# 13 Exercise Interventions in Patients with Diabetes and Peripheral Artery Disease

Mary M. McDermott

Lower extremity peripheral artery disease (PAD), or atherosclerosis of the arteries supplying the lower extremities, affects approximately 8.5 million people in the United States and more than 200 million people worldwide [1–3]. People with PAD have an increased rate of acute coronary events, stroke, and mortality compared to those without PAD [3, 4]. Insufficient oxygen supply to the lower extremities during walking activity leads to ischemic lower extremity muscle, resulting in pain, tightness, weakness, or other discomfort in lower extremity muscle during walking activity. It is well established that people with PAD have greater functional impairment, more rapid functional decline, and higher rates of mobility loss than those without PAD [5–9].

Diabetes mellitus is a major risk factor for PAD [1–3, 10]. Of five studies that assessed the association of diabetes mellitus with PAD, four reported a significant independent association of diabetes mellitus with increased prevalence of PAD, with odds ratios ranging from 1.9 to 4.0 [11–14]. A fifth study, the Framingham Offspring Study, reported a significant association of diabetes mellitus with PAD that was no longer statistically significant in a multivariable-adjusted model [15]. Diabetes mellitus is associated with a twofold increased risk of intermittent claudication, the most classic symptom of PAD [2]. More severe diabetes mellitus and more long-standing diabetes mellitus are associated with higher risks of PAD [2, 10, 16]. As the prevalence of obesity increases, the prevalence of diabetes mellitus will also increase. Thus, the number of people in the world with PAD and diabetes is likely to grow in the foreseeable future.

## Diabetes and Clinically Important Outcomes in PAD Patients

Among patients with PAD, those with diabetes mellitus have more adverse outcomes than those without diabetes mellitus. People with PAD and diabetes mellitus have a threefold higher risk of mortality and a fivefold higher rate of amputation compared to people with PAD who do not have diabetes [2, 17]. They also have greater functional impairment and faster functional decline than those without diabetes [18]. In a cross-sectional study of 460 patients with PAD recruited from several medical centers in Chicago, those with diabetes walked significantly shorter distances in the 6-min walk test (1040 vs. 1168 ft, $P < 0.001$), had slower fast-paced walking velocity (0.83 vs. 0.90 m/s, $P < 0.001$), and had a poorer short physical performance battery score (7.3 vs. 8.6, $P < 0.001$). People with more severe diabetes mellitus, determined by the use

M. M. McDermott (✉)
Northwestern University Feinberg School of Medicine, Department of Medicine, Division of general internal medicine and geriatrics, Chicago, IL, USA
e-mail: mdm608@northwestern.edu

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**Table 13.1** Characteristics of peripheral artery disease in the setting of diabetes mellitus

| Characteristic | Findings compared to people with PAD who do not have diabetes mellitus |
|---|---|
| Distribution of lower extremity atherosclerosis | People with diabetes mellitus have more distal atherosclerosis than those without diabetes mellitus |
| Leg symptoms | People with PAD and diabetes mellitus have a higher prevalence of atypical leg symptoms than those without diabetes mellitus |
| Functional impairment | People with PAD and diabetes mellitus have even greater functional impairment than people with PAD who do not have diabetes mellitus |
| Endovascular interventions for PAD | People with PAD and diabetes mellitus have poorer outcomes after endovascular revascularization compared to those without diabetes mellitus |
| Supervised treadmill exercise therapy | People with PAD and diabetes have significant benefits from supervised treadmill exercise. Whether the magnitude of benefit is similar between people with and without diabetes mellitus is unclear |
| Home-based walking exercise therapy | People with PAD and diabetes benefit from home-based walking exercise |

of diabetes medication, performed more poorly on functional testing than those not using diabetes medications [18]. Table 13.1 summarizes some clinically important differences in characteristics of patients with PAD with vs. without diabetes mellitus.

