Endovascular treatment for intermittent claudication

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Policy contains: Atherosclerosis; endovascular treatment; intermittent claudication; peripheral artery disease; revascularization.

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Benefit Coverage Determination

Requests for endovascular revascularization for treatment of intermittent claudication require prior authorization.

Endovascular revascularization for treatment of intermittent claudication is clinically proven and, therefore, medically necessary for members with peripheral artery disease when all of the following criteria are met (Conte, 2015; Gerhard-Herman, 2017):

- **Significant functional or lifestyle-limiting disability.**
- **Hemodynamically significant aortoiliac occlusive disease, femoropopliteal disease, or multivessel tibial disease with a stenosis of at least 50%.**
- **Failure of at least 12 weeks of guideline-directed pharmacotherapy or exercise therapy, or both, to control symptoms.**
- **Documented discontinuation or reduction of smoking and other tobacco use for at least 12 weeks.**
- **There is a reasonable likelihood of symptomatic improvement with endovascular treatment.**
- **The benefits of treatment outweigh the potential risks.**

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Limitations

All other uses for endovascular revascularization for members with intermittent claudication are investigational/not clinically proven, and therefore, not medically necessary, as their effectiveness has not been established, including, but not limited to (Conte, 2015; Gerhard-Herman, 2017):

- **Treatment of asymptomatic disease, regardless of hemodynamic measures or imaging findings demonstrating presence of disease.**
- **Treatment of isolated infrapopliteal artery disease.**
- **Treatment done solely to prevent progression to chronic limb ischemia.**

Alternative covered services

Guideline-directed risk reduction measures (e.g., diet and smoking cessation), pharmacotherapy (antiplatelet drugs, statins, or medications to lower blood pressure), supervised exercise therapy, home-based exercise therapy, and open surgical revascularization.

Background

The main cause of peripheral artery disease is atherosclerosis that reduces perfusion in peripheral arteries, particularly of the legs and feet (Sartipy, 2018). About 20% to 50% of patients diagnosed with peripheral artery disease are asymptomatic but may have functional impairment when tested. Symptomatic disease may present as intermittent claudication or with signs or symptoms consistent with limb-threatening ischemia (e.g., presence of ischemic rest pain, arterial insufficiency ulcers, and gangrene).

The Society for Vascular Surgery (Conte, 2015) defines intermittent claudication as a "reproducible discomfort in a specific muscle group, caused by arterial obstruction proximal to the affected muscle bed, which is induced by exercise and then relieved with rest." The most common indicators include muscle pain, heaviness, weakness, or cramping in the lower extremities that begins with physical activity and stops within minutes after resting. An atypical form of intermittent claudication presents with exertional discomfort that does not consistently resolve with rest. Patients with intermittent claudication are also at high risk of atherosclerotic morbidity (National Heart, Lung, and Blood Institute, 2020).

Current clinical management for intermittent claudication encompasses risk factor control, diagnosis, and medical and surgical treatment. Risk factors for peripheral artery disease include increasing age, smoking history, family history and genetics, unhealthy lifestyle habits, medical conditions related to metabolic conditions, elevated blood cholesterol and blood pressure, and obesity (National Heart, Lung, and Blood Institute, 2020). African Americans and Native Americans are at higher risk for peripheral arterial disease than Hispanics, Latinos, or whites. While men and women have a similar risk of developing peripheral artery disease, women are more likely than men to have asymptomatic disease but also have more complications, such as problems walking.

The primary method for diagnosis is the ankle-brachial index test at rest (National Heart, Lung, and Blood Institute, 2020). An ankle-brachial index less than or equal to 0.9 identifies hemodynamically significant peripheral artery disease (Conte, 2015). When the ankle-brachial index is borderline or normal (greater

than 0.9) and symptoms suggest claudication, an exercise ankle-brachial index test may be indicated. Other tests include the six-minute walk test, noninvasive Doppler imaging, pulse volume recording, and angiography. In patients with advanced age or long-standing diabetes mellitus, renal insufficiency, and arterial calcifications, a resting ankle-brachial index of greater than 1.4 indicates noncompressible arteries. In this case, a toe-brachial index reading of 0.7 or less supports a diagnosis of peripheral arterial disease (Gerhard-Herman, 2017). An assessment of functional impairment specific to arterial insufficiency and its perceived effect on quality of life should be conducted from the patient's perspective, as there is a poor correlation between degree of disability in claudication and both physiologic testing and anatomic findings (Conte, 2015).

