Clinical Policy Bulletin:  
Peripheral Vascular Stents

Number: 0785

Policy

Aetna considers peripheral artery stenting by means of Food and Drug Administration-approved stents* medically necessary in any of the following situations:

- Primary therapy for common iliac artery stenosis and occlusions.
- Primary therapy for external iliac artery stenoses and occlusions.
- Primary therapy for chronic mesenteric ischemia.
- Primary therapy for individuals with symptomatic posterior cerebral or cerebellar ischemia caused by subclavian artery stenosis (subclavian steal syndrome) who are at high-risk of surgical complications.
- Primary therapy for individuals with symptomatic extremity ischemia caused by subclavian artery stenosis (in cases for stenting of the subclavian artery following percutaneous transluminal angioplasty).
- Salvage therapy for brachiocephalic arteries: subclavian steal syndrome, upper extremity claudication, ischemic rest pain of the arm and hand, non-healing tissue ulceration, and focal gangrene.
- Salvage therapy for common and external iliac arteries for a sub-optimal or failed result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis greater than 50%, or flow-limiting dissection).
- Salvage therapy for femoral, popliteal, and tibial arteries for a sub-optimal or failed result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis greater than 50%, or flow-limiting dissection).
- Salvage therapy for femoral-popliteal arterial lesions for a sub-optimal result from balloon dilation.
- Salvage therapy for infra-popliteal arterial lesions for a sub-optimal result from balloon dilation.

Aetna considers peripheral artery stenting experimental and investigational in any of the following situations (not an inclusive list) because its effectiveness for these indications has not been established:

- Celiac artery stenting in the treatment of celiac artery compression syndrome.
- Primary therapy for tibial artery stenosis and occlusions.
- Primary therapy for infra-popliteal lesions.
- Primary or salvage therapy for atherosclerotic reno-vascular disease (e.g., renal artery stenosis).
- Primary or salvage therapy for aorto-iliac arterial lesions.
- Primary or salvage therapy for popliteal artery aneurysm.

Aetna considers the Zilver PTX Drug-Eluting Peripheral Stent medically necessary for the primary treatment of femoropopliteal artery disease.
Aetna considers the Gore Viabahn PTFE-coated Endoprosthesis medically necessary for improving blood flow in persons with symptomatic peripheral arterial disease in superficial femoral artery lesions.

Aetna considers peripheral venous stents medically necessary for the following indications (not an all-inclusive list)

- Hemodialysis access graft/fistula: stenosis, restenosis, and occlusion.
- Superior vena cava: superior vena cava syndrome, post radiation venous stenosis, and congenital stenosis

Aetna considers peripheral venous stents experimental and investigational for the treatment of recurrent phlebitis because their effectiveness for this indication has not been established.

* All drug-eluting arterial stents and polytetrafluoroethylene (PTFE)-covered arterial stents other than the Gore Viab PTFE-coated stent and the Zilver PTX-Drug-Eluting stent are considered experimental and investigational for treat of peripheral vascular diseases because their effectiveness for this indication has not been established.

See also CPB 0295 - Peripheral Atherectomy and Thrombectomy Devices; CPB 0458 - Peripheral Vascular Rehabilitation Programs; CPB 0531 - Balloon-Expandable Venous Stents; and CPB 0621 - Drug-Eluting Stents.

**Background**

Peripheral vascular disease (PVD) stems from restriction of blood flow in vessels that lead to the extremities (i.e., arms and legs) as well as internal organs (e.g., kidney and stomach). There are 2 types of PVD: (i) functional, and (ii) organic. Functional PVD does not involve defects in the structure of the blood vessels; it is usually transient and related to spasm of the vessels (e.g., Raynaud's disease). It can be triggered by smoking, cold temperatures, emotional stress or working with vibrating machinery. Organic PVD is caused by inflammation and tissue damage in the blood vessels (e.g., peripheral artery disease [PAD]). It is caused by fatty build-ups in arteries that block normal circulation; and is more common than functional PVD.

Peripheral artery disease affects 3 major arterial segments: (i) aorto-iliac arteries, (ii) femoro-popliteal (FP) arteries (iii) infra-popliteal (primarily tibial) arteries. The disease is usually classified based on claudication, rest pain, or de of tissue loss due to chronic ischemia. Peripheral artery disease is an important cause of morbidity that affects up million people in the United States. Physicians can identify patients who are at risk for the disease with a question and the ankle brachial index (ABI). The ABI can be attained by measuring the blood pressure (BP) at the brachial and at the posterior tibialis artery by means of sonography. The ankle systolic BP is divided by the brachial BP, both measured in the supine position. Normally, the ratio is more than 1; in severe disease, it is less than 0.5. More than 70% of patients diagnosed with the disease remain stable or improve with conservative management. Those who do not improve may undergo contrast angiography or magnetic resonance angiography, which may be used in plan graft surgery or percutaneous intervention. In particular, patients with critical limb ischemia (CLI) should undergo interventions for re-vascularization. Re-vascularization methods have entailed surgical as well as endovascular approaches. Surgical bypass, atherectomy, and endarterectomy have been used to restore peripheral circulation. However, the invasiveness and complications of surgical interventions have resulted in the development of endovascular procedures. Percutaneous transluminal angioplasty (PTA) and/or stenting have been employed as primary and salvage therapy for PAD (De Sanctis, 2001; Ouriel, 2001; Balk et al, 2008; AHA, 2009).

There are 2 basic types of stents: (i) balloon-expandable (BE), and (ii) self-expandable (SE). The former uses an angioplasty balloon to expand and set the stent within the arterial segment (e.g., the Palmaz stent); although it has supplanted by the next generation of SE stents for arterial occlusive lesions. Self-expanding stents may have been in longer occlusive lesions as primary therapy, especially in the FP segment, where PTA and BE stents may be associated with higher rates of re-stenosis and failure. The SE stent depends on the unique properties of a metal (e.g., nitiol) or alternatively the weave of the stent, to assume a pre-configured shape within the vessel lume
The Wallstent, an example of the latter, is composed of elgaloy, a variant of stainless steel, and the radial force imparted by the weave density determines expansion. The SE stent may be post-dilated to ensure strut apposition to the arterial wall. The patency rates of SE stents appear to be superior to BE stents (Balk et al, 2008).

New materials have been added to conventional stents in an attempt to improve their effectiveness. The standard (whether BE or SE) is bare-metal, with no added materials. Covered stents use a synthetic fabric, such as polytetrafluoroethylene (PTFE), which covers the metal component of the stent and acts as an exoskeleton. However, animal studies did not support the proposed advantage of the covered stent that it lowers the incidence of neointimal hyperplasia, which can hasten re-stenosis. While the incidence of neointimal hyperplasia was reduced in the mid-portion of the graft, it was comparable to that of controls at the proximal and distal ends of the covered stent. One advantage of a stent graft is that a longer infra-inguinal lesion can be treated. In theory, the synthetic fabric of the covered stent excludes the atherosclerotic plaque from the lumen. In addition, the combination of the nitinol exoskeleton and the fabric cover yields a flexible, but structurally stable device, which is particularly advantageous for the femoro-popliteal segment (Balk et al, 2008).

Drug-eluting stents (DES) that usually contain sirolimus (rapamycin) have been used "off-label" for patients with PV disease. Other treated stents have been developed such as the Carbostent, which has a thin coating of carbon designed to reduce its interaction with platelets. "Off-label" use of stents is problematic because the device does not follow the conventional FDA approval process. Randomized controlled trials (RCTs) are underway, one that compares P alone to PTA and a biliary stent in the superficial femoral and proximal popliteal arteries; another RCT has been performed, which examines a bare nitinol biliary stent in the same anatomical segment. Neither of these trials has been published in peer-reviewed journals (Balk et al, 2008). The National Institute for Health and Clinical Excellence guideline on "Lower limb peripheral arterial disease: Diagnosis and management" (2012) recommended the use of metal stents where stenting is indicated for intermittent claudication because of a lack of evidence of superior clinical outcomes with DES.

There is no consensus on the diagnosis or treatment of renal artery stenosis (RAS). The consequences of renal ischemia are hypertension, neuroendocrine activation, and renal insufficiency, which can result in acceleration of atherosclerosis, further renal dysfunction, myocardial infarction (MI), heart failure, stroke, and death. Whether re-vascularization improves clinical outcomes when compared with optimal medical therapy is unclear.

There is insufficient evidence of the effectiveness of stenting over percutaneous transluminal angioplasty (PTA) for artery stenosis. An assessment prepared for the Agency for Healthcare Research and Quality (2007) concluded that "overall, there is insufficient evidence to determine whether angioplasty with stenting is better treatment for [atherosclerotic renal artery stenosis] than aggressive medical therapy alone." The report also concluded that there is no difference in the long-term kidney function of people who have angioplasty compared with people who have medical therapy alone." The report also noted that there is insufficient evidence to determine whether angioplasty reduces the number of antihypertensive medications required after the procedure, and there is no research about how angioplasty and medical therapy compare in treating people who have acutely decompensating hemodynamic and kidney function.

The American Heart Association (AHA)'s symposium on atherosclerotic peripheral vascular disease -- intervention renal artery disease (Rocha-Singh et al, 2008) stated that the treatment of atherosclerotic renal artery disease is evolving and remains controversial. Renal artery stenting is widely available and frequently used to treat patients with renal artery stenosis and poorly controlled hypertension and/or renal insufficiency. However, it is still unclear if percutaneous re-vascularization adds incremental value to optimal medical therapy to prevent the adverse outcomes of renal artery disease. Accordingly, the AHA recommended that physicians enroll hypertensive patients with atherosclerotic RAS into the CORAL trial to acquire outcomes and selection data.

More recently published systematic evidence reviews (e.g., Kumbhani et al, 2011) have found no significant difference in clinical outcomes in persons with renal artery stenosis managed with stenting and persons managed medically. Ongoing clinical trials such as the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial will ultimately help to determine the best strategies to limit the morbidity and mortality associated with renal artery stenosis.
Cooper and colleagues (2006) stated that the Cardiovascular Outcomes in Renal Atherosclerotic Lesions Trial (COPRAS) is a randomized clinical study contrasting optimal medical therapy alone to stenting with optimal medical therapy for patients with atherosclerotic RAS on a composite cardiovascular and renal endpoint: cardiovascular or renal death hospitalization for congestive heart failure, stroke, doubling of serum creatinine, and need for renal replacement therapy. The secondary endpoints evaluate the effectiveness of re-vascularization in important subgroups of patients and with respect to all-cause mortality, kidney function, renal artery patency, microvascular renal function, and BP control.