## Medical Management of Walking Impairment in PAD

A major treatment goal for PAD is to improve functional performance. Although lower extremity revascularization improves walking performance in PAD, many patients with PAD and diabetes mellitus are not candidates for endovascular revascularization, which is the most common and least invasive form of lower extremity revascularization for PAD. Endovascular revascularization is more effective when performed in the proximal arteries (i.e., the aortoiliac arteries). However, diabetic patients with PAD have more distal and more diffuse atherosclerosis than those with PAD and diabetes mellitus [7]. Therefore, many patients with PAD and diabetes mellitus are not candidates for endovascular revascularization. In addition, few medications have been identified that meaningfully improve walking performance in PAD patients. Just two medications, cilostazol and pentoxifylline, are FDA approved for treating PAD-associated walking impairment [19–23]. Of these two medications, benefits from cilostazol are modest, and recent evidence suggests that pentoxifylline is not much better than placebo for improving walking performance in PAD [19, 20]. Current clinical practice guidelines recommend against pentoxifylline for improving walking performance in patients with PAD [20]. Cilostazol improves treadmill walking performance in people with PAD and intermittent claudication by approximately 25% or approximately 40 m in maximal treadmill walking distance [19–25]. However, side effects from cilostazol are common and include headache, diarrhea, light-headedness, and palpitations. One study reported that as many as 20% of patients who were prescribed cilostazol for PAD-related walking impairment discontinued the drug due to side effects [26].

## Supervised Treadmill Exercise for Peripheral Artery Disease

Consistent evidence from randomized clinical trials demonstrates that supervised treadmill exercise significantly and substantially improves pain-free and maximal treadmill walking distance in patients with PAD [27–32]. Supervised treadmill exercise sessions typically take place in a cardiac rehabilitation or hospital setting and consist of walking exercise on a treadmill, supervised by a nurse, exercise physiologist, or other trained personnel with knowledge of exercise treatment in PAD. Supervised exercise is typically conducted 3 days per week for a minimum of 12 weeks. The walking exercise program should be tailored to the individual patient with PAD. Many patients with PAD begin the supervised treadmill exercise program by walking a total of 10–15 min in the initial exercise sessions. Since PAD is associated with pain, weakness, or other disabling leg symptoms during walking exercise, PAD patients typically need to alternate walking exercise with rest periods. Patients should be encouraged to increase walking exercise time each week by about 5 min per session, until a total of 40–50 min of walking exercise is achieved per session (excluding rest periods). Improvement in walking endurance and leg symptoms in response to supervised exercise training does not begin immediately but typically is appreciated by the patient with PAD approximately 4–6 weeks after the start of the exercise program [33, 34]. Maximum improvement in treadmill walking performance occurs approximately 12 weeks after the start of supervised exercise training, while improvement in 6-min walk performance continues during the 3- to 6-month period after the start of supervised exercise [30, 35]. Once a supervised treadmill exercise program is completed, benefits in treadmill walking performance are largely sustained, up to 12 months after completion of the supervised exercise [27]; however benefits in the 6-min walk are not durable after a supervised exercise intervention is completed. The more favorable sustained effect of supervised treadmill exercise on treadmill walking performance vs. 6-min walk performance may be related to a learning effect observed after treadmill exercise on the treadmill walking outcome that is not observed for the 6-min walk outcome [36].

In a meta-analysis of 25 randomized trials of supervised exercise in patients with PAD, supervised treadmill exercise was associated with a 180-m greater increase in maximal treadmill walking distance and a 128-m greater increase in pain-free treadmill walking distance, compared to the control group that did not receive exercise [28]. Supervised treadmill exercise also achieves clinically important improvement in 6-min walk distance in patients with PAD [29–30, 32]. The effects of supervised treadmill exercise on physical activity and quality of life are variable. Supervised treadmill exercise has not been shown consistently to improve physical activity or quality of life [27, 29, 37].

