Comprehensive Endovascular Therapy for Femoropopliteal Arterial Atherosclerotic Occlusive Disease

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Treatment of the patient with symptomatic femoropopliteal atherosclerotic disease is evolving. The superficial femoral artery is a common site for infrainguinal atherosclerotic disease, particularly the portion of the superficial femoral artery that lies within the adductor canal of the thigh. Standard therapy is an exercise program and risk factor modification. Surgery is reserved for patients in whom medical treatment fails. Endoluminal intervention coupled with aggressive proactive medical management is replacing these conventional paradigms. Endovascular therapy results in immediate symptom relief. Initial technical success rates of 90% to 95% have been achieved for stenotic lesions, and rates of 80% to 95% for complete occlusions. Longterm patency is often questioned, but modern series suggest it might be a durable option, particularly if systemic risk factors are aggressively controlled. Anatomic failures do not correlate with clinical failures. This review outlines the current management of superficial femoral artery atherooclusive disease.

Clinical problem
Peripheral arterial disease (PAD) of the lower extremities remains one of the often unrecognized manifestations of systemic atherosclerosis symptomatically affecting between 3% and 7% of the population and up to one in five patients older than 75 years of age. It has a major detrimental impact on quality of life and is an unrecognized marker of multisystem vascular disease. The risk of disease increases two- to threefold for every 10-year increase in age after the age of 40 years, with men developing claudication about twice as commonly as women. The Framingham Study estimates the incidence of PAD at 26.6 per 1,000 men and 13.3 per 1,000 women less than 65 years old, but in approximately 20 per 1,000 men and women over 65 years of age. Mortality in claudicants is up to four times that in the non-claudicant age-adjusted population. Approximately 55% of claudicants will die from heart disease: 10% from a stroke and 10% from abdominal vascular pathology. Less than 20% of claudicants will die from a nonvascular cause. The strength of association is so strong that even an asymptomatic patient with a slightly reduced ankle brachial index (ABI) of 0.9 has a twofold relative risk of a coronary event.

Anatomic distribution is important. Patients with isolated aortoiliac disease tend to be younger and have a lower likelihood of preexisting coronary heart disease. Those with femoropopliteal disease, infragenicular disease, or multilevel disease tend to have the lowest ABI and the highest likelihood of coronary heart disease. This review will concentrate on the patient with femoropopliteal disease.

Anatomy
The superficial femoral artery (SFA) is a muscular artery, which is unique in that it is the longest artery in the body, and courses through the thigh in the muscular adductor canal, exiting at a fixed point. The geometry and elasticity of the SFA are markedly influenced by its proximity to musculature, its continuous mobility, and its location between two joints. So it undergoes additional mechanical forces not seen in other arteries. It has unique elastic wall recoil properties that affect its conformability and resilience. The flow in the SFA is also different than in many vessels treated with angioplasty; it has high resistance characteristics and disturbed flow. Nonlaminar flow results in increased predisposition to
the development of arteriosclerosis and intimal hyperplasia.28,29

Pathophysiology
Although arteriosclerosis is a systemic disease affecting all arteries within the human body, the SFA, because of its anatomy and physiology, is very susceptible to arteriosclerosis and can demonstrate all aspects of atherosclerotic plaque development. Arteriosclerosis may be defined as “a space occupying lesion or plaque of the inner coat of larger arteries that is focal, has a pattern of occurrence, is composed of an excess of fat, of an increased number of artery wall and inflammatory cells and their connective tissue products, and that may show calcification and ulceration, narrows the arterial lumen, may obstruct blood flow through the artery and may be associated with a local thrombus.”30,31

In atherogenesis, the arterial endothelium is considered chronically damaged by serum lipids, turbulent blood flow, and chronic inflammation. This injury leads to lipid accumulation and oxidation and the adhesion of monocytes and platelets with time. The aggregation of monocytes within the subendothelium constitutes the first stage of a “fatty streak.” These cells, in concert with a damaged or “activated” endothelium, synthesize and release growth factors and cytokines, leading to the migration and proliferation of smooth muscle cells and the recruitment of additional blood cells, particularly macrophages, filled with oxidized lipids or “foam cells.”32 An acellular core develops because of the toxic effects of oxidized lipoproteins. Oxidation of lipoproteins causes additional tissue injury and increased accumulation of blood cells and lipids. With time, this process results in the formation of an atheromatous plaque with a fibrous cap, an acellular core, and a surrounding myoproliferative and chronic inflammatory response.

Reports by the Committee on Vascular Lesions of the Council on Arteriosclerosis have established a new classification system for the various types of lesions (I to VI) described in arteriosclerosis (Fig. 1).30,31 In the older terminology, the fatty streak consists of types I, II, and III lesions; the intermediate or fibrofatty lesion, types III, IV, and Vα; and the fibrous plaque or advanced complicated lesion, types Vb, Vc, and VI.30 The SFA demonstrates all these lesions, but by the time the lesion is symptomatic (ie, manifested by claudication) the fibrous plaque or advanced complicated lesion predominates commonly with associated in situ thrombosis or occlusion.33

Fibrous plaques may be dynamic lesions that are in a continuous state of flux or those that are not enlarging and are considered stable or quiescent. Those that are expanding or have thinning of the plaque cap represent unstable or vulnerable lesions.30,31 The findings that the plaques are dynamic have increased the interest in medical therapies to induce stabilization, regression, or both in plaque morphology. Plaque growth, whether slow or abrupt, is usually associated with surface erosion, internal hemorrhage, luminal thrombosis, a combination of these processes, or gradual vessel occlusion.30,31

The classic plaque represents a raised fibrofatty lesion with a necrotic core and a fibrous outer coat. Within the plaques are degenerating blood elements, foam cells, cholesterol crystals, granulation tissue, smooth muscle cells, myofibroblasts, capillaries, calcium, iron pigment, giant cells, mononuclear leukocytes, and necrotic debris. Adjacent to the internal elastic membrane, which often exhibits numerous focal disruptions and duplications, the plaque is frequently characterized by a prominent deposition of elastin and collagen in an onion skin pattern. The most hazardous component of the atherosclerotic lesion is the plaque margin, where the fibrous cap of the lesion is thinned and eroded by macrophages and metalloproteinases they secrete.34 Sudden death from myocardial infarcts or acutely ischemic limbs are from these ruptures or fissures in the margins of the fibrous cap.35