Tuttle and colleagues (1998) reported their 5-year experience with the intra-vascular stent for the treatment of ostial RAS. A total of 129 patients (63 men and 66 women) and 148 arteries were included in this study. The mean age of the patients was 71 +/- 10 years; 98% were hypertensive and 57% had renal dysfunction. Angiographical characteristics of RAS were unilateral in 78%, bilateral in 15%, and single kidney in 7%. The technical success rate was 98% for stent versus 11% for percutaneous renal angioplasty (PTRA) in the ostial location. The stent re-stenosis rate (angiographical) was 14% at 8 +/- 5 months. Systolic and diastolic BPs were as follows: baseline, 158 +/- 3; 6 months, 149 +/- 3 and 81 +/- 2 mm Hg; 12 months, 149 +/- 3 and 79 +/- 2 mm Hg; and 24 months, +/- 3 and 79 +/- 2 mm Hg. Follow-up values were significantly lower than baseline (p < 0.05). The number of medications for hypertension initially decreased from 2.2 +/- 0.1 at baseline to 1.6 +/- 0.1 and 1.8 +/- 0.1 at 1 and 3 months, respectively (p < 0.05). By 6 months, however, the number of medications had increased and was not significantly different from before stent placement. Renal function was stable in the group as a whole: Cockcroft-Gault creatinine clearance (C-G CrCl) at baseline was 40 +/- 2 ml/min; at 6 months, 36 +/- 3 ml/min; at 12 months, 39 +/- 2 ml/min; and at 24 months, 39 +/- 4 ml/min. When stratified by degree of renal function, values were similarly stable: Patients with a baseline serum creatinine level of 2 mg/dL or less had C-G CrCl values as follows: baseline, 53 +/- 1 mg/dL; 6 months, 43 +/- 4 mg/dL; 12 months, 46 +/- 4 mg/dL; and 24 months, 52 +/- 5 mg/dL. Those with a baseline serum creatinine level greater than 2 mg/dL had C-G CrCl values as follows: baseline, 26 +/- 2 mg/dL; 6 months, 34 mg/dL; 12 months, 32 +/- 6 mg/dL; and 24 months, 23 +/- 3 mg/dL. Of 8 patients who were dialysis-dependent, 4% recovered renal function with a mean serum creatinine level of 2.3 +/- 0.5 mg/dL at 15 +/- 6 months (range of 9 months). The authors concluded that stent placement for the treatment of atherosclerotic ostial RAS has a high success rate and a low rate of re-stenosis. Control of hypertension improves in most patients. Renal function stabilizes or improves in the majority of patients, even those with severe renal failure. The authors reported that these favorable outcomes are maintained long-term.

In a prospective non-randomized trial, Zähringer et al (2007) evaluated the patency of sirolimus-eluting stents (SES) compared to bare-metal stents (BMS) in the treatment of atherosclerotic RAS. A total of 105 consecutive symptomatic patients (53 men; mean age of 65.7 years) with RAS were treated with either a bare-metal (n = 52) or a drug-eluting 53) low-profile Palmaz-Genesis peripheral stent at 11 centers. The primary endpoint was the angiographical results measured with quantitative vessel analysis by an independent core laboratory. Secondary endpoints were technical and procedural success, clinical patency [no target lesion re-vascularization (TLR)], BP and anti-hypertensive drug use, worsening of renal function, and no major adverse events at 1, 6, 12, and 24 months. At 6 months, the in-stent diameter stenosis for BMS was 23.9% +/- 22.9% versus 18.7% +/- 15.6% for SES (p = 0.39). The binary stenosis rate was 6.7% for SES versus 14.6% for the BMS (p = 0.30). After 6 months and 1 year, TLR rate was 7 and 11.5%, respectively, in the BMS group versus 1.9% at both time points in the SES group (p = 0.21). This rate remained stable up to the 2-year follow-up; but did not reach statistical significance due to the small sample. Even early as 6 months, both types of stents significantly improved BP and reduced anti-hypertensive medication compared to baseline (p < 0.01). After 6 months, renal function worsened in 4.6% of the BMS patients and in 6.9% of the SE group. The rate of major adverse events was 23.7% for the BMS group and 26.8% for the SES at 2 years (p = 0.39). The authors concluded that the angiographical outcome at 6 months did not show a significant difference between and SES. Renal artery stenting with both stents significantly improved BP. They stated that future studies with a larger patient population and longer angiographical follow-up are needed to determine if there is a significant benefit of D treating ostial RAS.
Corriere et al (2008) retrospectively examined peri-procedural morbidity and early functional responses to primary artery angioplasty and stenting (RA-PTAS) for patients with atherosclerotic reno-vascular disease (RVD). Consecutive patients undergoing primary RA-PTAS for hemodynamically significant atherosclerotic RVD with hypertension and ischemic nephropathy were identified from a prospectively maintained registry. Hypertension responses were determined based on pre- and post-intervention BP measurements and medication requirements. Estimated glomerular filtration rate (eGFR) was used to determine renal function responses. Both hypertension and renal function responses were assessed at least 3 weeks after RA-PTAS. Stepwise multi-variable regression analysis was used to examine associations between BP and renal function responses to RA-PTAS and select clinical variables. A total of 110 primary RA-PTAS were performed on 99 patients with atherosclerotic RVD with a mean angiographic diameter-reducing stenosis of 79.2 +/- 12.9%. All patients had hypertension (mean of 3.4 +/- 1.3 anti-hypertensive agents). Mean pre-intervention eGFR was 49.9 +/- 22.7 ml/min/1.73 m², and 74 patients had a pre-intervention eGFR of less than 60 ml/min/1.73 m². The technical success rate for RA-PTAS was 94.5%. The peri-procedural complication rate was 1%; there were no peri-procedural deaths. Statistically significant decreases in mean systolic BP (161.3 +/- 25.2 mm Hg versus 148.5 +/- 25.2 mm Hg post-intervention, p < 0.0001), diastolic BP (78.6 +/- 13.3 mm Hg versus 72.5 +/- 13.5 mm Hg post-intervention, p < 0.0001), and number of anti-hypertensive agents (3.3 +/- 1.2 versus 3.1 +/- 1.3 post-intervention, p = 0.009) were observed. Assessed categorically, hypertension response to RA-PTAS was cured in 12%, improved in 20.5%, and unchanged in 78.4%. Categorical eGFR response to RA-PTAS was improved in 27.7%, unchanged in 65.1%, and worsened in 7.2%. Multi-variable stepwise regression analysis revealed associations between pre- and post-intervention systolic BP (p < 0.0001), diastolic BP (p < 0.0001), and eGFR (p < 0.0001), as well as a trend toward improved diastolic BP response among patients managed with staged bilateral intervention (p = 0.0589). The authors concluded that primary RA-PTAS for atherosclerotic RVD was associated with low peri-procedural morbidity and mortality but only modest early improvements in BP and renal function. They stated that results from ongoing prospective trials are needed to assess the long-term outcomes associated with RA-PTAS and clarify its role in the management of atherosclerotic RVD.

The American Heart Association (AHA)'s symposium on atherosclerotic peripheral vascular disease -- intervention for renal artery disease (Rocha-Singh et al, 2008) had the following statements:

1. The treatment of atherosclerotic renal artery disease is evolving and remains controversial. Renal artery stenting is widely available and frequently used to treat patients with RAS and poorly controlled hypertension and/or renal insufficiency. However, it is still unclear if percutaneous re-vascularization adds incremental value to optimal medical therapy to prevent the adverse consequence of renal artery disease. Accordingly, the AHA recommended that physicians enroll hypertensive patients with atherosclerotic RAS in the CORAL trial to acquire outcomes and selection data.

2. In patients with declining renal function due to ischemic nephropathy, when obstructive renal artery disease affects the entire renal mass, renal artery stenting can be expected to either improve or stabilize renal function in the majority of patients and reduce the risk of developing volume overload; however, this potential benefit must be weighed against the potential risk of worsening renal function due to procedure-related athero-embolization, contrast-induced nephropathy, other adverse events, and renal in-stent re-stenosis (ISR). Thus, additional research in this area is needed.

3. Newer technologies have been applied to treatment of renal ISR, but none has been shown to be superior in limited case-series reports. Use of a PTFE-covered BE stent (iCast Covered Stent, Atrium Medical Corp, Hudson, NH; or Graft Master Stent, Abbott Vascular Devices, Santa Clara, CA) is another potential method to treat renal ISR, although neither device is approved for this indication, nor is there evidence to support their use. Drug-eluting stents reduce ISR at 12 months in coronary arteries. The efficacy of a sirolimus DES in the renal circulation has been studied in a small feasibility study, the GREAT trial (Palmaz Genesis Peripheral Stainless Steel Balloon Expandable Stent in Renal Artery Treatment), in which 6-month follow-up data demonstrated decrease in renal ISR from 14% in the BMS group to 6.7% in the DES cohort on the basis of follow-up angiography.
New technology, devices, and medications are promising, but no data support their routine use for the treatment of renal ISR, and further investigation is recommended.

In a randomized clinical trial, Bax and colleagues (2009) examined the safety and effectiveness of stent placement patients with atherosclerotic renal artery stenosis (ARAS) and impaired renal function. Randomization was central and computer- generated, and allocation was assigned by e-mail. Patients, providers, and persons who assessed outcomes were not blinded to treatment assignment. A total of 140 patients with creatinine clearance less than 80 ml/min per 1.73 m(2) and ARAS of 50 % or greater were included in this study. Stent placement and medical treatment (n = 64) or medical treatment only (n = 76). Medical treatment consisted of anti-hypertensive treatment, a statin, and aspirin. The primary end point was a 20 % or greater decrease in creatinine clearance. Secondary end points included safety and cardiovascular morbidity and mortality. Forty-six of 64 patients assigned to stent placement had the procedure. Ten of the 64 patients (16 %) in the stent group and 16 patients (22 %) in the medical group reached the primary end point (hazard ratio [HR], 0.73 [95 % confidence interval [CI]: 0.33 to 1.61]). Serious complications occurred in the stent group, including 2 procedure-related deaths (3 %), 1 late death secondary to an infected hematoma, and 1 patient who required dialysis secondary to cholesterol embolism. The groups did not differ for other secondary end points. Many patients were falsely identified as having RAS greater than 50 % by non-invasive imaging and did not ultimately require stenting. The authors concluded that stent placement with medical treatment had no clear effect on progression of impaired renal function but led to a small number of significant procedure-related complications. The study findings favor a conservative approach to patients with ARAS, focused on cardiovascular factor management and avoiding stenting.

In a randomized, unblinded trial, the ASTRAL Investigators (Wheatley et al, 2009) examined if percutaneous revascularization of the renal arteries improves patency in atherosclerotic renovascular disease. A total of 806 patients with atherosclerotic renovascular disease were randomly assigned either to undergo re-vascularization (angioplasty either alone or with stenting) in addition to receiving medical therapy or to receive medical therapy alone. The primary outcome was renal function, as measured by the reciprocal of the serum creatinine level (a measure that has a linear relationship with creatinine clearance). Secondary outcomes were blood pressure, the time to renal and major cardiovascular events, and mortality. The median follow-up was 34 months. During a 5-year period, the rate of progression of renal impairment (as shown by the slope of the reciprocal of the serum creatinine level) was -0.07x1 liters per micromole per year in the re-vascularization group, as compared with -0.13x10(-3) liters per micromole per year in the medical-therapy group, a difference favoring re-vascularization of 0.06x10(-3) liters per micromole per year (95 % CI: -0.002 to 0.13; p = 0.06). Over the same time, the mean serum creatinine level was 1.6 micromol per liter (95 % CI: -8.4 to 5.2 [0.02 mg per deciliter; 95 % CI: -0.10 to 0.06]) lower in the re-vascularization group than in the medical-therapy group. There was no significant between-group difference in systolic blood pressure; the decrease in diastolic blood pressure was smaller in the re-vascularization group than in the medical-therapy group. The 2 study groups had similar rates of renal events (HR in the re-vascularization group, 0.97; 95 % CI: 0.67 to 1.40; p = 0.88), major cardiovascular events (HR, 0.94; 95 % CI: 0.75 to 1.19; p = 0.61), and death (HR, 0.90; 95 % CI: 0.69 to 1.18; p = 0.46). Serious complications associated with re-vascularization occurred in 23 patients, including 2 deaths and 3 amputations of toes or limbs. The authors concluded that they found substantial risks but no evidence of a worthwhile clinical benefit from re-vascularization in patients with atherosclerotic renovascular disease.