The goals of treatment are multifold: cardiovascular risk reduction; symptom reduction; activity participation improvement; amputation risk reduction; and quality of life improvement. Depending on disease severity, associated complications at presentation, and desired treatment goals, individualized treatment may consist of lifestyle changes, supervised exercise in a health care setting, a home exercise program, pharmacotherapy (antiplatelet drugs, statins, or medications to lower blood pressure), or revascularization procedures (National Heart, Lung, and Blood Institute, 2020).

Revascularization is indicated when lesions are hemodynamically significant (Conte, 2015). Angiography (computed tomography, magnetic resonance, or catheter-based) and duplex ultrasound are used to determine the arterial anatomy, and the extent of disease. Endovascular techniques to treat claudication include balloon dilation (angioplasty), atherectomy, covered stents, drug-eluting stents, cutting balloons, and drug-coated balloons. Choice of endovascular technique depends on lesion characteristics (e.g., anatomic location, lesion length, degree of calcification), operator experience, and patient preferences.

Findings

Development of catheter-based endovascular technologies and noninvasive imaging techniques, along with shifts in reimbursement toward outpatient and office-based procedures, has lowered the threshold for vascular intervention. This has resulted in a dramatic increase in the use of invasive procedures to treat intermittent claudication, particularly in the ambulatory setting (Conte, 2017). Clinical regulatory trials used as the basis for marketing approval failed to apply clinically meaningful endpoints and contributed to the rapid dissemination of these interventions despite their unclear effectiveness.

The natural history of intermittent claudication is characterized by a slow, progressive functional decline. There is a lack of evidence related to lower limb prognosis to assist in predicting which patients with intermittent claudication are likely to deteriorate to critical limb ischemia. Such uncertainty has led to considerable practice variability with respect to when to offer revascularization (Hicks, 2020), and evidence-based guidelines were produced to improve clinical decision-making.

The Society for Vascular Surgery (Conte, 2015) and the American College of Cardiology/American Heart Association (Gerhard-Herman, 2017) developed guidelines for management of intermittent claudication. These guidelines support revascularization to improve claudication symptoms, functional status, and quality of life, as opposed to limb salvage, but not as a first-line treatment option (Conte, 2015; Gerhard-Herman, 2017). This rationale is based on a low risk of progression of intermittent claudication to chronic limb-threatening ischemia, as major amputation occurs in less than 5% of affected patients with appropriate risk factor modification.

Low-quality evidence comparing surgical and endovascular therapy suggests they are likely to have similar efficacy overall, although open surgery may be preferred for more distal disease and disease involving the common or deep femoral arteries. Long-term patency is greater in the aortoiliac than in the femoropopliteal segment, where greater lesion length, occlusion rather than stenosis, the presence of multiple and diffuse lesions, poor-quality runoff, diabetes mellitus, chronic kidney disease, renal failure, and smoking diminish durability.

The guidelines identified substantial evidence from several systematic reviews and meta-analyses of seminal randomized controlled trials comparing endovascular procedures to various combinations of medical treatment with or without supervised or unsupervised exercise programs. The definition of clinical success varied using different endpoints and enrolled patients with anatomic disease distribution at different levels. Despite these limitations, the evidence suggested both endovascular and surgical therapy were effective for reducing pain and improving walking distance, quality of life, and ambulatory function. Both forms of revascularization appeared superior to medical therapy for limb-related outcomes, but not necessarily to supervised exercise training for functional outcomes.

Recommendations from The Society for Vascular Surgery (Conte, 2015), presented with the strength of the recommendation and supportive evidence, are as follows:

- **In the absence of symptoms, invasive treatment for peripheral arterial disease is not recommended, regardless of hemodynamic measures or imaging findings demonstrating presence of disease (strong recommendation; moderate-quality evidence).**
- **First-line treatment should consist of risk reduction strategies — lifestyle modification, anti-atherosclerotic medical therapies, and exercise programs — because patients with intermittent claudication are at increased risk for cardiovascular events but at very low risk for amputation (strong recommendation; variable-quality evidence).**
- **Endovascular (angiogram, angioplasty, or stent) or surgical treatment is recommended for patients with significant functional or lifestyle-limiting disability when:**
    - **There is a reasonable likelihood of symptomatic improvement with treatment.**
    - **Pharmacologic therapy, exercise therapy, or both have failed.**
    - **The benefits of treatment outweigh the potential risks (strong recommendation; moderate-quality evidence).**
- **Choice of invasive treatment should be individualized. The modality offered should provide a reasonable likelihood of sustained benefit to the patient (a greater than 50% likelihood of clinical efficacy for at least two years). Anatomic patency (freedom from hemodynamically significant restenosis) is a prerequisite for sustained efficacy (strong recommendation; low-quality evidence).**
- **Endovascular treatment of tibial disease should be reserved for multivessel disease with a stenosis of at least 50%. The preferred endovascular approach generally targets the proximal lesions first, which may resolve symptoms. Endovascular treatment for isolated infrapopliteal disease is of unproven benefit, could possibly be harmful, and is not recommended (strong recommendation; low-quality evidence).**