Numerous clinicopathologic investigations have demonstrated that surface weakness is the most common feature of an unstable plaque.30,31,36 Microscopically, the observed sites of injury span a broad morphologic range, from minimal surface erosions to lacerations that extend deep within the plaque. The result of these injuries is exposure of the luminal blood to a thrombogenic surface, setting the stage for acute thrombosis. Plaque rupture can also lead to hemorrhage within the atheroma.34 Although the region of hemorrhage consists primarily of red blood cells, the surfaces along the ruptured tract are often lined by aggregates of platelets. Plaque hemorrhage can also develop by an en-

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<th>Abbreviations and Acronyms</th>
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<tr>
<td>ABI = ankle brachial index</td>
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<td>PAD = peripheral artery disease</td>
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<td>PTA = percutaneous transluminal angioplasty</td>
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<td>SFA = superficial femoral artery</td>
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tirely different mechanism. Within the core of a soft atheroma, primary disruption of capillary channels derived from the vasa vasorum may occur and lead to rapid plaque enlargement. Small hemorrhages are frequently observed in nonruptured plaques. Mechanical stress points for eccentric lesions have been identified at the junction of the plaque with more normal appearing arterial wall and along the center of the plaque. This is likely the basic plaque morphology that is encountered during percutaneous transluminal angioplasty (PTA) of the SFA.

**Classification of disease**

In addition to the atherosclerotic lesion characteristics, there is an anatomic classification of disease based on angiography or alternative imaging (duplex, computerized tomographic angiography, or magnetic resonance angiography). The Transatlantic Intersocietal Commission (TASC) has stratified femoropopliteal disease into four categories: A, B, C, and D. These categories are used for clinical reporting purposes. The definitions are shown in Table 1, and angiographic examples are given in Figure 2.

**Established and emerging risk factors for femoropopliteal disease**

Claudication is strongly associated with multiple cardiovascular risk factors (Table 2). Of these, smoking and diabetes mellitus correlate most strongly, and 70% to 90% of claudicants are either current or ex-smokers. Cigarette smoking is associated with a marked increased risk for peripheral arteriosclerosis. Followup of smokers versus ex-smokers at 7 years shows critical limb ischemia in 16% of smokers and none in the ex-smokers. The 10-year incidence of myocardial infarction is five times greater in the smoking group than in ex-smokers (53% versus 11%, respectively). At 10 years followup, cardiovascular-related mortality in the smok-

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**Figure 1.** Atherosclerotic plaque. The Committee on Vascular Lesions of the Council on Arteriosclerosis has established a new classification system for the various types of lesions (I–VI) described in arteriosclerosis (Fig. 1). In the older terminology, the fatty streak consists of types I, II, and III lesions; the intermediate or fibrofatty lesion, types III, IV, and Va; and the fibrous plaque or advanced complicated lesion (types Vb, Vc and VI). The superficial femoral artery demonstrates all these lesions, but by the time the lesion is symptomatic (ie, manifested by claudication), the fibrous plaque or advanced complicated lesion predominates, commonly with associated in situ thrombosis or occlusion. (From: Stary HC, Chandler AB, Glagov S, et al. A definition of initial fatty streak and intermediate lesions of arteriosclerosis: A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Arterioscler Thromb 1994;14:840–856, with permission.)
ing group is more than 50%, three times that of the nonsmoking group.

Elevated cholesterol has been shown in the Framingham study to be a weak but important increased risk factor for claudication. Lipid profile abnormalities, such as elevated serum triglyceride levels and reduced high density lipoproteins, have been found in the majority of patients in studies of intermittent claudication, and there is a strong inverse relationship between high-density lipoprotein levels and claudication severity. Lipoprotein (a) levels have been shown to correlate with LDL, cholesterol, fibrinogen levels, and PAD severity. Studies of lipid-lowering drugs and subsequent vascular events have focused mainly on coronary disease as a more frequent end point.

It has been estimated that 50% of diabetic patients have evidence of PAD. Diabetic patients suffer from both micro- and macrovascular disease manifested often as ischemia, but more frequently as motor or sensory neuropathies. But a study of 100 consecutive nondiabetic patients attending a vascular clinic showed abnormal glucose tolerance tests in 40%, despite the fact that all 40 patients had normal random or fasting blood glucose levels. There are three clues that might help identify patients who have a diabetic tendency: first, a distal distribution of PAD in a diabetic pattern; second, a raised ABI in the presence of symptoms of intermittent claudication; and third, a diabetic picture in the lipid profile. The relative risk for developing PAD in the presence of both smoking and diabetes mellitus is three- to fourfold higher than with the presence of one factor alone.

Markers of inflammation have been associated with development of arteriosclerosis and cardiovascular events. In particular, C-reactive protein is independently associated with PAD, even in patients with normal lipid levels. In the Physicians Health Study, an elevated C-reactive protein level was a risk factor for development of symptomatic PAD and also a risk for peripheral revascularization. High C-reactive protein levels are independent predictors of poor PTA outcomes after revascularization.

Elevated plasma homocysteine levels appear to be independent risk factors for PAD. Although B-vitamin supplements can lower homocysteine levels, the evidence for benefits from supplementation in preventing cardiovascular events is lacking. There are suggestions that elevated homocysteine levels are associated with restenosis after percutaneous transluminal coronary angioplasty. One study suggests that treatment with a combination of folate (1 mg), vitamin B12 (400 mcg), and pyridoxine (10 mg) may reduce the rate of coronary restenosis and the need for revascularization compared with placebo controls.