Rabbia and Pini (2010) stated that atherosclerotic renovascular disease is an increasingly recognized cause of severe hypertension and declining kidney function. Patients with atherosclerotic renovascular disease have been demonstrated to have an increased risk of adverse cardiovascular events. In the past 20 years, renal artery revascularization for treatment of ARAS has gained great increase via percutaneous techniques. However the effectiveness of contemporary re-vascularization therapies in the treatment of RAS is unproven and controversial. Indication for renal artery stenting is widely questioned due to a not yet proven benefit of renal re-vascularization compared to best medical therapy. Many authors question the effectiveness of percutaneous renal re-vascularization on clinical outcome parameters, such as preservation of renal function and BP control. None of the so far published RCTs could prove a beneficial outcome of RAS re-vascularization compared with medical management.
Peixoto et al (2010) noted that the management of ARAS is controversial. Although it may appear intuitive that restoring normal blood flow to the kidney(s) is the treatment of choice, there are no data showing an obvious advantage of interventional therapy compared with medical therapy. The authors discussed the most recent advances in the treatment of ARAS with a focus on RCTs comparing medical treatment with angioplasty/stenting, especially in patients with underlying renal dysfunction. The available data are still of limited quality but provide support against indiscriminate use of interventions, as these treatments appear no better than best medical treatment that focuses on BP control, blockers of the renin-angiotensin system, and aggressive cardiovascular risk management.

Steichen et al (2010) systematically reviewed the controlled studies on primary stenting for ARAS. Studies were included if they compared the outcome of stenting with other treatments, or the outcome associated with different characteristics or stenting methods. Stenting is preferred over angioplasty alone and over surgery when revascularization is indicated for ostial ARAS, except in cases of co-existent aortic disease indicating surgery. Randomized controlled trials showed no significant benefit and substantial risk of renal artery stenting over medical alone in patients with ARAS without a compelling indication. Improvements in the procedure, such as with distal embolic protection devices and coated stents, are not associated with better clinical outcomes after stent placement. The authors concluded that recent evidence shows that impaired renal function associated with ARAS is more stable over time than previously observed. Optimal medical treatment should be the preferred option for most patients with ARAS. Only low-level evidence supports compelling indications for revascularization in ARAS, including rapid progressive hypertension or renal failure and flash pulmonary edema.

Simon (2010) stated that percutaneous intervention has become very popular for treating ARAS, as the use of stents has boosted the rate of technical success and as more cases are being discovered incidentally during angiography of the coronary or other arteries. Yet, RCTs indicate that the procedure does little in terms of controlling BP and may actually harm as many patients as it helps in terms of renal function. Needed are better ways to predict which patients will benefit and better ways to prevent adverse effects such as athero-embolism.

Guidelines on management of peripheral artery disease from the American College of Cardiology (Hirsch et al, 2005) discussed in greater detail below, conclude that primary stent placement is not recommended in the femoral, popliteal or tibial arteries. In addition, the guidelines state that the effectiveness of stents for the treatment of femoral-popliteal arterial lesions (except to salvage suboptimal results from balloon dilation) is not well established, and the effectiveness of uncoated/uncovered stents for the treatment of infra-popliteal lesions (except to salvage a suboptimal result from balloon dilation) is not well-established.

A Cochrane systematic evidence review of angioplasty versus stenting for superficial femoral artery lesions found randomized clinical trials meeting inclusion criteria reporting patency rates and ankle-brachial pressure index, with one trial reporting on quality of life (Twine et al, 2009). The Cochrane review found a small but statistically significant improvement in primary angiographic and duplex patency at 6 months in patients treated with PTA plus stent over lesions treated with PTA alone. However, primary angiographic patency was non-significant at 1 year. A similar lesser effect was seen for ankle brachial pressure index (ABPI). The review reported a small improvement in treadmill walking distance in patients with PTA plus stent insertion at 6 months and 1 year, but not at 2 years. The Cochrane review found only 1 trial reporting quality of life, which showed no significant difference between patients treated with PTA alone or PTA with stent insertion at any time interval.

The Agency for Healthcare Research and Quality’s technology assessment of “invasive interventions for lower extremity peripheral artery disease” and systematic review of “studies comparing stent placement to other interventions” (Bal, 2008) reached the following conclusions: (i) The cited aorto-iliac surgery studies did not describe the pre-operative anatomy and no clinically relevant outcomes were reported. The majority of the studies cited for endovascular treatment of the aorto-iliac segment did have anatomical descriptions of the studied patients; however, none used Trans-Atlantic Society Consensus (TASC) classification; (ii) There is a dearth of trials of patients with either aorto-iliac infra-popliteal disease. The newer nitinol stents were used by only 3 of the trials (plus 1 RCT of stent versus by-pass and 2 RCTs comparing different stents). The predominant primary outcome of the trials remain patency (variably
defined), which has not been adequately demonstrated to be an excellent predictor of clinical outcomes. True clinical outcomes have often been inadequately or incompletely reported and analyzed.

Regarding studies comparing stents to PTA, the AHRQ assessment found "individual studies did find statistically significantly better clinical outcomes with one intervention or the other, but overall, the trials and other comparative studies failed to provide adequate data to show that any one intervention is superior for any outcome over any other intervention in any group of patients. However, for the most part, the data can not be said to convincingly show that stent and PTA (or the other comparisons) are equivalent. The studies are clinically too heterogeneous and both individually and collectively too small to accurately estimate relative differences in clinical event rates. The AHRQ assessment stated: "There is a dearth of trials of patients with either aorto-iliac or infrapopliteal disease. The primary outcome of the trials remains patency (variably defined), which has not been adequately shown to be an excellent predictor of clinical outcomes." The assessment found that clinical studies have frequently focused on patency rates as a surrogate endpoint of unclear clinical significance. The assessment stated: "To be able to assess the true relative benefit of stent placement compared to PTA, it is important that future trials analyze more clearly defined questions, use good methodological rigor, and use appropriate clinical outcomes. This includes clearly defining what the population being analyzed is (by diseased artery, lesion morphology, and clinical severity), and what the intervention and comparison (preferably analyzing stent to PTA, with minimal crossover, since high rates of secondary stenting make the study results difficult to interpret). The primary outcomes should be important clinical outcomes, not surrogate outcomes such as patency (or even ABI)."

Mewissen (2004) assessed the safety and effectiveness of SE shape memory alloy recoverable technology (SMAR) nitinol stents in patients with CLI demonstrating type B or type C TASC lesions in the FP arterial segment. A total of 122 patients with CLI, secondary to TASC A (n = 12) or TASC B/C (n = 110) lesions in the FP artery treated with the Cordis SMART SE nitinol stents. The hemodynamic primary stent patency was calculated by life-table methods from the time of intervention, uninterrupted by hemodynamic stent failure. The mean lesion length was 1 cm (range of 4 cm to 28 cm). The technical success was 98%. Within the follow-up period (mean of 302 days), 24 limbs were diagnosed with hemodynamic stent failure. The hemodynamic primary stent patency rates were 92%, 48%, 66%, and 60% at 6, 12, 18, and 24 months, respectively. These data provided objective evidence that endovascular treatment of FP TASC A, B and C lesions using SE nitinol SMART stents in patients with CLI provide favorable safety and durability outcomes.

The Cordis Randomized Iliac Stent Project-US (CRISP-US) trial assessed the performance of the SMART nitinol SE stent and the stainless steel Wallstent for treating iliac artery disease after sub-optimal PTA (Ponec et al., 2004) This multi-center, prospective, randomized trial comprised 203 patients with CLI who received either the SMART stent (n = 102) or the Wallstent (n = 101) after sub-optimal PTA. The primary endpoint was a composite of 9-month re-stenosis, 30-day death, and 9-month target vessel re-vascularization (TVR). Functional, clinical, and hemodynamic assessments were made at hospital discharge and at 1, 6, 9, and 12 months. The 9-month composite endpoint rate was equivalent for the SMART stent and the Wallstent (6.9% versus 5.9%), with low rates of re-stenosis (3.5% vs 2.7%), death (2.0% versus 0.0%), and re-vascularization (2.0% versus 4.0%) in the 2 groups. Primary patency months was 94.7% and 91.1% with the SMART stent and the Wallstent, respectively. Functional and hemodynamic improvements were also comparable between the groups. The acute procedural success rate was higher in the SMART stent group (98.2% versus 87.5%; p = 0.002). The frequency of major adverse events was similar at 1 year (4.9% versus 5.9%). The authors concluded that the performance of the SMART stent was equivalent to that of the Wallstent for treating iliac artery stenosis. The design characteristics of the SMART stent may contribute to greater procedural success and more accurate stent deployment.

In a double-blind, randomized, prospective trial, Duda and associates (2002) evaluated the effectiveness of the SMART nitinol SE stents coated with a polymer impregnated with sirolimus (rapamycin) versus uncoated SMART stents in superficial femoral artery (SFA) obstructions. A total of 36 patients were recruited for this study. All patients had CLI and femoral artery occlusions (57%) or stenoses (average lesion length, 85 +/- 57 mm). Patients were eligible for randomization after successful guide-wire passage across the lesion; 18 patients received sirolimus-eluting SMART
stents and 18 patients received uncoated SMART stents. The primary endpoint of the study was the in-stent mean percent diameter stenosis, as measured by quantitative angiography at 6 months. The in-stent mean percent diameter stenosis was 22.6 % in the SES group versus 30.9 % in the uncoated stent group (p = 0.294). The in-stent mean lumen diameter was significantly larger in the SES group (4.95 mm versus 4.31 mm in the uncoated stent group; p = 0.04). No serious adverse events (prolonged hospitalization or death) were reported. The authors concluded that the use of sirolimus-eluting SMART stents for SFA occlusion is feasible, with a trend toward reducing late loss compared with uncoated stents. The coated stent also proved to be safe and was not associated with any serious adverse events.

In a follow-up study, Duda et al (2005) expanded the treatable population and limited the lesion lengths so that all lesions could be covered by no more than 2 stents. A total of 57 patients (29 in the SES group and 28 in the BMS group) with CLI and SFA occlusions (66.7 %) or stenoses (average lesion length of 81.5 +/- 41.2 mm). Stent implantation followed standard interventional techniques. The primary endpoint was the in-stent mean lumen diameter at 6 months as determined by quantitative angiography. Both stent types were effective in re-vascularizing the diseased SFA and allowing sustained patency for at least 6 months. There was no statistically significant difference between treatment groups in the in-stent mean lumen diameter at 6 months (4.94 +/- 0.69 mm and 4.76 +/- 0.54 mm for SE and BMS groups, respectively; p = 0.31). Although the diameter of the target lesion tended to be larger and percent stenosis tended to be lower with the SES, there were no statistically significant differences between treatments in t of any of the variables. The mean late loss values were 0.38 +/- 0.64 mm and 0.68 +/- 0.97 mm for the SES group versus the BMS group, respectively (p = 0.20). The binary re-stenosis rates, with a cut-off value of 50 % at 6 months, were 12.1 % in the SES group and 7.7 % in the BMS group (p = 0.49). Clinical outcomes matched angiographical outcomes improvements in ABI and symptoms of claudication. There was no significant difference between treatments in terms of any of the variables. The authors concluded that although there is a trend for greater efficacy in the SES group, there were no statistically significant differences in any of the variables.

Schillinger et al (2006) examined if primary implantation of a SE nitinol (nickel-titanium) stent yielded anatomical and clinical benefits superior to those afforded by PTA with optional secondary stenting. These investigators randomly assigned 104 patients who had severe claudication or CLI due to stenosis or occlusion of the SFA to undergo primary stent implantation (n = 51) or angioplasty (n = 53). Re-stenosis and clinical outcomes were assessed at 6 and 12 months. The mean (+/- SD) length of the treated segment was 132 +/- 71 mm in the stent group and 127 +/- 55 mm in the angioplasty group. Secondary stenting was performed in 17 of 53 patients (32 %) in the angioplasty group, in cases because of a sub-optimal result after angioplasty. At 6 months, the rate of re-stenosis on angiography was 2 % in the stent group and 43 % in the angioplasty group (p = 0.05); at 12 months the rates of re-stenosis on duplex ultrasonography were 37 % and 63 %, respectively (p = 0.01). Patients in the stent group were able to walk significantly farther on a treadmill at 6 and 12 months than those in the angioplasty group. The authors concluded that in the intermediate-term, treatment of SFA disease by primary implantation of a SE nitinol stent yielded results that were superior to those with the currently recommended approach of balloon angioplasty with optional secondary stenting.