## Supervised Treadmill Exercise in Patients with PAD and Diabetes Mellitus

Since diabetes mellitus is a major risk factor for PAD, many PAD participants in randomized clinical trials of supervised exercise have diabetes. In three of the largest randomized trials of supervised exercise in PAD patients, the prevalence of diabetes mellitus was 36–45% [29, 30, 32]. Despite this, relatively few studies have specifically assessed how diabetes mellitus affects responsiveness to supervised treadmill exercise in patients with PAD. A systematic review identified just three studies that had evaluated the impact of diabetes mellitus on improvement in treadmill walking performance in patients with PAD, after a supervised treadmill exercise program [38]. Of the three studies [39–41], two were small randomized trials of 27 and 60 participants, respectively. In post hoc analyses, Gardner et al. reported that PAD participants without diabetes mellitus increased their maximal treadmill walking distance by 57%, compared to 30% in the PAD participants with diabetes mellitus [40]. However, a significant interaction between diabetes mellitus and improvement in maximal treadmill walking distance following supervised exercise was not observed. Allen et al. reported significant improvement in maximal treadmill walking distance among 13 patients with diabetes mellitus and 14 without diabetes mellitus, respectively, but did not statistically compare the degree of improvement in participants with vs. without diabetes mellitus. An observational study from the Netherlands evaluated changes in treadmill walking performance in 775 patients with PAD referred for supervised treadmill exercise, according to presence or absence of diabetes mellitus [41]. Of the 775 PAD patients referred for supervised treadmill exercise, 230 (30%) had diabetes mellitus. At baseline, those with diabetes mellitus had significantly poorer maximal treadmill walking distance than those without diabetes mellitus. Just 440 of the 775 patients with PAD were available for follow-up. There was no difference in the degree of improvement in maximal treadmill walking distance between those with and without diabetes mellitus (270 m vs. 400 m) [41]. The overall conclusion of the review was that there were insufficient data to determine whether diabetes mellitus impairs response to supervised treadmill exercise in patients with PAD [38]. However, it is important to point out that participants with diabetes mellitus in all trials improved their treadmill walking performance following supervised exercise.

In another review of randomized trials of supervised exercise that included greater proportions of patients with PAD and diabetes mellitus, the authors reported that absolute improvement in treadmill walking performance following exercise intervention was poor [42]. However, patients with PAD and diabetes mellitus typically have poorer functional performance and shorter treadmill walking distance at baseline than PAD patients with no diabetes mellitus [18, 41]. Thus, the percent improvement in treadmill walking distance, or the degree of improvement relative to baseline, is a more relevant metric for comparison than absolute improvement in treadmill walking distance. Available evidence suggests that patients with PAD and diabetes mellitus improve their walking performance following supervised treadmill exercise interventions [38–42].

## How to Implement a Supervised Treadmill Exercise Program for Patients with PAD and Diabetes Mellitus

Supervised treadmill exercise programs must be tailored for the individual patient. It is ideal to have a treadmill for exercise that can accommodate speeds as low as 0.50 miles per hour, since some patients with PAD, especially those with diabetes mellitus, cannot tolerate high exercise speeds [18]. In addition, some PAD patients with diabetes are unable to complete more than 10–15 min of walking exercise per session in their first week of exercise. Patients with PAD should aim to increase the total number of minutes walking for exercise each session by 5 min per week, until they achieve 40–50 min of walking exercise per session. Patients with PAD should also be instructed to alternate periods of walking exercise with rest during a typical treadmill exercise session. Based on current evidence, PAD patients should be advised to walk to near-maximal leg pain for maximum gains in exercise capacity. There is also some evidence to suggest that patients with PAD who walk at a slow or comfortable pace can still achieve significant gains in walking endurance [28]. Based on current evidence, if a patient with PAD is able to walk for treadmill exercise for 10 min without experiencing ischemic leg symptoms, the workload should be increased, by increasing either the speed or grade of the treadmill [29, 30].

## Centers for Medicare and Medicaid Services Coverage for Supervised Exercise in PAD

Until recently, many PAD patients in the United States did not have access to supervised treadmill exercise because of lack of medical insurance coverage. In 2017, the Centers for Medicare and Medicaid Services (CMS) released a decision memorandum, indicating that they would begin providing coverage for supervised exercise for patients with symptomatic PAD [43]. This change in policy by CMS is expected to make supervised treadmill exercise more accessible to many PAD patients.

In order to provide coverage, CMS requires that supervised exercise for PAD must be ordered during a face-to-face physician office visit, during which cardiovascular disease risk factors must be addressed. CMS provides coverage for 12 weeks and 36 sessions of supervised exercise for symptomatic PAD. The supervised exercise must take place in a hospital setting or medical office affiliated with a hospital and must be conducted by qualified personnel with training in basic and advanced cardiac life support and PAD-related

**Table 13.2** Elements of supervised exercise required for coverage by the Centers for Medicare and Medicaid 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 weeks of exercise sessions that occur three times weekly |
| After completing 12 weeks of supervised exercise, an additional 36 sessions may be prescribed, with written justification, after the first 12 weeks is 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 advance life support and exercise therapy for PAD |
| Exercise must be supervised by a physician, physician's assistant, or nurse practitioner/clinical nurse specialist |

[a]Reprinted with permission from the American College of Cardiology [58].

exercise therapy [43]. A physician must be on-site. After the 12 weeks and 36 sessions of supervised exercise are completed, CMS may provide coverage for an additional 36 sessions of supervised exercise therapy, if a physician can justify the need for the additional sessions. Table 13.2 summarizes characteristics of supervised exercise programs that are covered by CMS.