Platelet aggregability has been shown to be 30% higher in patients with peripheral vascular disease even if they are asymptomatic. Antiplatelet therapy has, not surprisingly, shown considerable reductions in fatal and nonfatal vascular events in high-risk vascular patients, eg, claudicants. The risk reduction for antiplatelet therapy versus placebo in the claudicant population was 46% for nonfatal stroke, 32% for nonfatal myocardial infarction, and 20% for death from a vascular cause. Even low risk patients on antiplatelet therapy have shown small, but considerable, risk reduction. Claudication progression, as measured by angiography, has also been shown to be inhibited in antiplatelet-treated patients. A randomized, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE) had a large subgroup of patients with atherosclerotic vascular disease. Clopidogrel was shown to bring about a small, but substantial, risk reduction. Claudication progression, as measured by angiography, has also been shown to be inhibited in antiplatelet-treated patients. A randomized, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE) had a large subgroup of patients with atherosclerotic vascular disease.
Hemostatic abnormalities are found frequently in PAD and could contribute to pathogenesis or be markers of disease progression. The presence of the lupus anticoagulant and elevated markers of platelet activation (beta thromboglobulin levels) has been associated with peripheral arteriosclerosis. Hemostatic abnormalities are present in diabetic patients, with greater evidence of thrombin generation than in nondiabetic patients. Clinical studies on patients undergoing peripheral bypass surgery have demonstrated the presence of a definite subset of patients with abnormal coagulation profiles. After adjustment for age and gender, von Willebrand factor, fibrin, D-dimer, and urinary fibrinopeptide A are elevated in claudicants, and the risk for claudication is substantially raised with unit changes in each factor.

Male patients with PAD have been demonstrated to have normal prothrombin and partial thromboplastin times. In addition, there appear to be no notable differences in alpha 2 macroglobulin, C1 inactivator, and antithrombin III. Enhanced levels of fibrinogen, α1-antitrypsin, thrombin/antithrombin III complex, α2-plasmin inhibitor/plasmin complex, and thrombomodulin were documented in claudicants. Compared with healthy control subjects, patients with PAD showed higher t-PA antigen, PAI-1 antigen, and D-dimer levels both at rest and after exercise. Thrombin formation is enhanced in these patients with PAD after submaximal treadmill exercise. Cumulatively, these data suggest that patients with PAD suffering from claudication are relatively hypercoagulable. The significance of such findings is unknown, and to date, no hemostatic factor or combination has been associated with failure or restenosis of PTA in PAD.

Management of patients with PAD

General

The management of patients with intermittent claudication has traditionally focused on relief of symptoms. But the realization that claudication is part of a generalized vascular disease with high mortality has led to a recent and substantial broadening of treatment strategies. The main goals of medical care should be reduction in cardiovascular risk on a systemic basis accompanied by alleviation of the symptoms of intermittent claudication. Current recommendations are that all PAD pa-
Table 2. Optimal Medical Management in the Patient with Peripheral Artery Disease: Goals, Interventions, and Recommendations

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<th>Smoking</th>
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<td>Goal: Complete cessation. No exposure to environmental tobacco smoke.</td>
<td>Ask about tobacco use status at every visit. In a clear, strong, and personalized manner, advise every tobacco user to quit. Assess the tobacco user's willingness to quit. Assist by counseling and developing a plan for quitting. Arrange followup, referral to special programs, or pharmacotherapy. Urge avoidance of exposure to secondhand smoke at work or home.</td>
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<th>Blood pressure control</th>
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<td>Goal: &lt; 140/90 mmHg; &lt; 130/85 mmHg if renal insufficiency or heart failure is present; or &lt; 130/80 mmHg if diabetes is present.</td>
<td>Promote healthy lifestyle modification. Advocate weight reduction; reduction of sodium intake; consumption of fruits, vegetables, and low-fat dairy products; moderation of alcohol intake; and physical activity in persons with blood pressure of ≥ 130 mmHg systolic or 80 mmHg diastolic. For persons with renal insufficiency or heart failure, initiate drug therapy if blood pressure is ≥ 140/90 mmHg if 6 to 12 mo of lifestyle modification is not effective, depending on the number of risk factors present. Add blood pressure medications, individualized to other patient requirements and characteristics (eg, age, race, need for drugs with specific benefits).</td>
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<td>Goal: An overall healthy eating pattern.</td>
<td>Advocate consumption of a variety of fruits, vegetables, grains, low-fat or nonfat dairy products, fish, legumes, poultry, and lean meats. Match energy intake with energy needs and make appropriate changes to achieve weight loss when indicated. Modify food choices to reduce saturated fats (&lt; 10% of calories), cholesterol (&lt; 300 mg/d), and trans-fatty acids by substituting grains and unsaturated fatty acids from fish, vegetables, legumes, and nuts. Limit salt intake to &lt; 5 g/d. Limit alcohol intake (≤ 2 drinks/d in men, ≤ 1 drink/d in women) among those who drink.</td>
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<td>Primary goal: LDL-C &lt; 70 mg/dL. Secondary goal: If triglycerides &gt; 200 mg/dL, non HDL &lt; 30 mg/dL. Other targets: triglycerides &lt; 150 mg/dL, HDL &gt; 40 mg/dL in men, &gt; 50 mg/dL in women.</td>
<td>Initiate lifestyle changes consisting of dietary modification, including use of plant sterols (&lt; 2 g/d) and increased fiber. Rule out secondary causes. Start drugs and advance dose to bring LDL-C to goal. Usually statin or combination of drugs with a statin. If non HDL-C elevated, consider lifestyle changes, or niacin or fibrates. If HDL-C low, consider niacin or fibrates.</td>
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<td>Goal: At least 30 min of moderate-intensity physical activity on most (and preferably all) days of the week.</td>
<td>If cardiovascular, respiratory, metabolic, orthopaedic, or neurologic disorders are suspected, or if patient is middle-aged or older and is sedentary, consult physician before initiating vigorous exercise program. Moderate-intensity activities (40% to 60% of maximum capacity) are equivalent to a brisk walk (15–20 min per mile). Additional benefits are gained from vigorous-intensity activity (&gt; 60% of maximum capacity) for 20–40 min on 3–5 d/wk. Recommend resistance training with 8–10 different exercises, 1–2 sets per exercise, and 10–15 repetitions at moderate intensity ≥ 2 d/wk. Flexibility training and an increase in daily lifestyle activities should complement this regimen.</td>
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<td>Goal: Achieve and maintain desirable weight body mass index 18.5–24.9 kg/m². When body mass index is ≥ 25 kg/m², waist circumference at iliac crest level ≤ 40 inches in men, ≤ 35 inches in women.</td>
<td>Initiate weight-management program through caloric restriction and increased caloric expenditure as appropriate. For overweight or obese persons, reduce body weight by 10% in first year of therapy.</td>
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<td>Goals: Normal fasting plasma glucose (&lt; 110 mg/dL) and near normal HbA1c (&lt; 7%).</td>
<td>Initiate appropriate hypoglycemic therapy to achieve near-normal fasting plasma glucose or as indicated by near-normal HbA1c. First step is diet and exercise. Second-step therapy is usually oral hypoglycemic drugs; sulfonylureas and/or metformin with ancillary use of acarbose and thiazolidinediones. Third-step therapy is insulin. Treat other risk factors more aggressively (eg, change blood pressure goal to &lt; 130/80 mmHg and LDL-C goal to &lt; 100 mg/dL).</td>
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<th>Aspirin</th>
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<td>Goal: All patients on an antiplatelet agent.</td>
<td>Patients should be on 81 mg of aspirin/d unless contraindicated. Clopedigrel may also be considered at 75 mg/d.</td>
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patients should receive antiplatelet therapy, stop smoking, exercise, and be screened and treated for hyperlipidemia, hypertension, diabetes, and hypercoagulability in accordance with national guidelines and community standards (Table 2).