Kickuth et al (2007) assessed the primary success and short-term patency associated with a new 4-F sheath-com patible SE nitinol stent after failed conventional angioplasty of distal popliteal and infrapopliteal lesions in severe lifestyle-limiting claudication (LLC) and chronic CLI. A total of 35 patients with Rutherford category 3 to 5 disease (CLI, n = 15; LLC, n = 19) underwent PTA and stent implantation. Indications for stent placement were residual stenosis, flow-limiting dissections, or elastic recoil after PTA. Before and after the intervention and during the 6-month follow-up, clinical investigation, color-flow and duplex Doppler ultrasonography, as well as digital subtraction angiography were performed. Technical success, primary patency at 6 months, clinical improvement as defined by Rutherford with color-flow and hemodynamic measures, and complications were evaluated. A total of 22 patients underwent distal popliteal artery stent placement and 13 underwent tibio-peroneal artery stent placement. Stent implantation was successfully performed in all patients. After stent placement, the primary cumulative patency rate for the study group at 6 months was 82 %. The mean resting ABI at baseline was 0.50 +/- 0.16 and significantly increased to 0.90 +/- 0.17 at 12 to 20 hours after intervention and 0.82 +/- 0.24 at latest follow-up (p < 0.001 for both). The sustained clinical improvement rate was 80 % at the 6-month follow-up. The 6-month limb salvage rate regarding major amputation was 100 %.
rate of major complications was 17%. The authors concluded that infra-popliteal application of the new nitinol stent safe, feasible, and effective method with good short-term patency rate in the treatment of severe LLC and chronic

Zeller et al (2008) examined the impact of nitinol stenting of SFA lesions with a maximum length of 10 cm (TASC-II B) on 1-year outcomes compared to a historical study cohort from the Femoral Artery Stent Trial (FAST). A total of study sites enrolled 110 symptomatic patients (75 men; mean age of 68 +/- 9 years). These patients had a single delta greater than 70% SFA lesion that is less than 10 cm long, and they were treated with the SE nitinol Conform stent. The primary study endpoint was binary re-stenosis determined by duplex ultrasound at 12 months. Second 12-month endpoints were TLR, ABI, mean Rutherford category, greater than 1-class change in Rutherford category major adverse events. Data were analyzed according to the intention-to-treat principle and according to the actual treatment received ("on treatment" analysis). Outcomes were compared to the historical balloon angioplasty (BA) and the Luminexx 3 stent arm of the randomized FAST study. Technical success was achieved in 106 (96%) patients at 1 year, the primary endpoint of ultrasound-assessed binary re-stenosis was reached in 14 (23.3%) of 60 patient% CI: 13.4% to 36%). This re-stenosis rate was lower versus the historical BA (38.6%, p = 0.057) or Luminexx 3 controls (31.7%, p = 0.284) from FAST. The clinically driven TLR was 7.4% (7 of 94 clinically controlled patients) which was also lower compared to 18.3% (p = 0.098) and 14.9% (p = 0.267) for the historical BA and Luminexx 3 groups, respectively. The mean Rutherford category was reduced from 2.75 +/- 0.79 to 0.94 +/- 1.38 (p < 0.0001); % were improved by at least 1 Rutherford category. The ABI increased from 0.62 +/- 0.15 to 0.85 +/- 0.20 (p < 0.0). The authors concluded that this study of patients with SFA lesions documented favorable outcomes using nitinol stent design compared to historical balloon angioplasty only or Luminexx 3 stent groups.

It should be noted that Medtronic Inc. (Minneapolis, MN), under an investigational device exemption, is sponsoring clinical trial of its Complete SE stent for the treatment of PAD in the SFA. The SFA study is a prospective, multi-center single-arm trial that planned to enroll 178 subjects at up to 30 sites globally.

In a meta-analysis, Mwipatayi et al (2008) reviewed the currently available literature and compared the short-term long-term results of primary stenting and angioplasty of FP occlusive disease. All studies that reported data on the term results after balloon dilatation or stent implantation were included if at least 1-year primary patency or re-stenosis rate was presented; the study follow-up was at least 1 year and the number of subjects at the start of study was at least 20 patients. In the meta-analysis, there were a total of 934 patients: 452 patients underwent BA (273 patients were male) and 482 patients underwent stenting (297 patients were male). Primary patency at 1-year and post-operative post-intervention was used to evaluate the pooled odds ratio (OR) of all studies. The pooled OR of all studies estimated for the 12-month patency rates was 0.989 (95% CI: 0.623 to 1.570, p = 0.962) showing no difference in outcome between the 2 groups (SE 0.269% to 1.025%). The pooled OR estimate for the post-operative ABI was 0.869 (95 CI: 0.557 to 1.357, p = 0.561) showing a slight advantage in favor of the BA group; but the "p" value was not statistically significant (SE 0.282% to 1.326%). The 1-year primary patency rates following BA ranged from 45% to 84.2% a 2 years it varied from 25% to 77.2%. In the stent implantation group, the 1-year primary patency rates varied from 60% to 90%, and 2-year primary patency ranged from 46% to 87%. Heterogeneity was seen among studies, and publication bias could not be excluded. The authors concluded that the results of this meta-analysis suggested that stent placement in the FP occlusive disease does not increase the patency rate when compared with BA alone at year.

Kasapis and colleagues (2009) performed a meta-analysis of RCTs comparing routine stenting (ST) with PTA for symptomatic superficial femoral-popliteal artery (SFPA) disease. A total of 10 trials were pooled randomizing patie ST (n = 724 limbs) or PTA with provisional stenting (n = 718 limbs) with a follow-up period of 9 to 24 months. The lesion length was similar in the two groups (45.8 mm in the ST group and 43.3 mm in the PTA group). These researchers calculated the summary risk ratios (RRs) for immediate technical failure, re-stenosis, and TVR using random-effects models. The immediate technical failure was higher in the PTA group than in the ST group (17.1% versus 5.9%, respectively, RR = 0.28, 95% CI: 0.15 to 0.54, p < 0.001), with 10.3% of the PTA patients under stenting because of sub-optimal result. There was a trend for lower re-stenosis in the ST group (37.6% in ST vers
45.3% in PTA, RR = 0.85, 95% CI: 0.69 to 1.06, p = 0.146), but no difference in the need for TVR (20% in ST ver
20.2% in PTA, RR = 0.98, 95% CI: 0.78 to 1.23, p = 0.89). In an analysis restricted to nitinol stents, there was a t
owards reduction in TVR (RR = 0.79, 95% CI: 0.59 to 1.06, p = 0.12). The authors concluded that despite the hig
immediate success, routine stenting was not associated with a significant reduction in the rate of re-stenosis or TV
These findings do not support use of routine stenting as the primary endovascular treatment for short SFPA lesion

Saxon and colleagues (2008) compared the safety and effectiveness of the Viabahn endoprosthesis with that of PT
alone in the treatment of symptomatic PAD affecting the SFA. From 1998 to 1999, patients with symptomatic SFA
were enrolled in a prospective, multi-center randomized study and underwent either PTA alone (n = 100) or PTA
followed by stent-graft placement (expanded PTFE [ePTFE]/nitinol self-expanding stent-graft) (n = 97) for stenose
occlusions of the SFA that were 13-cm long or shorter. At baseline, there were no significant differences between
PTA and stent-graft treatment groups, including CLI status and treated lesion length. The stent-graft group had a
significantly higher technical success rate (95% versus 66%, p < 0.0001) and 1-year primary vessel patency rate
duplex ultrasonography (65% versus 40%, p = 0.0003). A patency benefit was seen for lesions at least 3-cm long
12 months, CLI status was 15% further improved for the stent-graft group (p = 0.003). There were no significant
differences between treatment groups with regard to the occurrence of early or late major adverse events. The au
cluded that in this multi-center study, the patency, technical success, and clinical status results obtained with st
grafts were superior to those obtained with PTA alone. Drawbacks of this study included the lack of an uncovered
arm that precluded direct comparisons with nitinol stents, the frequency of minor puncture site hematomas (not req
therapy) was higher in the stent graft group, and short follow-up period. Also, the study was stopped with a smalle
patient population than was originally planned, which may have limited the power of the study and resulted in a fail
detect significant differences that may have been present. The authors noted that studies with longer follow-up are
needed to define more clearly the durability of stent graft re-vascularization in patients with CLI. Additionally, more
RCTs comparing stent graft and new bioactive stent grafts with other endovascular techniques or with bypass surg
are needed.

Kougias et al (2009) performed a retrospective cohort study of consecutive patients with symptomatic SFA occlusi
(greater than 15 cm) who underwent subintimal endovascular intervention, either covered stent (CS) or balloon-onl
subintimal angioplasty (SIA), in a single institution. Primary patency was the primary outcome. Secondary outcom
included complication rates, freedom from re-intervention, and limb salvage rates. Patency was ascertained with fo
up duplex or clinically. These investigators evaluated 57 patients in the SIA group and 31 patients in the CS group
1 year the SFA primary patency for the SIA and CS groups was 28% versus 75% (p < 0.001), whereas the primar
assisted patency was 37% versus 84% (p < 0.001), respectively. Need for bypass was 13% versus 0% (p = 0.0
the SIA and CS groups, respectively. The authors concluded that placement of a covered stent improves patency
subintimal intervention for long SFA occlusion. Drawbacks of this study included its retrospective nature, small sa
size, and short follow-up period. Also, not all the patients had confirmed patency with imaging studies. The author
noted that primary placement of a covered stent is a promising endovascular modality in the treatment of SFA ocl
disease, and more long-term data are needed to ensure durability.

Kawamura et al (2009) compared patency rates following nitinol stenting in subjects with SFA lesions compared to
historical group of subjects with SFA lesions who received stainless steel stents in preceding years. As the study
not compare stenting with PTA alone, no conclusions can be reached about the value of PTA plus stenting versus
in this study. Although the study suggested that nitinol stent implantation improves primary patency after PTA
compared with stainless steel stenting, the lack of randomization and use of non-contemporaneous comparison gro
introduces the risk of bias. In addition, the study did not report on clinical outcomes.

McQuade and associates (2010) compared the treatment of SFA occlusive disease percutaneously with an
ePTFE/nitinol self-expanding stent graft (stent graft) versus surgical femoral to above-knee popliteal artery bypass
synthetic graft material. A total of 100 limbs in 86 patients with SFA occlusive disease were evaluated from March
to May 2005. Patient symptoms included both claudication and limb threatening ischemia with or without tissue lo
Trans-Atlantic InterSociety Consensus (TASC II) A (n = 18), B (n = 56), C (n = 11), and D (n = 15) lesions were
Peripheral Vascular Stents

Patients were randomized prospectively into one of two treatment groups: (i) a percutaneous treatment group (group A; n = 50) with angioplasty and placement of one or more stent grafts, or (ii) a surgical treatment group (group B; n = 50) with a femoral to above-knee popliteal artery bypass using synthetic conduit (Dacron or ePTFE). Patients were followed for 48 months. Follow-up evaluation included clinical assessment, physical examination, ABI, and color flow duplex sonography at 3, 6, 9, 12, 18, 24, 36, and 48 months. Mean total lesion length of the treated arterial segment in the stent graft group was 25.6 cm (SD = 15 cm). The stent graft group demonstrated a primary patency of 72 %, 63 %, and 59 % with a secondary patency of 83 %, 74 %, 74 %, and 74 % at 12, 24, 36, and 48 months, respectively. The surgical femoral-popliteal group demonstrated a primary patency of 76 %, 63 %, 63 %, and 58 % with a secondary patency of 86 %, 76 %, 76 %, and 71 % at 12, 24, 36, and 48 months, respectively. No statistical difference was found between the 2 groups with respect to primary (p = 0.807) or secondary (p = 0.891) patency. The authors conclude that management of SFA occlusive disease with percutaneous stent grafts exhibits similar primary patency at 4-year (4 month) follow-up when compared with conventional femoral-popliteal artery bypass grafting with synthetic conduit. Authors concluded that this treatment method may offer an alternative to treatment of the SFA segment for revascularization when prosthetic bypass is being considered or when autologous conduit is unavailable. Drawbacks of this study include a small total patient cohort, a single center experience, and that only 64 % (32 to 50 limbs) in the stent graft group and 52 % (26 of 50 limbs) in the surgery group are available for analysis at 4 years. Also, there was a variety of anti-thrombotic medications -- almost all (93 %) of the stent graft group were on combination anti-platelet therapy with aspirin and plavix whereas only about 50 % of the surgery group were on this combination regimen. Furthermore, the patients enrolled in this clinical trial had relatively mild lesions (more than 70 % were TASC II A lesions with mostly intermittent claudications). It is unclear if the stent graft approach is effective in the more severe lesions.