## Home-Based or Unsupervised Walking Exercise in People with PAD and Diabetes Mellitus

For many patients with PAD, participation in supervised treadmill exercise can be difficult even when paid for by medical insurance. In an analysis of 1541 patients with PAD who were eligible to participate in randomized trials of supervised exercise, and therefore had free access to supervised exercise, 69% declined participation, because of inconvenience, lack of interest, or comorbidities that interfered with participation [44]. When supervised exercise is inconvenient or not feasible, home-based or unsupervised exercise may be an effective alternative to supervised treadmill exercise. While home-based exercise was previously considered not an effective therapy for people with PAD, early studies of home-based walking exercise in PAD did not incorporate behavioral change therapies [45–47]. More recent randomized clinical trial evidence demonstrates that when behavioral change methods are incorporated into the intervention, home-based exercise therapy can significantly improve walking endurance in PAD patients [31, 32, 48]. However, close monitoring of the PAD patient is required to ensure ongoing adherence to home-based exercise [49].

Three large clinical trials, published between 2011 and 2014, demonstrated that home-based exercise can improve walking performance in PAD patients [31, 32, 48]. The largest of these three trials was the Group-Oriented Arterial Leg Study (GOALS), which tested the efficacy of a Group-Mediated Cognitive Behavioral (GMCB) intervention to help patients with PAD adhere to a home-based walking exercise program [48]. In the GOALS trial, 192 participants with PAD were randomized to either a GMCB intervention or an attention control group for 6 months [48]. The GMCB intervention used behavioral change methods including self-monitoring, goal setting, group support, and self-efficacy to help people with PAD adhere to a home-based walking exercise program. During the first 6 months of the GOALS intervention, PAD participants in the intervention met in groups once per week at the exercise center with other PAD patients and a coach. The coach led group discussions that fostered group support and focused on specific behaviors necessary for successful behavior change, including goal setting, self-efficacy, self-monitoring, and overcoming obstacles to exercise adherence. PAD participants in the GOALS intervention were instructed to walk for exercise 5 days per week, gradually building up to 40–50 min of walking exercise per session, at a pace that elicited moderate to severe ischemic leg symptoms. Participants were instructed to stop and rest in between bouts of ischemia-inducing walking exercise activity. After 6 months, participants in the GMCB home-based exercise intervention group significantly improved their 6-min walk distance (primary outcome) by 54 m relative to the control group, consistent with a large meaningful improvement [49]. Pain-free treadmill and maximal treadmill walking time also improved significantly compared to the control group [48]. The home-based exercise intervention also significantly improved physical activity levels and participants' perception of walking endurance, measured by the Walking Impairment Questionnaire (WIQ) distance score, compared to the control group. Furthermore, in subgroup analyses, the intervention significantly improved 6-min walk in participants both with and without diabetes mellitus, respectively [48]. Specifically, 6-min walk distance increased by 53 m among participants without diabetes mellitus and by 54 m among participants with diabetes mellitus.

After 6 months of the weekly on-site sessions, participants in the GOALS intervention were transitioned from the weekly group meetings to telephone contact only and received periodic telephone calls from the coach between months 7 and 12. At 12-month follow-up, 6 months after the more intensive on-site study intervention was completed, change in 6-min walk distance compared to baseline remained significantly better in the intervention group compared to the control group, consistent with a durable benefit from the intervention [50].