**Smoking**

Smoking cessation is a priority in the addicted claudicant. More than 75% of claudicants who already smoke will have tried and failed to quit smoking. Up to 25% of patients will try to follow clinical advice to stop smoking, but more than 75% of these will recommence in less than 3 months.82 With medical advice alone, only 5% of claudicants will have longterm success in quitting.83 Nicotine replacement therapy such as chewing gum, transdermal patches, nasal sprays, and inhalers are effective in helping patients stop. A metaanalysis of trials shows a 1.5- to 2-fold increase in cessation rate, with nasal spray and inhaled nicotine showing most success.84 Combining nicotine replacement therapy with treatments such as an inhaler with a patch increases the success rate to nearly 20% at 1 year.85

Amfebutamone or bupropion (Zyban, GlaxoSmithKline) is an atypical antidepressant that has recently been licensed as an aid to smoking cessation. It reduces the hypertensive, cardiac, and other side effects of nicotine withdrawal. Trials suggest up to 30% 1-year cessation rates, with a dose-related response.86 The goals for the care of these patients should be accessible specialist smokers’ clinics, where counseling, education, and support by specialists in tobacco cessation can be combined with appropriate pharmacologic treatment.87

**Exercise**

Exercise therapy produces considerable improvements in the symptoms of claudicants.88-90 Physical improvements gained from an exercise regimen are both multifactorial and systemic.91 These include compensatory adaptations and redistribution of peripheral blood flow, changes in oxidative capacity of skeletal muscle with greater use of oxygen, changes in blood composition, inhibition of additional atherosclerotic disease, and improvements in the cardiorespiratory system.92 A study of 34 claudicants after a supervised exercise regimen over 6 months found a doubling of pain-free walking distance.1 There was also a mean drop in systolic blood pressure of 5.7% and a fall in mean cholesterol levels of 5.2%. Concerns about claudicants developing an inflammatory-type response during walking, which may be harmful, appear unfounded. Regular exercise training produces a reduction in the inflammatory markers associated with endothelial damage.93 So evidence suggests that patients following an exercise regimen improve both claudication distance and cardiovascular risk profile.

Three separate metaanalyses of exercise regimen trials identified similar components in the most successful programs.94-96 Common factors were exercise duration of greater than 30 minutes per session, frequency of at least three sessions per week, walking as the mode of exercise, exercising to near maximal pain tolerance, and a program lasting 6 months or longer. In claudicants, there appears to be equal benefit if the patient undergoes upper limb exercise or lower limb exercise. Pain-free and maximum walking distance improvements were seen with both forms of exercise.97 This is likely a function of total body conditioning because all exercise should give improvements in cardiovascular function; walking will give additional adaptive benefits in the muscle groups affected by claudication. The role of supervised exercise classes versus best exercise advice given in clinic has still to be determined on a large trial basis.

**Lipid lowering therapy**

Patients with symptomatic peripheral vascular disease should be considered within the high risk groups as defined by the Adult Treatment Panel III (ATP-III) of the National Cholesterol Education Program.99,100 The goal of lipid lowering therapy should be set at a LDL-cholesterol level of ≤ 70 mg/dL. Hypertriglyceridemia (> 200 mg/dL) is also prevalent in the peripheral vascular disease population and should be treated.101 The Adult Treatment Panel III identifies the sum of LDL and very-low density lipoprotein (VLDL), termed non-HDL cholesterol, (=[cholesterol]-[HDL]) as a secondary target for therapy in patients with high triglycerides (≥ 200 mg/dL). The goal for these patients is non-HDL cholesterol of ≤ 30 mg/dL.99,100 Despite the known lipid profile abnormalities in claudicants and the proved and theoretic advantages of lipid-lowering drugs,46,99,102 few studies have targeted relief of claudication symptoms as an end point.103,104 A recent review by the Cochrane peripheral vascular disease group identified only seven suitable randomized trials of lipid lowering therapy (not statins) in patients with lower limb arteriosclerosis.104,105 Lipid lowering therapy results in a marked but unimportant reduction in mortality and no change in nonfatal events. Two of these trials did demonstrate a substantial
The role of lipid-lowering regimens in the treatment of claudication has recently been readdressed. The Scandinavian Simvastatin Survival Study (4S) had demonstrated that subjects randomized to simvastatin had a 38% reduction in new or worsening claudication compared with subjects randomized to placebo, and several recent studies demonstrated improved walking ability in patients treated with statin compared with patients without a statin, independent of cholesterol levels and other potential confounders.

**Pharmacologic therapy**

Multiple drugs and regimens have been tested in claudication; five oral drugs have been licensed for the treatment of claudication. Two of these, inositol nicotinate, and cinnarizine, have not been established as effective when compared with placebo. Pentoxifylline (oxypentixyline) has been shown, in a metaanalysis, to improve walking distance by 29 meters over placebo (the improvement was approximately 50% compared with baseline in the placebo group; pentoxifylline provided an additional 30% improvement). Naftidrofuryl has shown an increase in walking distance of up to 30% when compared with a placebo at 6 months. Cilostazol, a phosphodiesterase inhibitor, has shown a 40% increase in walking distance at 3 months and has become the drug of choice in the pharmacologic management of claudication. Oral drug therapy should always be combined with exercise and risk factor modification.