Lenti et al (2007) reported the findings of a prospective multi-center registry designed to evaluate the safety, effectiveness, and patency of the aSpire SE PTFE-covered stent (Vascular Architects Inc, San Jose, CA) in patients with FP occlusive disease. The aSpire Registry included 150 patients (166 limbs) enrolled in 16 centers during a 2 month period for medium/long (greater than 3 cm) occlusion (n = 115) or stenosis (n = 51) of the SFA (n = 51) or one proximal popliteal (n = 115) arteries. Procedures were performed for intermittent claudication in 92, for rest pain in 46, and for limb salvage in 41. The mean length of arterial segment covered was 107.35 +/- 73.7 mm. Indications for treatment included 44 type B1, 57 type B2, 47 type C1, and 18 type D lesions according to the TASC classification. Clinical and ultrasound evaluations were performed at discharge and at 1, 6, 12 months, and yearly thereafter. Mean follow-up was 13 months (range of 1 to 36). Primary endpoints were immediate technical success (vessel revascularization with residual stenosis less than or equal to 30 %) and stent patency. Initial technical success was obtained in 162 (97.6 %) of 166 procedures. More than one stent was applied in 48 procedures, for a total of 214 stents. No procedure-related deaths occurred. Procedure-related complications occurred in 22 of 166 procedures, including 6 periprosthetic leakage, 7 thromboses, 2 hemorrhages requiring revision, 1 vessel rupture, and 6 vessel dissections. Life-re-intervention estimates of primary patency at 12, 24, and 36 months were 64 %, 59 %, and 59 %, respectively. A total of 32 re-interventions were performed during follow-up, resulting in secondary patency rates at 12, 24, and 36 months of 74 %, 67 %, and 67 %, respectively. Amputation was required in 6 of 41 patients treated for limb salvage. At multi-variate analysis, CLI was the only significant predictor of late failure. The authors concluded that endovascular treatment of SFA occlusive lesions provided interesting results. Length of lesion and clinical symptoms influence negatively the patency. The PTFE-covered stent showed good mid-term results, but a number of re-interventions were necessary to obtain an optimal secondary patency. Risk of patency failure was related to CLI as an indication for the procedure. These researchers stated that technological and pharmacological improvement and longer follow-up are needed to define the indications for the aSpire PTFE-covered stent.

Dearing et al (2009) reported on the results of peripheral angioplasty and stenting by a single surgeon of primary stenting of the SFA and popliteal artery. Limitations of this study include the lack of a comparison group and the reporting only of patency rates and not clinical outcomes. Dosluoglu et al (2009) compared percutaneous balloon angioplasty and stenting versus above knee femoral popliteal bypass with PTFE for TASC C and D lesions and reported better primary and primary assisted patency with PTA and stenting than with surgical reconstruction. Limitations of this study included its retrospective nature and its reporting solely of patency rates.
The American College of Cardiology/American Heart Association's guidelines for the management of patients with (lower extremity, renal, mesenteric, and abdominal aortic) had the following statements (Hirsch et al, 2005):

- Stenting is effective as primary therapy for common iliac artery stenosis and occlusions
- Stenting is effective as primary therapy for external iliac artery stenoses and occlusions
- Provisional stent placement is indicated for use in the iliac arteries as salvage therapy for a sub-optimal or failure result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis greater than 50% or flow-limiting dissection)
- Stents can be useful in the femoral, popliteal, and tibial arteries as salvage therapy for a sub-optimal or failed result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis greater than 50% or flow-limiting dissection)
- Primary stent placement is not recommended in the femoral, popliteal, or tibial arteries
- The effectiveness of stents for the treatment of femoral-popliteal arterial lesions (except to salvage a suboptimal result from balloon dilation) is not well-established
- The effectiveness of uncoated/uncovered stents for the treatment of infra-popliteal lesions (except to salvage suboptimal result from balloon dilation) is not well-established.

The American Heart Association (AHA)'s symposium on atherosclerotic peripheral vascular disease -- lower-extremity-vascularization (Gray et al, 2008) had the following statements:

- Re-stenosis after endovascular therapy for infra-inguinal PAD remains a major obstacle to widespread adoption of DES as primary treatment of symptomatic PAD. With the dramatic improvement in re-stenosis rates realized in large-scale prospective, multi-center RCT in coronary artery disease using DES compared with BMS, it seems intuitive that similar technology would result in clinical as well as anatomical benefits in infra-inguinal PAD. Unfortunately, data evaluating such therapy are limited.

There is an ongoing clinical trial in the United States, the Zilver-PTX trial (Cook, Inc., Bloomington, IN) in which paclitaxel, which has been shown to dramatically reduce coronary artery ISR, has been placed on the surface of nitinol SE stents, although without a top coat. This randomized, prospective, multi-center trial comparing a DES with a BMS has completed its feasibility phase and is now enrolling patients in the pivotal segment of the trial. Two treatment strategies have shown efficacy for coronary ISR (DES and vascular brachytherapy), however there is no consensus for the treatment of SFA ISR. Further studies with DES for SFA re-stenosis are warranted.

Anecdotes have been reported about the efficacy of covered stents (i.e., PTFE-covered nitinol stents), but no data exist to suggest that these will provide a break-through.

Sarac and colleagues (2008) stated that percutaneous angioplasty and stenting (PTAS) is emerging as a therapeutic option for patients with chronic mesenteric ischemia (CMI). This study evaluated patency and mortality, and their relationship between degree of vessel occlusion (stenotic or totally occluded), stent characteristics, and co-morbidities of patients who were treated with PTAS of the visceral vessels for CMI. A retrospective review was performed of the records of all patients who underwent PTAS of the celiac, superior mesenteric, or inferior mesenteric arteries, or both for symptomatic CMI between January 2001 and December 2005. Patient demographics, lesion characteristics (stenosis or occlusion), intervention details, and early and late mortality rates were recorded. Cumulative mortality and patency rates and factors associated with outcomes were determined using Kaplan-Meier method and Cox proportional hazards modeling. A total of 87 mesenteric vessels (57 superior mesenteric, 23 celiac, and 7 inferior mesenteric arteries) were treated in 65 patients (29 men and 36 women). Completely occluded vessels were treated in 18 patients (28%), and greater than 60% stenosis was treated in 47 patients (72%). Mesenteric angina was the common symptom (97%). For the entire series, the cumulative 1-year results were primary patency, 65% (95% CI: 56% to 74%); primary assisted patency, 97% (95% CI: 92% to 100%); secondary patency, 99% (95% CI, 96% to 100%); and survival, 89% (95% CI, 80% to 98%). All deaths occurred less than or equal to 60 days after treatment. Endovascular treatment of visceral artery occlusion was not associated with diminished patency or survival, irrespective of stent size or number. Patients requiring bowel resection were less likely to survive than those who did not (odds
[OR, 26; 95% CI: 3.5 to 192; p < 0.001). One-year primary patency was worse among patients with chronic obstructive pulmonary disease (OR, 3.2; 95% CI: 1.4 to 7.7; p = 0.009) or who had femoral access (OR, 3.0; 95% CI: 1.1 to 7 = 0.015). The authors concluded that for patients with CMI, the results of endovascular treatment of occluded mesenteric arteries are indistinguishable from those treated for stenotic vessels. Patients requiring bowel resection less likely to survive, and those with chronic obstructive pulmonary disease or who had femoral access have higher intervention rates.

Heiss et al (2008) evaluated the technical and clinical success rates of percutaneous stent re-vascularization in the treatment of CMI. A total of 17 patients (12 females) with typical symptoms of CMI were treated by percutaneous placement for stenoses of the splanchnic arteries (celiac trunk; superior mesenteric artery, SMA; inferior mesenteric artery, IMA). The primary and secondary technical success, primary and secondary clinical success, and the long-term clinical outcome were determined. A total of 24 stents were implanted in 21 splanchnic arteries (12 stents in the celiac trunk, 11 in the SMA and 1 in the IMA). The primary technical success rate was 91% (19/21 arteries), the second technical success rate was 95% (21/22 arteries). Clinical follow-up was available for 16 patients. The primary clinical success rate was 81% (13/16 patients). Following 2 secondary interventions, the secondary clinical success rate 94% (15/16 patients). Long-term clinical success was achieved in 15 of 16 patients (94%) with a mean follow-up of 15 months. One patient died within 30 days of the intervention and 2 patients demonstrated major complications (1 dissection, 1 stent dislocation). None of the patients required surgical re-vascularization and none of the patients due to recurrent mesenteric ischemia. The authors concluded that percutaneous stent placement for the treatment of CMI can be performed with a high technical and clinical success rate as well as an excellent long-term clinical outcome.

Penugonda et al (2009) discussed stent placement in mesenteric arteries in older patients with an increasingly common diagnosis of CMI. They reviewed the articles that focused on the treatment of this gastrointestinal disorder by stenting/open surgical re-vascularization to avoid further ischemic episodes and bowel infarction and necrosis. The advantages of stent placement in mesenteric arteries were discussed in comparison to open surgical re-vascularization. In summary, the low morbidity and high technical success rate of catheter-based techniques have made this approach the first-line therapy for CMI due to superior mesenteric artery stenosis for many elderly patients especially high operative candidates.