Findings in the GOALS trial were confirmed in two other randomized trials of home-based exercise in people with PAD [31, 32]. One of these trials randomized 180 participants with PAD and intermittent claudication to one of the three groups: supervised treadmill exercise, home-based walking exercise, and an attention control group for 12 weeks [32]. In the supervised treadmill exercise group, participants performed treadmill walking exercise to maximal ischemic leg pain, 3 days per week, for up to 40 min per session. In the home-based walking exercise group, participants walked for exercise at home 3 days per week, at a self-selected pace, for up to 45 min per session. PAD participants in the home exercise group wore an activity monitor during exercise and returned to the medical center at 1-, 4-, 8-, and 12-week follow-up to meet with a study investigator, review their step count data, and set goals for the next 4 weeks. After 12 weeks, both exercise groups significantly improved their 6-min walk distance, maximum treadmill walking distance, and pain-free treadmill walking distance, relative to the control group. Furthermore, the home-based walking exercise group improved their 6-min walk distance more than the supervised treadmill exercise group. At 12-week follow-up, 6-min walk distance increased by 45 m in the home-based exercise group, by 15 m in the supervised exercise group, and by 45 m in the home-based exercise group. Since corridor walking more closely simulates over ground walking, home-based exercise programs may be more helpful in achieving improved walking in daily life for people with PAD. In summary, home-based walking exercise interventions that include regular visits to the medical center improve walking performance in PAD patients, including those with diabetes mellitus [48]. Table 13.3 summarizes evidence from both supervised and home-based exercise trials regarding benefits of supervised and home-based exercise interventions in PAD participants with and without diabetes mellitus.

In another randomized trial of home-based walking exercise intervention that included only patients with PAD and diabetes mellitus, the findings were somewhat different. Collins et al. randomized 145 participants with PAD and diabetes to a behavioral intervention vs. an attention control group for 6 months [51]. The intervention consisted of an individualized counseling session at baseline, followed by one walking session per week with an instructor and other patients with PAD at an exercise center and 3 days of walking at home each week, for up to 50 min of exercise per session. Participants in the intervention also received bi-weekly telephone calls, in which an instructor reviewed their walking progress and provided feedback. The attention control group received bi-weekly calls from a study investigator during which the participant and study investigator discussed glucose control, blood pressure, and cholesterol levels during the previous month. After 6 months, there were no differences in treadmill walking performance between the home-based walking exercise intervention and the control group. Therefore, in this study of participants with diabetes mellitus and PAD, a

**Table 13.3** Studies comparing improvement in walking performance between PAD participants with and without diabetes mellitus

| Study | Sample size | Study design | Primary findings | Comments |
|---|---|---|---|---|
| *Supervised treadmill exercise interventions* | | | | |
| Van Pul et al. [41] | *N* = 755<br>*N* = 230 (30%) with diabetes mellitus | Observational longitudinal analysis of patients referred to supervised treadmill exercise in the Netherlands | At 3-month follow-up, maximal treadmill walking distance increased by 73% in people without diabetes vs. 67% in people with diabetes. At 6-month follow-up, maximal treadmill walking distance increased by 100% and 91%, respectively ($P = 0.48$ for comparison of change between those with and without diabetes) | Follow-up data were available for just 440 of 755 participants |
| Allen et al. [39] | *N* = 27<br>*N* = 13 (48%) with diabetes | Randomized trial of supervised exercise in PAD. Data analyzed according to the presence vs. absence of diabetes | At 3-month follow-up, PAD participants with diabetes increased maximal treadmill walking performance by 52%, and those without diabetes increased maximal treadmill walking performance by 29% | Small sample size is a study limitation |
| Gardner et al. [40] | *N* = 60<br>*N* = 25 (42%) with diabetes mellitus | Randomized trial of supervised exercise in PAD | At 3-month follow-up, maximal treadmill walking distance increased by 57% (198 m) in participants with diabetes vs. 30% (87 m) in those without diabetes | Small sample size is a study limitation |
| *Home-based walking exercise interventions* | | | | |
| McDermott et al. [48] | *N* = 194<br>64 (33%) had diabetes | Randomized clinical trial of home-based exercise using a group-mediated cognitive behavioral intervention | At 6-month follow-up, 6-min walk distance increased by 53 m among participants without diabetes and by 54 m among participants with diabetes mellitus | Improvement in 6-min walk distance is consistent with a large meaningful change |
| McDermott et al. [49] | *N* = 200<br>67 (33.5%) had diabetes | Randomized clinical trial of telephone counseling + wearable device to improve walking ability in PAD | At 9-month follow-up, there was no improvement overall in 6-min walk distance between the intervention and control groups. Results did not differ by the presence vs. absence of diabetes | |

home-based exercise intervention did not improve treadmill walking performance more than a control group. Both groups (intervention and control group) improved in this trial, and the 6-min walk test was not measured.