**Gene therapy**

Molecular therapies to induce angiogenesis are appealing in the claudicant population because the ischemia is subacute, time for angiogenesis to occur is available, and collateral development is associated with improved symptoms and increased walking distance. Molecular therapies that result in increased levels of vascular endothelial growth factor, fibroblast growth factor, and hepatocyte growth factor have been used in claudication populations. The RAVE Trial (Regional Angiogenesis with Vascular Endothelial Growth Factor in Peripheral Arterial Disease) concluded that a single unilateral IM administration of adenoviral vascular endothelial growth factor provided a 121% increase in walking distance at 12 weeks compared to placebo. The most recent Therapeutic Angiogenesis with Recombinant Fibroblast Growth Factor-2 for Intermittent Claudication (TRAFFIC) study has shown that intrarterial fibroblast growth factor will result in a considerable increase in walking time at 90 days. These therapies are not readily available and have not been compared with standard aggressive medical and endoluminal management of claudication.

**Endoluminal procedures**

Because of the introduction of PTA in 1964 by Dotter and Judkins and its refinements by Gruntzig, PTA has grown into a viable alternative to surgical intervention in most arterial beds. The diseased SFA may be approached with a repertoire of techniques. The conventional approach is to access the SFA in an antegrade manner and negotiate a guide wire through the target lesion before performing PTA. A similar approach can be achieved in short segment occlusions. An antegrade transfemoral approach has initial technical success rates of 90% to 95% for stenotic lesions and 80% to 95% for complete occlusions. Use of the retrograde transpopliteal approach can increase the original technical success rate by an additional 6%. But longer occlusions require additional techniques. Percutaneous intentional extraluminal recanalization, or subintimal angioplasty or Bolia angioplasty, is a technique used to recannulize chronic occlusions. It intentionally achieves a dissection plane in the vessel wall to circumvent a total occlusion. Gaining luminal access into the distal target vessel remains the Achilles’ heel of this approach. Recently, the use of intravascular ultrasound to identify and guide a needle from the false dissected lumen into the true lumen has been shown to be effective. Percutaneous intentional extraluminal recanalization through the retrograde popliteal approach can be achieved in up to 80% of patients.

**Pathology of angioplasty and stenting**

Angioplasty is a controlled injury to the vessel wall. Although there is no apparent loss of cells from the media of the vessel wall after balloon injury, studies show that approximately 20% of total wall DNA is lost. Some of this loss is of endothelial origin, but a considerable amount reflects injury to the underlying medial smooth muscle cells. In the immediate aftermath of angioplasty, programmed cell death, or apoptosis, can be identified at 1 to 2 hours and disappears by 4 hours. No apoptosis can be identified in the wall after injury at 3 days but by day 7, 50% of the cells again show signs of apoptosis and by day 14, the number of apoptotic cells is again markedly decreased.
Smooth muscle cell proliferation within the media, which is normally less than 1%, increases to more than 20% within 48 hours after angioplasty. The fraction of cells proliferating reaches a maximum between 3 and 7 days and occurs as a synchronous wave of entry into the S phase of the medial smooth muscle. This first phase of smooth muscle cell proliferation appears to be driven by basic fibroblast growth factor released from dead and damaged cells in the vessel wall after balloon injury, and approximately 80% to 90% of this response can be prevented by inhibition with basic fibroblast growth factor antibodies. Four weeks after injury, the medial proliferative response returns to baseline levels. Intracoronary radiation after angioplasty inhibits this first wave of cell proliferation and prevents adventitial proliferation. By day 8 after the injury, smooth muscle cells are observed on the luminal side of the internal elastic lamina and appear to have migrated to the luminal surface through fenestrations in the internal elastic lamina. The number of smooth muscle cells in the intima increases to a maximum at 2 weeks after injury, and about 30% of medial smooth muscle cells may migrate from the media to the intima. This migration of cells requires degradation of the cage of matrix surrounding each cell by proteases and the synthesis of new matrix molecules. Migration of the smooth muscle cells from the media to the intima across the internal elastic lamina is mediated in part by platelet derived growth factor. Smooth muscle cell migration is unaffected by irradiation and antimitotic drugs. Once within the intima, approximately 50% of the smooth muscle cells

Figure 3. Therapeutic results. (A) This panel of angiograms of the superficial femoral artery shows a Transatlantic Intersocietal Commission B lesion (left [L]; arrows). This lesion was successfully treated with balloon angioplasty. Luminal diameter is improved with evidence of a nonflow limiting dissection in the wall (right; arrows). The patient experienced symptomatic relief. (B) This panel of angiograms of the superficial femoral artery shows a nonocclusive Transatlantic Intersocietal Commission C lesion (left [L]; arrow). This lesion was successfully treated with balloon angioplasty (right; arrow) and symptom relief has been maintained for 2 years. (C) This panel of angiograms of the superficial femoral artery shows a long Transatlantic Intersocietal Commission D lesion (left [L]) approached from the popliteal approach. The vessel was successfully recanalized and primarily stented along its entire length (middle [M]). Flow was restored with no defects (right). The patient experienced symptomatic relief, which lasted for 6 months. In-stent restenosis was encountered and successfully treated with balloon angioplasty. Symptom relief has been maintained for an additional 12 months. CFA, common femoral artery; SFA, superficial femoral artery; PFA, profunda femoris artery.
proliferate (a second phase of mitosis). In the intima, a second phase of cellular proliferation is first noted at day 7 and reaches a maximum at 1/4 days before returning to baseline by 28 days.136 But it may continue for up to 12 weeks in areas where reendothelialization takes longer to complete. This second phase of smooth muscle cell replication in the intima appears to be mediated by autocrine and paracrine factors and remains poorly understood. It also appears that the thickness of the intimal hyperplasia peaks within 1 month, and its rapid development is from both cellular elements and the production of proteoglycans.