The American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines (Gerhard-Herman, 2017) recommends revascularization as a reasonable treatment option for the patient with lifestyle-limiting claudication with an inadequate response to guideline-directed management and therapy. Specific recommendations are as follows:

- **Endovascular procedures are an effective revascularization option for patients with lifestyle-limiting claudication and hemodynamically significant aortoiliac occlusive disease (strong recommendation, high-quality evidence).**
- **Endovascular procedures are reasonable as a revascularization option for patients with lifestyle-limiting claudication and hemodynamically significant femoropopliteal disease (moderate recommendation, moderate-quality evidence from randomized studies).**
- **The usefulness of endovascular revascularization for patients with claudication due to isolated infrapopliteal artery disease is unknown (weak recommendation; limited data suggesting benefits outweigh risks).**
- **Endovascular procedures should not be performed in patients with peripheral artery disease solely to prevent progression to chronic limb ischemia (strong recommendation, moderate-quality nonrandomized evidence of harm).**

Subsequently published evidence of randomized controlled trials confirm the robustness of these recommendations for patients with intermittent claudication due to femoropopliteal or aortoiliac peripheral artery disease (Djerf 2020; Fakhry, 2018; Klaphake, 2018; Mullins, 2021; van den Houten, 2019). Moderate-quality evidence supports a clinically meaningful functional benefit from structured exercise therapy and home-based exercise therapy compared to usual care (no exercise). There is less confidence in the evidence of functional benefit derived from endovascular revascularization alone. Combination treatment of endovascular revascularization and conservative noninvasive treatment (best medical therapy or structured exercise therapy) may confer a synergistic statistical benefit in function and disease-specific quality of life, but that benefit appears to dissipate over time. Inadequate sample size likely contributes to the failure to reach statistical significance in many follow-up studies.

A Cochrane review (Fakhry, 2018) of 10 randomized controlled trials (n = 1,087 participants) compared endovascular revascularization to either no specific treatment or conservative therapy (supervised exercise or pharmacotherapy with cilostazol 100 milligrams twice daily), or compared a combination therapy of endovascular revascularization plus conservative therapy versus conservative therapy alone. The quality of the evidence ranged from low to high due to substantial heterogeneity and small sample size. Any statistically significant benefit in functional performance, number of secondary invasive interventions, or disease-specific quality of life of endovascular revascularization over comparators decreased during long-term follow-up.

The results of both this Cochrane review and another systematic review and meta-analysis of seven randomized controlled trials (Klaphake, 2018) suggest improved benefits to walking performance and quality of life may occur when endovascular revascularization is combined with conservative therapy rather than delivered alone. A network meta-analysis (van den Houten, 2019) of eight low-quality trials (n = 656 patients) found no statistically significant differences in daily physical activity measures among supervised exercise, home-based exercise, and endovascular revascularization treatment up to six months follow-up.

Djerf (2020) examined the long-term benefit of revascularization in 158 patients with intermittent claudication based on the results of the Invasive Revascularization or Not in Intermittent Claudication (IRONIC; U.S. National Library of Medicine, 2019) randomized controlled trial. After five years of follow-up, a strategy incorporating revascularization with best medical therapy plus structured exercise therapy conferred no long-term improvement in health-related quality of life or walking capacity compared to a noninvasive treatment strategy.

Regarding infrapopliteal disease, the decision of whether to intervene in patients with intermittent claudication is complex and multifactorial. Mullins (2021) queried the Vascular Quality Initiative for 34,944 peripheral vascular interventions performed for intermittent claudication between 2003 and 2018, of which 1,045 (3.0%) were infrapopliteal interventions, In multivariable analysis, isolated infrapopliteal intervention (odds ratio 6.47, 95% confidence interval 6.45 to 6.49, *P* < .0001) and combined above- and below-knee interventions (odds ratio 2.32, 95% confidence interval 2.31 to 2.33, *P* < .0001) were associated with higher amputation rates. The Mullins study confirms the current guidelines' recommendations for caution in treating isolated infrapopliteal disease with endovascular approaches.

References

On February 9, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "Peripheral Vascular Diseases" (MeSH), "lower extremity" (MeSH), "intermittent claudication" (MeSH), and "endovascular procedures" (MeSH). We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

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