## Practical Aspects of Prescribing Home-Based Walking Exercise for Patients with PAD and Diabetes Mellitus

Prior to initiating a new home-based exercise program, it is reasonable for PAD patients with diabetes mellitus to complete a baseline treadmill cardiac stress test to evaluate them for significant coronary ischemia, which may become manifest during walking exercise as leg symptoms improve. A regular treadmill exercise stress test (without imaging) should be sufficient to evaluate most PAD patients for coronary ischemia prior to initiating a new exercise program. PAD patients whose baseline treadmill exercise stress test indicates coronary ischemia should undergo additional evaluation prior to initiating an exercise intervention.

Effective home-based exercise programs for people with PAD have used activity monitors and/or incorporated throughout the intervention principles of behavioral change theory [31, 32, 48]. Behavioral change techniques that have been successful for promoting home-based walking exercise in PAD have included goal setting, building self-efficacy, monitoring progress, and a "coach" to whom the patient feels accountable [31, 32, 48]. Therefore, patients with PAD engaged in home-based exercise should be advised to write down walking exercise goals and record their walking exercise activity each week, and this information should be reviewed periodically by a coach or a clinician who provides regular feedback to the patient. Successful home-based programs have incorporated coach contact with the participant as infrequently as monthly [32]. A home-based exercise intervention for PAD participants that consisted of providing a wearable activity monitor and telephone coaching was not effective [49]. Thus, available evidence suggests that effective home-based exercise programs for PAD may require ongoing contact with a coach, at least during the first 6 months of the intervention [49–52].

## Additional Alternative Exercise Strategies for PAD Patients

Relatively few exercise modalities other than walking exercise have been studied for PAD patients. Several randomized trials that implemented upper and lower limb ergometry, or upper and lower extremity cycling, improved walking performance in people with PAD and intermittent claudication [53–55]. Zwierska et al. randomized 104 participants with PAD into an upper limb aerobic ergometry intervention, a lower limb aerobic ergometry intervention, or a non-exercise control group for 6 months [53]. Exercise sessions occurred twice per week and consisted of 2 min of arm or leg cranking ergometry exercise followed by 2 min of rest for a total of ten cycles (20 min of exercise per session). After 6 months of ergometry exercise, the maximal walking distance, measured by a shuttle-walk test, increased by 29% in the upper limb ergometry group and by 31% in the lower limb ergometry group. The improvement in walking endurance following upper limb exercises is unexpected and counterintuitive, as exercise benefits are highly specific to an imposed demand. Improved cardiovascular fitness following upper limb exercise may contribute to improved walking endurance as a result of systemic improvement in endothelial function or if poor cardiorespiratory fitness contributed importantly to the functional impairment, rather than atherosclerotic obstruction of the lower extremity arteries. It is apparent that more studies are needed to define the specific mechanisms involved. These trials have not evaluated benefit specifically in people with PAD and diabetes mellitus.

## Resistance Exercise Training for PAD Patients

Lower extremity resistance training has been evaluated in PAD patients in several randomized clinical trials [29, 56, 57]. In the largest of these trials, 156 participants with PAD were randomized to supervised treadmill exercise, supervised resistance training, or a control group for 6 months. At 6-month follow-up, supervised treadmill exercise achieved a statistically significant and clinically meaningful improvement in 6-minute walk performance (+35.9 meters vs. the control group), while supervised lower extremity resistance training did not improve the six-minute walk more than the control group (+12.4 meters). Resistance training has not been separately evaluated in PAD participants with diabetes mellitus, to the author's knowledge.

## Conclusions

Diabetes mellitus is common in PAD patients. Patients with PAD and diabetes mellitus have significantly greater impairment in walking endurance and higher rates of mobility loss than those without diabetes mellitus. The distribution of lower extremity atherosclerosis in people with PAD makes these less well suited for endovascular revascularization, which is most beneficial when performed for more proximal lower extremity stenosis.

Patients with peripheral artery disease with and without diabetes mellitus benefit from both supervised and home-based walking exercise. The magnitude of improvement following supervised treadmill exercise may be less for patients with PAD and diabetes mellitus compared to patients with PAD who do not have diabetes mellitus. Nevertheless, evidence supports that exercise interventions are effective in improving walking performance or exercise capacity in PAD patients with and without diabetes mellitus and therefore exercise should be considered as part of the therapeutic strategy of these patients.

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