Associated with the changes in the intima and media, there are substantial changes in the adventitia, as evidenced by increased cell proliferation and growth factor synthesis in the adventitia relative to the media after angioplasty. In the adventitia, there is a marked infiltrate of cells termed “myofibroblasts” by day 2, which by day 14, can represent up to 50% of cells within the intima.133,134 The presence of myofibroblasts is common in wound healing and leads to contraction of the wound. A similar phenomenon may occur in the healing vessel. Injured vessels can undergo chronic elastic recoil or negative remodeling, resulting in loss of luminal dimensions without an additional increase in neointimal area. Retrieved atherectomy material from primary and restenotic lesions has shown that the proportion of cells, which can be demonstrated to be proliferating in the restenotic lesion, is low,135 but that migratory activity and collagen synthesis of human smooth muscle cells from the restenotic lesions are greatly elevated, strongly supporting the concept that remodeling is important in the final determination of luminal diameter.136,137

The degree of intimal hyperplasia that develops in a vessel is dependent on the length and depth of the injury.138 Minimal intimal proliferation occurs when the media is uninjured, but intimal hyperplasia increases in proportion to the depth of the medial injury, indicating that the proliferative response reflects the direct injury to the smooth muscle cells.139,140 In addition, distention of smooth muscle cells without severe endothelial cell injury has been shown to result in smooth muscle cell proliferation. The length of the injury influences the duration of the reendothelialization process. Reendothelialization occurs from the margins of the denuded area and possibly from the endothelial cells of the vasa vasorum. The longer there is an incomplete endothelial cell covering, the greater time the smooth muscle cells are without the modulating influence of the endothelial cells, and the longer the replication phases of the smooth muscle cells will be.121,123 After deep vessel wall injury, luminal narrowing may be less dependent on intimal hyperplasia formation and more dependent on vessel wall remodeling.141 Medial damage is accompanied by a massive adventitial cell proliferation,142 which, in time, provides cells capable of contraction and negative remodeling.

**Intravascular stents**

The biology of in-stent restenosis is different than that seen after balloon angioplasty.143 A stent is generally used if the result of balloon angioplasty is technically unsatisfactory or if there is arterial occlusion, immediate elastic recoil, flow-limiting dissection, or restenosis. The response of a vessel to a stent is dependent on the stent design, length, composition, delivery system, and deployment technique.144 In-stent restenosis is classified on the basis of length of restenosis in relation to stented length. Four categories of in-stent restenosis have been defined: focal (≤ 10 mm length), diffuse (> 10 mm length) proliferative (> 10 mm length and extending outside the stent), and occlusion.145 After balloon angioplasty, there is thrombus formation, intimal hyperplasia development, elastic recoil, and negative remodeling. In contrast, after stent placement, elastic recoil and negative remodeling are eliminated146 and thrombus formation followed by intimal hyperplasia development are the main contributors to in-stent restenosis.147

Patients with diabetes and earlier restenosis have a higher rate of in-stent restenosis,148 and there is a correlation with prolonged in-stent thrombus and hyperglycemia.149 Stent placement in a vessel results in generalized injury to the length of the vessel exposed and in more focal injuries at the areas of strut placement. Intravascular ultrasound has demonstrated that stents do not always completely oppose the vessel wall along its entire length, resulting in uneven injury along its length.146 After stent placement, the surface of the metal implanted into the vessel is covered by a strongly adherent monolayer of protein within 5 seconds. After 1 minute the surface is covered by fine layers of proteins, predominantly fibrinogen.150 The holes between the stent wires are filled with thrombus and the adherence of platelets and leukocytes is enhanced by disturbance of electrostatic equilibrium.151,152

The basic mechanisms of smooth muscle cell prolif-
eration and migration after stent placement are the same as those after balloon injury.153 The intimal hyperplasic process in a stent is more prolonged and robust than in a balloon-injured artery and is proportional to the depth of injury the recipient vessel sustains154 and the inflammatory response induced.155 It can often be much more pronounced at the ends than in the body of the stent. In addition, the adventitial response is prolonged, with adventitial giant cell body formation noted. Stents prevent chronic elastic recoil and cause progressive atrophy of the media.156

Outcomes
National reporting standards for vascular procedures define three categories of clinical success: anatomic, hemodynamic, and clinical (Table 3). A composite analysis of all published trials of PTA with or without stenting in the femoropopliteal arteries showed patencies of 71%, 59%, and 53% at 1, 3, and 5 years, respectively (Fig. 4). Technical success was 90%, with a complication rate of 10% (Table 4). Multiple factors can adversely affect patency; these include presenting symptoms (claudication versus critical ischemia), type of lesion (stenosis versus occlusion), length of lesion (< 10 cm and > 10 cm), and distal runoff157-160 (Table 5). The presence of diabetes also influences longterm patency.161

Jorgenson and colleagues162 suggested that restricting the area of dilation and using the smallest necessary balloon to reduce vessel wall injury would be beneficial, but the clinical benefit of this approach has not been shown. Prolonged dilation, although a safe procedure, does not result in superior longterm patency rates.163 Two studies suggested that no factor contributed to longterm failure.164,165 Patients with diabetes have been shown to have worse outcomes than patients without diabetes.158,161,166,167 Patients treated for critical ischemia have lower patency rates than patients treated for claudication.158,159,167,168 Stenoses are associated with better patency than occlusions, but if technical failures are excluded, patency rates are similar between both lesions.158-160,169-171

Concentric lesions have also been found to be more favorable than eccentric lesions158,172 and focal stenoses fare better than long segment lesions.158,166,167,172,173 In most cases, poor runoff correlates with worse outcomes.160,167,172 There is a high incidence of thrombosis within hours of angioplasty of total occlusions, which is independent of the length of the lesion.174 Predictors of immediate PTA failure are diastolic hypertension and the percent stenosis.164 Male gender and presence of a lower atherosclerotic burden are associated with a lower complications rate.117

London and associates175 demonstrated that continued smoking, poor runoff, and length of occlusion were important risk factors for occlusion after percutaneous intentional extraluminal recanalization. In a prospective registry, Laxdal and coworkers176 showed that subintimal angioplasty has a poor patency at 18 months, and the

<table>
<thead>
<tr>
<th>Technical complication</th>
<th>Literature (%)</th>
<th>Maximum to accept (%)</th>
</tr>
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<tbody>
<tr>
<td>Acute operation</td>
<td>&lt;1</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Severe hematoma</td>
<td>&lt;2</td>
<td>&lt;4</td>
</tr>
<tr>
<td>Acute occlusion</td>
<td>&lt;0.5</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>&lt;0.1</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Perforation</td>
<td>&lt;0.1</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

Table 4. Reported and Maximal Limitations to Accept Technical Complications with Percutaneous Transluminal Angioplasty (Society of Cardiovascular and Interventional Radiology 1990)
major factors contributing to occlusion are the presence of diabetes and critical ischemia.