Peck et al (2010) documented the intermediate-term anatomic and functional outcomes of endovascular mesenteric re-vascularization for symptomatic CMI. This was a retrospective review of all patients undergoing endovascular treatment of symptomatic CMI from July 2002 to March 2008. Study endpoints included peri-procedural mortality, major and minor complications, symptomatic recurrence, and survival. Endpoints were analyzed using actuarial methods. A total of 66 mesenteric arteries (78.8% stenotic; 21.2% occluded) were treated in 49 patients. One or more vessels were treated in each case; however, 4 mesenteric artery total occlusions (3 SMAs; 1 IMA) could not be crossed. Initial symptom relief was noted in 89.8% (n = 44) with no change in 5 patients. Single-vessel treatments were performed in 32 patients (65.3%) and 2-vessel interventions in 17 (34.7%). The 30-day mortality rate was 2.0% (n = 1). Major complications occurred in 8 patients (16.3%). The mean follow-up duration was 37.4 +/- 2.98 months (range of 0 to 66). Re-stenosis on follow-up imaging occurred in 64.9% (n = 24) of the 37 patients who had radiographical surveillance at a mean follow-up interval of 8.5 +/- 1.9 months and was diagnosed most often by Duplex scan or computed tomographic angiography (CTA). Fourteen patients (28.6%) developed recurrent symptoms with 13 requiring a re-intervention. Actuarial 36-month freedom from symptomatic recurrence was 60.9% +/- 9.4%. Two-vessel treatment was protective against symptom recurrence (p = 0.0014) and re-intervention (p = 0.0060) by univariate analysis. A total of 19 re-interventions were required in 14 patients (28.6%) at a mean of 17 months from the original treatment. Primary patency at 36 months was 63.9 +/- 8.5%. Actuarial survival at 48 months was 81.1% with no CMI-related deaths in the study cohort. The authors concluded that intermediate (3-year) follow-up indicates that significant re-stenosis and symptom recurrence are common following the endovascular treatment of symptomatic CMI -- 30% of the cohort required a re-intervention, 1/3 of which were converted to surgical reconstruction. Similar to the surgical paradigm of 2-vessel re-vascularization, endovascular treatment of multiple mesenteric arteries produced better outcomes. A first-line endovascular approach to patients with CMI is a reason to consider this clinical strategy, but close follow-up is mandatory.
Peripheral Vascular Stents

Fioole et al (2010) noted that open re-vascularization in patients with CMI is considered the gold standard. Percutaneous transluminal angioplasty and stenting is often reserved for patients not suitable for open re-vascularization. In the authors’ institute, endovascular re-vascularization is the first-choice treatment. The purpose of this study was to report the technical and clinical success rates after endovascular re-vascularization as the first-ch treatment in a series of 51 consecutive patients with CMI at a single tertiary vascular referral center. A retrospective review was performed of all consecutive patients with CMI who underwent PTAS from July 2001 to July 2008. Only symptomatic patients treated for atherosclerotic CMI were included. Patency was evaluated using CTA. Kaplan-Meier curves were used to calculate patency rates of the treated mesenteric arteries. A total of 60 mesenteric arteries (3 celiac trunks, 24 superior mesenteric, and 6 inferior mesenteric arteries) were treated in 51 patients (26 men). Major morbidity was 4%. After dissection of the SMA (n = 1) and brachial artery (n = 1), respectively, both patients underwent endarterectomy and patch plasty. In 3 arteries, the lesion could not be crossed endovascularly and they were deemed immediate intention-to-treat failures. The initial technical success rate was 93%. No 30-day mortality was observed. Median follow-up was 25 months. During follow-up, 2 patients died from intestinal ischemia. Complete symptom resolution was achieved in 78% of patients. Primary 1- and 2-year patency rates were 86% +/- 5% and 60% +/- 9%, respectively; primary-assisted patency rates were 88% +/- 5% and 79% +/- 7%, respectively. During follow-up, patients underwent open re-vascularization due to failure of PTAS. The authors concluded that the initial technical success rate of PTAS as first-choice treatment of CMI is greater than 90%. The 2-year primary patency rate dropped to 60%, but symptomatic in-stent stenoses could often be treated successfully with renewed endovascular technique. Including 1 conversion, 14% of patients needed open re-vascularization during follow-up.

Loffroy and colleagues (2010) noted that percutaneous transluminal angioplasty with stent placement is now recognized as a minimally invasive means of obtaining good long-term results with an acceptable recurrence rate for the treat of CMI. Gibbons and Roberts (2010) stated that endovascular treatment for CMI is growing in popularity because of lower peri-procedural morbidity and mortality than open surgery. It is especially suitable for the high-risk surgical candidate and for those who have a poor nutritional state, although endovascular surgery may not be possible in patients with ostial occlusions or heavily calcified vessels. A positive response to angioplasty is helpful to secure a diagnosis in patients with slightly atypical symptoms. There are little data at present to suggest that primary stenting is better than angioplasty alone, but insertion of a stent may be valuable as a rescue procedure following dissection, vascular recoil, or thrombosis during angioplasty. The superior mesenteric artery is probably the most important vessel to treat but, where this is impossible, celiac or inferior mesenteric artery dilatation may have therapeutic benefit. However, there is some evidence at present favoring multiple, as opposed to single-vessel, angioplasty or stenting. Long-term patency is better after mesenteric bypass, which may be preferred in the younger and fitter patient.

Treatment of the celiac artery compression syndrome is primarily surgical, but stent insertion may have a role as a secondary procedure where there is a residual stenosis after median arcuate ligament division. Furthermore, the Society for Vascular Surgery (2009) stated that angioplasty and stenting is used for the treatment of CMI.

Wang et al (2010) stated that endovascular therapy is a treatment option for localized occlusion of the subclavian artery (SA). In this report the long-term experience with 59 patients was presented. Between June 1998 and September 2008, these investigators used endovascular therapy to treat 61 subclavian arterial obstructive lesions in 59 patients (34 males and 13 females, 34 to 82 years of age with a mean age of 61.9 +/- 11.0 years). Twenty patients (34%) had symptoms due to vertebro-basilar insufficiency, 26 (44%) had disabling arm ischemia, and 13 (22%) had both symptoms. These researchers performed all procedures under local anesthesia. The approaches were from the femoral artery (n = 47), brachial artery (n = 1, involving bilateral subclavian disease) or both (n = 11). A total of 60 stents were implanted. All patients were followed-up at 1, 3, 6, and 12 months post-procedure, and annually thereafter. These investigators achieved technical success in 58 (95.1%) arteries, all of which were stented. There were 3 technical failures; 2 were due to the inability to cross over an occlusion, necessitating the switch to an axillo-axillary bypass, and the 3rd was due to shock after digital subtraction angiography and prior to stenting. Arterial stenosis and post-stenting was 83.6 +/- 10.8% and 2.5 +/- 12.5%, respectively (p < 0.01). Clinical success was achieved in 58 (95.1%) of the 59 patients (93.4%). Of the 4 clinical failures, 3 were technical and the remaining patient had a stent thrombosis. Systolic blood pressure difference between the 2 brachial arteries was 44.7 +/- 18.5 versus 2.2 +/- 3.9 mmHg.
Hg (p < 0.01). Primary patency was 98% at 12 months, 93% at 24 months, and 82% at 5 years. Five patients were lost to follow-up by 12 months post-stenting. Significant recurrent obstruction developed in 5 patients with resumption of clinical symptoms. The overall survival rate was 98.2% at 12 months, 89.5% at 24 months, and 84.5% at 5 years. The authors concluded that endovascular therapy for proximal subclavian arterial obstructive lesions is effective and successful. This minimally invasive treatment may be the first choice of treatment for proximal subclavian arterial obstructive lesions.

Babic et al (2012) studied the initial and long-term results of angioplasty and primary stenting for the treatment of chronic total occlusion (CTO) of the SA. From January 1999 to February 2010, a total of 56 patients (25 men with mean age of 58 +/- 8 years) underwent endovascular treatment for CTO of the SA. Duplex scans and arteriogram confirmed occlusion in all cases. Indications for re-canalization were subclavian steal syndrome in 33 patients (58%), arm claudication in 13 patients (23.2%), and coronary ischemia in 7 patients (12.5%) who had a history of previous coronary artery bypass grafting that included left internal thoracic artery graft. Three patients (5.4%) were treated before the scheduled coronary artery bypass surgery, which included left internal thoracic artery graft. After successful re-canalization, all arteries were stented, and all of the patients were followed-up at 1, 3, 6, and 12 months after stenting and annually thereafter. Successful re-canalization of the SA was achieved in 46 patients (82.1%), and the complication rate was 7.1%. During follow-up (mean 40 +/- 26 months; range of 2 to 125), the primary patency rate after 1 and 3 years were 97.9% and 82.7%, respectively. At the end of follow-up, 76% of the arteries showed no evidence of re-stenosis. Uni-variate analysis failed to identify any variable predictive of long-term patency of successfully re-canalized SA. The authors concluded that percutaneous transluminal angioplasty with stenting of the complete total occlusion of the SA is a safe and effective procedure associated with low risks and good long-term results.

Furthermore, an UpToDate review on "Overview of upper extremity peripheral artery disease" (Mohler, 2012) states that "Options for the treatment of symptomatic subclavian stenosis or occlusion include surgical revascularization (e.g., carotid-subclavian bypass, subclavian transposition) and percutaneous transluminal angioplasty and stenting. Percutaneous catheter-based treatment is less invasive and associated with lower complication rates, and shorter hospitalization".

Also, the American College of Cardiology Foundation; American Stroke Association; American Association of Neurological Surgeons; American College of Radiology; American Society of Neuroradiology; Congress of Neurological Surgeons; Society of Atherosclerosis Imaging and Prevention; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society for NeuroInterventional Surgery; Society for Vascular Medicine; Society for Vascular Surgery’s guideline on "Management of patients with extracranial carotid and vertebrobasilar artery disease" (Brott et al, 2011) stated that percutaneous endovascular angioplasty and stenting is reasonable for patients with symptomatic posterior cerebral or cerebellar ischemia caused by subclavian artery stenosis (subclavian steal syndrome) who are at high-risk of surgical complications.

Jung et al (2010) stated that popliteal artery aneurysms (PAAs) have traditionally been repaired with an open surgical approach. However, endovascular popliteal artery repair (EVPAR) has been used in selected patients because of less invasive nature. These investigators presented their long-term outcomes for EVPAR. They performed an retrospective review of all patients who underwent EVPAR at a single academic institution between September 2 and March 2006. These patients were evaluated for patency, need for secondary intervention, amputation-free survival, and overall survival. A total of 15 limbs in 13 patients were treated with EVPAR during the study period. All EVPA were performed using the Viabahn(®) endoprostheses, with an average of 1.67 stents per limb. The mean age of patients was 74.6 years (range of 66 to 84). Technical success was achieved in 100% and all limbs had initial postoperative ankle-arm indices of greater than or equal to 1.0. Mean duration of follow-up was 54 months (range of 470). Two patients died of unrelated causes at 3 and 38 months with intact limbs, and 1 patient was lost to follow-up. Two limbs developed type I or III endoleaks, and were successfully treated with additional endovascular stent placement, resulting in a primary patency rate of 84.6% and secondary patency rate of 100%. There were no instances of limb loss during the follow-up period, yielding both amputation-free survival and overall survival rates.
85.7%. The authors concluded that long-term follow-up of this cohort of EVPAR patients suggested that in selected patients, this is a durable technique, capable of achieving excellent patency rates and limb preservation. Moreover, they stated that further large-scale clinical trials are needed to help define optimal candidates for this technique.

Pulli and colleagues (2012) retrospectively compared peri-operative (less than 30 days) and 2-year results of open endovascular management of PAAs in a single-center experience. From January 2005 to December 2010, a total of 59 consecutive patients were operated on at the authors' institution; in 43 cases, open repair was performed (group 1), whereas the remaining 21 cases had an endovascular procedure (group 2). Data from all the interventions were prospectively collected in a dedicated database, which included main pre-operative, intra-operative, and post-operative parameters. Early results in terms of mortality, graft thrombosis, and amputation rates were analyzed and compared by χ² text or Fisher exact test. The surveillance program consisted of clinical and ultrasonographic examinations at 1, 6, and 12 months and yearly thereafter. Follow-up results (survival, primary and secondary patellar limb salvage) were analyzed by Kaplan-Meier curves, and differences in the 2 groups were assessed by log-rank test. There were no differences between the 2 groups in terms of sex, age, risk factors for atherosclerosis, and co-morbidities; PAAs were symptomatic in 48% of cases in group 1 and in 29% in group 2 (p = 0.1). Fifteen patients mild-to-moderate acute ischemia due to PAA thrombosis underwent pre-operative intra-arterial thrombolysis, 13 in group 1 and 2 in group 2. In open surgery group, 9 cases were treated with aneurysmectomy and prosthetic graft interposition, and in 7 cases, the aneurysm was opened and a prosthetic graft was placed inside the aneurysm. In cases, ligation of the aneurysm with bypass grafting (21 prosthetic grafts and 6 autologous veins) was carried out. Group 2, 20 patients had endoprosthesis placement, whereas in the remaining patient, a multi-layer nitinol stent was used. There was 1 peri-operative death in a patient of group 2 who underwent concomitant endovascular aneurysm repair and PAA endografting. Cumulative 30-day death and amputation rate was 4.5% in group 1 and 4.7% in group 2 (p = 0.9). Follow-up was available in 61 interventions (96%) with a mean follow-up period of 22.5 months (range 6-60). Estimated primary patency rates at 24 months were 78.1% in group 1 and 59.4% in group 2 (p = 0.1). Free from re-intervention rates at 24 months were 79% in group 1 and 61.5% in group 2 (p = 0.2); estimated 24-month secondary patency rates were 81.6% in group 1 and 78.4% in group 2 (p = 0.9), and freedom from amputation rate were 92.7% and 95%, respectively (p = 0.7). The authors concluded that endovascular treatment of PAAs provides in the authors' initial experience, satisfactory peri-operative and 1-year results, not significantly different from those obtained with prosthetic open repair in patients with similar clinical and anatomical status. There is, however, a trend toward poorer primary patency rates among patients endovascularly treated, who also seem to require more frequent re-intervention.