If intravascular ultrasonography is used immediately after PTA, the extent of dissection, free lumen area, and diameter are predictive factors of patency. Factors of intravascular ultrasound that favor improved patency are the absence of calcification, dissection or plaque rupture, and a residual stenosis of less than 30%. Intravascular ultrasound predictor of failure at 1 and 6 months is initial residual stenosis after PTA. Similarly, pronounced residual stenosis (> 30%) on duplex ultrasound 1 day after PTA correlates with failure within 1 year; unfortunately, the converse is not true; a normal duplex at + 1 day cannot predict failure within 1 year. Plaque area increase and vascular remodeling contribute to lumen area change after PTA of the femoropopliteal artery on intravascular ultrasound study.

Table 5. Factors Influencing the Patency of Superficial Femoral Artery Interventions

<table>
<thead>
<tr>
<th>Factors</th>
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<tbody>
<tr>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>&lt; 2-cm lesions</td>
<td></td>
</tr>
<tr>
<td>Noncalcified lesions</td>
<td></td>
</tr>
<tr>
<td>&gt; 3.5-mm diameter vessel</td>
<td></td>
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<tr>
<td>No use of thrombolytics</td>
<td></td>
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<tr>
<td>Nonsmokers</td>
<td></td>
</tr>
<tr>
<td>Low C-reactive protein</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Occlusions</td>
<td></td>
</tr>
<tr>
<td>Segments stented &gt; 10 cm</td>
<td></td>
</tr>
<tr>
<td>&gt; 30% residual stenosis</td>
<td></td>
</tr>
<tr>
<td>Poor tibial runoff</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine &gt; 1.3 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Noncontributory</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Experience of operator</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacotherapy after PTA

The role of pharmacotherapy after PTA in the SFA has been driven by data derived from the coronary artery interventional literature. Heiss and associates demonstrated a major benefit of aspirin compared with placebo after PTA, but antiplatelet drugs have not shown a consistent benefit in preventing restenosis. Low dose aspirin appears as effective as high dose aspirin in the prevention of restenosis. The coronary literature supports the use of the combination of aspirin and clopidogrel after en-
doluminal intervention. No data are readily available for periphery interventions, but most centers add clopidogrel before and after intervention. The required duration of this additional therapy has not been tested. Whether statins are beneficial after peripheral angioplasty is unanswered by level 1 evidence, but given the fact that patients with SFA disease should have their cardiovascular risk factors managed aggressively, it is likely to be a moot point.

**Adjuvant stenting**

Four randomized studies comparing PTA alone versus PTA plus stent placement in the SFA all failed to demonstrate a benefit to stenting in terms of long-term patency and symptom relief.\(^\text{199-202}\) There is little evidence to support the superiority of endovascular stents over PTA alone in the femoropopliteal arteries. Their use should be confined at present to flow limiting dissections or inadequate results from balloon angioplasty alone.\(^\text{200,203,204}\) Cheng and coauthors\(^\text{205}\) suggested that major factors that impede stent patency were occlusions, stented segment length > 10 cm, procedure in claudicants, and the use of Memotherm (Bard) stents. Liermann and colleagues\(^\text{206}\) reported a primary patency rate of 82% after 18 months and noted a lower patency rate for stents placed in the distal portion of the SFA compared with the proximal portion. Strecker and associates\(^\text{170}\) reported a 2-year patency rate of 73% for stent placement for stenosis and 32% in occlusions.

Use of wall stents for short lesions and stenoses reveals a 1- to 2-year primary patency of 67%; for occlusions this dropped to 49%.\(^\text{171}\) One report suggested a high rate of early thrombosis and restenosis rate of 77% when wall stents are placed in the SFA.\(^\text{207}\) There are no peer reviewed data in press on the long-term performance of nitinol stents in the SFA. One report noted that the 12-month restenosis of nitinol stents was 46%, which was not influenced by the cumulative length or the number of stents placed, but was worsened in the presence of diabetes.\(^\text{208}\)

In a bid to counteract in-stent restenosis, covered stents have been proposed.\(^\text{209}\) There appears to be an initial gain in patency over the first 6 months.\(^\text{210}\) Although this strategy did prevent in-stent restenosis, it did not prevent development of intimal hyperplasia at the ends of the device.\(^\text{211}\) Reclosure rates of 32% to 43% in the first 12 to 18 months after implantation have been reported.\(^\text{211-214}\) Reconstructive operations in patients presenting with infrainguinal stent occlusion or restenosis appear to be associated with higher morbidity and major limb amputation rates.\(^\text{215}\)

**Drug eluting stents**

Although several drug eluting stents have been used in the coronary circulation, only one, the sirolimus eluting SMART stent (Cordis Endovascular), has data available for the periphery. The results of the SIROCCO studies showed that despite excellent 6-month patency observed in the bare nitinol stent group, comparative analysis revealed a reduction in neointimal hyperplasia in the sirolimus eluting stents.\(^\text{216,217}\) It did not appear that these stents had a major clinical effect.

**Atherectomy**

Debulking of lesions may enhance patency. Atherectomy devices and endovascular endarterectomy have been used to achieve these aims. Directional atherectomy appears to have a 75% patency at 24 months, but there is a high restenosis rate.\(^\text{218}\) Endovascular SFA endarterectomy appears to have a 65% technical success rate and a cumulative patency of 59% in patients in whom technical success can be achieved.\(^\text{219}\) Directional atherectomy has a patency of 57% at 2 years in patients with diabetes, complete luminal occlusion, or critical ischemia having lower patencies.\(^\text{220}\) Studies have suggested that debulking segments before adjunctive balloon angioplasty may offer advantages in reducing acute complications and improving long-term patency.\(^\text{221,222}\) In addition, treatment of in-stent restenosis may be helped by debulking before dilatation.\(^\text{223}\)

Several mechanical atherectomy devices have been used in the treatment of peripheral vascular disease. The Simpson Atherocath is commonly used to treat focal eccentric lesions in larger vessels and bypass graft anastomoses. It is limited by its high profile and side-cutting design. The Silverhawk catheter (Foxhollow Inc), which is derived from the Simpson catheter, has reduced these obstacles to catheter placement and use. Case series suggest that it has short-term benefits.\(^\text{224-226}\) Rotational atherectomy (Rotablator, Boston Scientific) uses a high speed rotating diamond coated burr to abrade lesions into microparticles that are dispersed down stream; it is very useful for heavily calcified lesions, but the consequences of distal embolization remain a considerable concern. The transluminal endarterectomy catheter (TEC) uses aspiration to collect debris shaved by a ro-
tating cutting head and appears more effective in treating soft or thrombus-containing obstructions. In a retrospective analysis of 35 SFAs treated with the transluminal endarterectomy catheter, the initial success rate was 100%, but the 5-year patency was 0%. Both the pullback atherectomy catheter and Redha-Cut (Sherine Med AG) catheter rely on first passing the obstruction with the entire device and then removing the material as the catheter’s cutting blades are pulled back across the lesion. In three prospective randomized trials, there was no difference between angioplasty and atherectomy for SFA disease.