Antoniou and associates (2012) noted that endovascular repair of PAAs is an emerging treatment in high-risk surgical patients. The location in a functionally demanding anatomical area creates limitations in terms of endograft patency. Technological advancements have been conscripted in an effort to circumvent such constraints. The multi-layer stent technology effects via hemodynamic modulation. These investigators employed the multi-layer stent to treat 6 asymptomatic PAAs in 3 patients. All procedures were successfully accomplished without any complications. Over mean follow-up period of 9 months, thrombosis occurred in 2 limbs, and blood flow was restored with thrombolysis achieving a primary and secondary patency rate at 6 months of 67% and 100%, respectively. Partial or complete thrombosis of the aneurysm sac was achieved in all aneurysms. The authors concluded that even though the use of a multi-layer stent in PAAs was safe in the short-term, their experience showed that close surveillance is needed. Furthermore, an UpToDate review on "Popliteal artery aneurysm" (Reed, 2012) does not mention the use of stenting as a therapeutic option.

Dake et al (2011) stated that sustained benefits of drug-eluting stents in femoropopliteal arteries have not been demonstrated. A prospective, multinational, randomized study was designed to compare the 12-month safety and effectiveness of a polymer-free, paclitaxel-coated nitinol drug-eluting stent (DES) with percutaneous transluminal angioplasty (PTA) and provisional bare metal stent (BMS) placement in patients with femoropopliteal peripheral arterial disease. In this study patients were randomly assigned to primary DES implantation (n=236) or PTA (n=238) and demographics and lesion characteristics were similar between groups. One hundred twenty patients had acute PTA failure and underwent secondary random assignment to provisional DES (n=61) or BMS (n=59). The 12-month rat
event-free survival and patency in the primary DES and PTA groups were evaluated. Compared with the PTA group, the primary DES group exhibited superior 12-month event-free survival (90.4% versus 82.6%; P=0.004) and primary patency (83.1% versus 32.8%; P<0.001). In secondary evaluations, the primary DES group exhibited superior clinical benefit compared with the PTA group (88.3% versus 75.8%; P<0.001). The provisional DES group exhibited superior primary patency (89.9% versus 73.0%; P=0.01) and superior clinical benefit (90.5% and 72.3%, P=0.009) compared with the provisional BMS group, and the stent fracture rate (both DES and BMS) was 0.9% (4/457). The authors concluded that femoropopliteal peripheral artery disease treatment with the paclitaxel-eluting stent was associated with superior 12-month outcomes compared with PTA and provisional BMS placement.

Lammer et al (2011) stated that a novel self-expanding drug-eluting stent was designed to slowly release everolimus to prevent restenosis following peripheral arterial intervention. They reported on the first-in-human Superficial Femoral Artery Treatment with Drug-Eluting Stents (STRIDES) trial, which was to evaluate the safety and efficacy of this device for the treatment of symptomatic superficial femoral and proximal popliteal arterial occlusive disease. One hundred patients were enrolled at 11 European investigative centers in a prospective, nonrandomized, single-arm trial. Enrollment criteria included severe symptomatic vascular disease, including a significant proportion of patients with critical limb ischemia (17%), diabetes (39%), and single-vessel outflow (26%). The mean lesion length was 9.0 ± 4.3 cm and nine percent of patients were available for 12-month follow-up, including duplex imaging in 90% and arteriography in 83%. Clinical improvement, defined as a sustained decrease in Rutherford-Becker clinical category, was achieved in 80% of patients and primary patency (freedom from ≥50% in-stent restenosis) was 94 ± 2.3% and 68 ± 4.6% at 6 and 12 months, respectively. Plain radiographic examination of 122 implanted devices at 12 months revealed no evidence of stent fracture. The authors concluded that the everolimus-eluting self-expanding nitinol stent can be successfully implanted in patients with severe peripheral arterial disease with favorable outcomes and clinical improvements observed in the majority of patients.

In November, 2012 the FDA approved use of the Zilver PTX Drug-Eluting Peripheral Stent (Zilver PTX Stent), which is the first drug-eluting stent indicated to re-open a particular artery in the thigh (femoropopliteal artery) when narrowed or blocked as a result of PAD. The device is contraindicated in patients with stenoses that cannot be dilated to permit passage of the catheter or proper placement of the stent, patients who cannot receive recommended drug therapy due to bleeding disorders, or women who are pregnant, breastfeeding, or plan to become pregnant in the next five years (FDA, 2012).

The Gore Viabahn Endoprosthesis has been approved by the FDA for improving blood flow in patients with symptomatic peripheral arterial disease in superficial femoral artery lesions with reference vessel diameters ranging from 4.8 to 8.0 mm. The Gore Viabahn Endoprosthesis is a flexible, metallic (made from nitinol) stent which is lined with expanded polytetrafluoroethylene (ePTFE). The device is mounted on the end of a delivery catheter and held in place by a release mechanism. The delivery catheter with the mounted endoprosthesis is inserted in the femoral artery through a puncture in the leg and threaded to the blocked section of the femoral artery. Once the device is positioned within the blocked area, it is freed from the delivery catheter by activation of the release mechanism. The device is expanded within the artery, opening the blocked area to improve blood flow. The delivery catheter is removed from the patient leaving the device within the femoropopliteal artery of the patient. According to the FDA (2012), the Gore Viabahn Endoprosthesis should not be used in patients who have a blockage where full expansion of the balloon dilatation catheter has not been achieved or where blockages cannot be dilated sufficiently to allow passage of the delivery system.

Saxon et al (2012) evaluated the performance of a heparin-bonded, expanded polytetrafluoroethylene (ePTFE)-lined nitinol endoprosthesis in the treatment of long-segment occlusive disease of the femoropopliteal artery (FPA). In a single-arm, prospective, 11-center study (VIPER [Gore Viabahn Endoprosthesis with Heparin Bioactive Surface in Treatment of Superficial Femoral Artery Obstructive Disease] trial), 119 limbs (113 patients; 69 men; mean age of 72 yrs), including 88 with Rutherford category 3-5 disease and 72 with Inter-Society Consensus for the Management of
Peripheral Arterial Disease (TASC II) C or D lesions of the FPA, underwent stent graft implantation. The mean lesion length was 19 cm; 56% of lesions were occlusions. Follow-up evaluations included color duplex ultrasonography patients, with patency defined as a peak systolic velocity ratio less than 2.5. At 12 months, Rutherford category an ankle-brachial index (ABI) were significantly improved (mean category improvement, 2.4; ABI increased from 0.6 ± 0.9 to 0.9 ± 0.19; p < 0.0001). Primary and secondary patency rates were 73% and 92%. The primary patency for de oversized less than 20% at the proximal landing zone was 88%, whereas the primary patency for devices oversiz greater than 20% was 70% (p = 0.047). Primary patency was not significantly affected by device diameter (5 ver 6 versus 7 mm) or lesion length (less than or equal to 20 cm versus greater than 20 cm). The 30-day major adverse event rate was 0.8%. The authors concluded that the heparin-bonded, ePTFE/nitinol stent graft provided clinical improvement and a primary patency rate of 73% at 1 year in the treatment of long-segment FPA disease.

Sixt et al (2008) reported that percutaneous transluminal angioplasty is an accepted and successful treatment stra in obstructive disease of the SA. These researchers evaluated the technical and clinical long-term outcome followin endovascular therapy. These researchers retrospectively analyzed 99 patients (mean age of 65 +/- 10 years) with interventions of the SAs and the brachiocephalic trunk with different etiologies [atherosclerosis (90%); Takayasu's arteritis (5%); thrombo-embolism (2%); external compression (1%); iatrogenic dissection (1%) and occlusion after graft implantation in type B dissection (1%)]. Primary success rate was 97% (100% for stenoses and 90% for occlusions). Treatment modalities included balloon angioplasty (PTA) alone (16%), stent implantation (78%), rot thrombectomy (2%) and atherectomy (1%). The primary 1-year patency rate of the whole study cohort was 87% being not significantly lower after PTA (75%) compared to stent assisted angioplasty (89%). After thrombectomy atherectomy no relevant restenosis were found. Multi-variable analysis of 1-year restenosis-free survival revealed younger age (p = 0.03) and stenting (p = 0.04) as independent predictor. The blood pressure difference between brachial limbs at baseline was 42 +/- 24 mmHg and dropped to 10 +/- 14 mmHg after the intervention and 15 +/- 20 mmHg 12 months, respectively (p = 0.01). The authors concluded that endovascular therapy of SA obstructions of various etiologies offers good acute success rates even in total occlusions; long-term patency rate is in favor of stent place

Park et al (2011) stated that since they reported about a landmark technique to re-open an occluded SA, they hav faced difficulty in using protection devices in the vertebral artery to protect against thromboembolism from the reverse steal phenomenon after angioplasty and stenting. Thus, they presented an optimal solution in using a protection device while re-canalizing the occluded SA. Among 21 cases of stenting for SA stenosis-occlusion, they applied the landmark technique at the opposite end of an occluded segment in 4 patients and used a protection device in 2 patients. Be the embolic protection device was placed in the vertebral artery via the brachial artery, optimal angioplasty and stenting via the brachial route were limited. Therefore, angioplasty via the trans-brachial approach was needed to be followed by stenting through a trans-femoral approach. They estimated the safe and optimal steps for placement and retrieval of protection devices in addition to stenting. The procedure was safely performed when a stent was introduced via the femoral artery and a protection device was used via the brachial artery. However, in cases when a guide-wire was passed via the transfemoral route, simultaneous use of 2 systems via the brachial route could cause friction of dev or trapping of protection devices in a stent. When a protection device was trapped in a deployed stent, they retrieved the protection device with a 4F angio-catheter by selectively rotating the catheter tip. To avoid such procedural difficulty, they recommended using a trans-brachial angioplasty followed by trans-femoral stenting while placing the protection device in the vertebral artery via the trans-brachial route. The authors concluded that if a guide-wire was passed through using a trans-femoral approach while performing the landmark technique, changing the stenting route from brachial to the femoral artery can be useful after securing the lumen in the occluded SA after angioplasty via the brachial artery.

Chatterjee et al (2013) stated that SA stenosis has long been treated with great success with bypass surgery. Percutaneous intervention, often used in combination with stent placement, has come into vogue for the past few years as a safe and effective therapeutic modality. These investigators compared angioplasty alone with angioplasty following stent placement by combining available data. The objective of this study was to perform a review of the available literature to compare the efficacy of percutaneous transluminal angioplasty (PTA) alone with PTA followed by stent placement for proximal SA stenosis. Successful re-canalization was defined as patency at the end of 1 year, and r
occlusions and re-stenoses were noted as events for the purpose of pooling the data. The authors searched the Specialized Register and the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, PubMed, EMBASE, and CINAHL databases for relevant trials/studies comparing PTA and PTA with stenting. Rev authors independently assessed the methodological quality of studies (focusing on the adequacy of the randomiza process, allocation concealment, blinding, completeness of follow-up evaluation, and intention-to-treat analysis) an selected studies for inclusion. All retrospective observational studies were also included in the analysis in the abs of double-blinded randomized trials for increasing sample size. All analyses were done using RevMan 5.0. Odds r was calculated using Mantel-Haenszel test with a fixed effect model. All included studies were assessed by all aut for potential sources of bias. A total of 8 studies were included in the analysis having 544 participants. Stenting af PTA was significantly superior to angioplasty alone for treatment of SA stenosis and maintenance of patency at 1 y as indicated by absence of events (p = 0.004; 95 % confidence interval, odds ratio 2.37 [1.32 to 4.26]) without sign complication rates for either procedure. The authors concluded that there is evidence in favor of stent placement a angioplasty for successful re-canalization of stenosed SAs and long-term maintenance of patency without significa increase in risk for major complications in subjects.