**Laser-assisted angioplasty**

Laser-assisted angioplasty increases luminal cross-sectional area by both athero-ablation and vessel expansion without calcium ablation. Technical success with laser-assisted angioplasty is as high as 91%. There appears to be better initial recanalization with laser-assisted angioplasty compared with PTA, but no longterm differences between PTA and laser-assisted angioplasty have been appreciated. Enclosed thrombolysis associated with PTA has no advantage over PTA alone.

**Brachytherapy**

Delivery of radiation to the injured field in a vessel has had beneficial effects. Endovascular radiotherapy can prevent intimal hyperplasia after stent implantation in femoropopliteal arteries, but it partially prevents healing of disrupted vessel surfaces. Gamma radiation induces positive vascular remodeling after balloon angioplasty. When doses of 12 to 14 Gy (gamma radiation) are applied endoluminally to the femoropopliteal segment after PTA, there is a twofold increase in 12-month patency compared with that in untreated controls. Similar results were noted in the Peripheral Artery Radiation Investigational Study trial.

**Cryotherapy**

Cryoplasty is a novel therapy that combines conventional balloon angioplasty with application of cryotherapy. Experimental data suggest that cryotherapy induces early arterial wall cell loss through apoptosis, but does not alter intimal hyperplasia development or eventual lumen area compared with conventional balloon angioplasty. The single system on the market at present uses a double balloon system that exerts 8 atm on the lesion and is accompanied by cold induced injury to the wall. The hope is that cryotherapy will allow more accurate angioplasty and induce apoptosis in the wall, reducing dissections and vessel response to injury. The final results of the cryovascular safety registry have shown, in 102 patients, a primary patency of 82% at 10 months. Longer-term data are required, although case series suggest that improved patency can be achieved up to 18 months.

**Exercise versus angioplasty**

Various trials have compared superficial femoral artery PTA to exercise therapy. They suggest that although PTA may give a short 3- to 6-month improvement in symptoms, exercise therapy has better results at 12 months. But at 5-year followup, there appears to be no difference between the groups. The loss of the initial advantage of PTA was attributable to restenosis of the dilated segment; those treated conservatively had a steadily increased benefit of exercise. The later loss of the advantage of exercise was probably from a lack of adherence to the exercise program. The best effect of exercise was found in patients with disease confined to the SFA in contrast to PTA, which had the best effect in iliac lesions. One study compared PTA with exercise with no treatment and suggested that PTA moderately but considerably improves quality of life at 1 year. All of these studies lacked sufficient power and the seminal group of PTA with supervised exercise is missing in all studies.

**Operation versus angioplasty**

When examining the benefits of exercise in the claudicant population, another question arises: “Is there a functional benefit of operation in the intermittent claudication population?” One study compared peripheral bypass operation, operation followed by 6 months of supervised exercise training with dynamic leg exercises, and 6 months of supervised training alone in 75 patients with claudication. At 13 months of randomization, walking ability was improved in all three groups. The most effective treatment for improving functional status was exercise training plus operation. The median changes in maximal walking distance were 173% for the surgical group, 263% for the group that received both supervised exercise and bypass, and 151% for the exercise group alone. The surgically treated patients increased their walking distance more than patients who...
received only exercise training did; they also had a greater rate of complications than the exercise groups.\textsuperscript{255}

**Economics**

In Sweden, the cost-effectiveness ratios (cost per month of patency) for PTA and local open thromboendarterectomy appear equivalent.\textsuperscript{256} For a decision and cost-effectiveness analysis of revascularization procedures for femoropopliteal disease (4,800 PTAs and 4,511 bypasses),\textsuperscript{257} six treatment strategies were analyzed: no treatment, initial PTA with no additional revascularization, initial PTA with subsequent PTA, initial PTA with subsequent bypass surgery, bypass surgery followed by no therapy, and bypass surgery followed by graft revision. The results showed that for a 65-year-old man with disabling claudication and a femoropopliteal stenosis or occlusion, an initial PTA strategy increased quality adjusted life years by 2 to 13 months and resulted in decreased lifetime expenditures as compared with bypass surgery. Sensitivity analysis showed that when the 5-year patency of PTA exceeds 30%, PTA is the preferred initial invasive strategy in patients with disabling claudication and femoropopliteal stenosis or occlusion.

In conclusion, aggressive proactive medical therapy in the claudicating patient remains the most important therapeutic step that should be initiated as soon as claudication is identified (Fig. 5). Exercise is important in this initial strategy, but will also contribute to improved symptom relief in many patients. In patients who still have severe lifestyle-limiting claudication that does not respond to the initial medical regimen, angioplasty of the SFA appears to be an appropriate intervention with success more likely in low-grade lesions compared with high-grade lesions. Adjuncts to a percutaneous approach have not proved consistently beneficial to date. Endoluminal intervention without aggressive lifestyle modifications is not recommended because the durability of the intervention is approximately 50% at 5 years and secondary interventions are often required to maintain patency.

**REFERENCES**


49. Ridker PM, Stampfer MJ, Rifai N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein fibrinogen homocysteine lipoprotein(a) and standard choles-


292 Davies et al Femoropopliteal Atherosclerotic Disease J Am Coll Surg


189. Zdanowski Z, Albrechtsson U, Lundin A, et al. Percutaneous transluminal angioplasty with or without stenting for femoro-


246. Davies et al. Femoropopliteal Atherosclerotic Disease J Am Coll Surg