An UpToDate review on “Overview of upper extremity peripheral artery disease” (Mohler, 2013) states that “Patien who do not have symptoms do not require intervention. Options for the treatment of symptomatic subclavian steno occlusion include surgical revascularization (e.g., carotid-subclavian bypass, subclavian transposition) and percutaneous transluminal angioplasty and stenting. Percutaneous catheter-based treatment is less invasive and associated with lower complication rates, and shorter hospitalization”.

In a prospective, randomized, single-blind, multicenter study, Lammer and colleagues (2013) hypothesized that endovascular treatment with covered stents has equal risks but higher efficacy than BMS in long FP artery disease total of 141 patients with symptomatic PAD were assigned to treatment with heparin-bonded, covered stents (Viaba = 72) or BMS (n = 69). Clinical outcomes and patency rates were assessed at 1, 6, and 12 months. Mean ± SD le length was 19.0 ± 6.3 cm in the Viabahn group and 17.3 ± 6.6 cm in the BMS group. Major complications within 30 days were observed in 1.4 %. The 12-month primary patency rates in the Viabahn and BMS groups were: intentio treat (ITT) 70.9 % (95 % CI: 0.58 to 0.80) and 55.1 % (95 % CI: 0.41 to 0.67) (log-rank test p = 0.11); treatment per protocol (TPP) 78.1 % (95 % CI: 0.65 to 0.86) and 53.5 % (95 % CI: 0.39 to 0.65) (HR: 2.23 [95 % CI: 1.14 to 4.34) rank test p = 0.009). In lesions greater than or equal to 20 cm, (TASC class D), the 12-month patency rate was significantly longer in VIA patients in the ITT analysis (VIA 71.3 % versus BMS 36.8 %; p = 0.01) and the TPP anal (VIA 73.3 % versus BMS 33.3 %; p = 0.004). Freedom from TLR was 84.6 % for Viabahn (95 % CI: 0.72 to 0.91) v 77.0 % for BMS (95 % CI: 0.63 to 0.85; p = 0.37). The ABI in the Viabahn group significantly increased to 0.94 ± 0 compared with the BMS group (0.85 ± 0.23; p < 0.05) at 12 months. The authors concluded that this randomized t symptomatic patients with PAD who underwent endovascular treatment for long FP lesions demonstrated significa clinical and patency benefits for heparin-bonded covered stents compared with BMS in lesions greater than or equ 20 cm and for all lesions in the TPP analysis. In the ITT analysis for all lesions, which was flawed by major protoco deviations in 8.5 % of the patients, the difference was not significant.

Cooper et al (2014) noted that atherosclerotic RAS is a common problem in the elderly. Despite 2 randomized tria did not show a benefit of renal-artery stenting with respect to kidney function, the usefulness of stenting for the prevention of major adverse renal and cardiovascular events is uncertain. These researchers randomly assigned participants who had atherosclerotic RAS and either systolic hypertension while taking 2 or more anti-hypertensive drugs or chronic kidney disease to medical therapy plus renal-artery stenting or medical therapy alone. Participant were followed for the occurrence of adverse cardiovascular and renal events (a composite end-point of death from cardiovascular or renal causes, MI, stroke, hospitalization for congestive heart failure, progressive renal insufficien the need for renal-replacement therapy). Over a median follow-up period of 43 months (interquartile range: 31 to 5 the rate of the primary composite end-point did not differ significantly between participants who underwent stenting addition to receiving medical therapy and those who received medical therapy alone (35.1 % and 35.8 %, respectiv HR with stenting, 0.94; 95 % CI: 0.76 to 1.17; p = 0.58). There were also no significant differences between the treatment groups in the rates of the individual components of the primary end-point or in all-cause mortality. Durin
follow-up, there was a consistent modest difference in systolic blood pressure favoring the stent group (-2.3 mm Hg % CI: -4.4 to -0.2; p = 0.03). The authors concluded that renal-artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to comprehensive, multi-factorial medical therapy in people atherosclerotic RAS and hypertension or chronic kidney disease.

The accompanying editorial (Bittl, 2014) of the afore-mentioned study concluded that “The CORAL trial is a definitive test of the usefulness of renal-artery stents for moderately severe atherosclerotic disease. The trial results send a message to patients and referring physicians. Until new treatments are found to be safe and effective, patients in everyday practice who have moderately severe atherosclerotic renovascular disease and either hypertension or chronic kidney disease should receive medical therapy to control blood pressure and prevent the progression of atherosclerosis but should not be corralled into getting a renal-artery stent.”

In a Cochrane review, Chowdhury et al (2014) examined the effect of PTA compared with PTA with BMS for SFA stenoses on vessel patency in people with symptomatic (Rutherford categories 1 to 6; Fontaine stages II to IV) low limb PVD. In addition, these researchers assessed the effectiveness of PTA and stenting in improving quality of life ABI and treadmill walking distance. For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Coordinator searched the Specialised Register (last searched August 2013) and the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 6). Randomized trials of angioplasty alone versus angioplasty with BM stenting treatment of superficial femoral artery stenosis were selected for analysis. Two review authors independently selected suitable trials, assessed trial quality and extracted data. Furthermore, these 2 review authors performed assessments of methodological quality and wrote the final manuscript. The third review author cross-checked all aspects of the review process. These investigators included 3 new studies in this update, making a total of 11 included trials with 1,387 participants. The average age was 69 years and all trials included men and women. Participants were followed for up to 2 years. There was an improvement in primary duplex patency at 6 and 12 months in participants treated with PTA plus stent over lesions treated with PTA alone (6 months: OR 2.90, 95 % CI: 1.17 to 7.18, p = 0.0005, 9 studies, 578 subjects; 12 months: OR 1.78, 95 % CI: 1.02 to 3.10, p = 0.04, 9 studies, 858 participants). This was by 24 months (p = 0.06). There was a significant angiographic patency benefit at 6 months (OR 2.49, 95 % CI: 1.44 to 4.17, p = 0.0005, 4 studies, 329 participants) which was lost by 12 months (OR 1.30, 95 % CI: 0.84 to 2.00, p = 0.20, 9 studies, 384 participants). Ankle brachial index and treadmill walking distance showed no improvement at 12 months (p = 0.49 and p = 0.57, respectively) between participants treated with PTA alone or PTA with stent insertion. Three trials (660 participants) reported quality of life, which showed no significant difference between participants treated with PTA alone or PTA with stent insertion at any time interval. Anti-platelet therapy protocols and inclusion criteria regarding affected arteries between trials showed marked heterogeneity. The authors concluded that although there was a short-term gain in primary patency there was no sustained benefit from primary stenting of lesions of the SFA in addition to angioplasty. Moreover, they stated that future trials should focus on quality of life for claudication and limb salvage in critical ischemia.

Humphries et al (2014) evaluated midterm outcomes of balloon-expandable bare-metal stents (BMSs) versus covered balloon-expandable (CBE) stents placed in the common iliac artery (CIA) for aorto-iliac occlusive disease. All endovascular interventions for symptomatic peripheral arterial occlusive disease performed at a single institution from 2006 to 2012 were reviewed. Patients undergoing stent placement in the CIA segment were included in the analysis. Demographic data, TASC classification, stent type, patency, and limb re-interventions were compared. For treatment of de-novo distal aorta or CIA stenosis, 254 procedures were performed in 162 patients. Balloon-expandable bare-metal stents were used in 190 arteries; CBE stents were used in 64 arteries. There was no difference in age, gender, or TASC classification between the 2 groups. Mean follow-up was 22 ± 16 months. Primary patency, assisted patency, and secondary patency were significantly better in the BMS group. Common iliac arteries treated with covered stents were more likely at 1 year or longer to require repeated intervention (HR, 2.5; 95 % CI: 1.2 to 5.3; p = 0.009); TASC classification did not predict need for re-intervention in either group. Multi-variate analysis revealed dual anti-platelet therapy to be the only other factor to affect patency during long-term follow-up. The authors concluded that in this study, BMSs had significantly better patency compared with CBE stents for treatment of aorto-iliac occlusive disease.
Moreover, they stated that a randomized trial comparing patency as well as re-stenosis rates with long-term follow-needed to determine if there is any benefit from use of covered stents in the aorto-iliac segment.

CPT Codes / HCPCS Codes / ICD-9 Codes

**Peripheral Artery Stenting:**

**CPT codes covered if selection criteria are met:**

37236
37237

**Other CPT codes related to the CPB:**

37226
37227
37236
37237
79560

**HCPCS codes covered if selection criteria are met:**

C1876  Stent, non-coated/non-covered, with delivery system [for femoropopliteal artery disease]
C1877  Stent, non-coated/non-covered, without delivery system [for femoropopliteal artery disease]

**HCPCS codes not covered for indications listed in the CPB:**

C1875  Stent, coated / covered, without delivery system

**ICD-9 codes covered if selection criteria are met:**

435.2  Subclavian steal syndrome
785.4  Gangrene

**ICD-9 codes not covered for indications listed in the CPB:**

440.1  Atherosclerosis of renal artery
447.4  Celiac artery compression syndrome

**Other ICD-9 codes related to the CPB:**

437.1  Other generalized ischemic cerebrovascular disease
440.1 - 440.9  Atherosclerosis
442.3  Other aneurysm of artery of lower extremity
443.0 - 443.9  Other peripheral vascular disease
444.0 - 444.9  Arterial embolism and thrombosis
445.01 - 445.89  Atheroembolism
447.1  Stricture of artery
453.0 - 453.9  Other venous embolism and thrombosis
557.1  Chronic vascular insufficiency of intestine
707.8  Chronic ulcer of other specified site [non-healing tissue ulceration]

**Gore Viabahn PTFE-coated Endoprosthesis:**

**HCPCS codes covered if selection criteria are met:**

C1874  Stent, coated/covered, with delivery system [not covered for other polytetrafluoroethylene (PTFE)-covered stents]

**ICD-9 codes covered if selection criteria are met:**

443.0 - 443.9  Other peripheral vascular disease

**Peripheral Venous Stents:**

**CPT codes covered if selection criteria are met:**

37238
37239

**Other CPT codes related to the CPB:**

37226
37227
79560

**HCPCS codes covered if selection criteria are met:**

C1860  Stent, noncoated/noncovered, with delivery system
C1877  Stent, noncoated/noncovered, without delivery system
C2617  Stent, noncoronary, temporary, without delivery system
C2625  Stent, noncoronary, temporary, with delivery system

**ICD-9 codes covered if selection criteria are met:**

996.1  Mechanical complication of other vascular device, implant, and graft [hemodialysis acces graft/fistula: stenosis and restenosis]
Other complications due to other vascular device, implant, and graft [hemodialysis access graft/fistula: occlusion]

**Other ICD-9 codes related to the CPB:**

- 444.21 - 444.22 Embolism and thrombosis of arteries of upper and lower extremity
- 459.2 Compression of vein [superior vena cava syndrome]
- 747.49 Other congenital anomalies of great veins [congenital stenosis of superior vena cava]
- 909.2 Late effect of radiation [post radiation venous stenosis]

The above policy is based on the following references:


52. Reed AB. Popliteal artery aneurysm. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed July 201
62. Mohler ER, III. Overview of upper extremity peripheral artery disease. UpToDate [serial online]. Waltham, MA: UpToDate; reviewed September 2013.