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Reference Summary

Peripheral Arterial Disease

guidelines

This summary of the ***ACC/AHA Guidelines for Management of Patients With Peripheral Arterial Disease*** (P.A.D.) is an introduction to the complete 2005 guidelines and is not meant to replace the full guide. The complete edition addresses the diagnosis and management of atherosclerotic, aneurysmal, and thromboembolic P.A.D. Although the term "peripheral arterial disease" encompasses a large series of disorders that affect arterial beds exclusive of the coronary arteries, the 2005 guidelines limit the scope to the disorders of the ***abdominal aorta***, ***renal and mesenteric arteries, and lower extremity arteries***. Clinical management guidelines for other arterial beds (e.g., the thoracic aorta, carotid and vertebral arteries, and upper-extremity arteries) have been excluded from the current guidelines to focus on the infradiaphragmatic arterial system, in recognition of the robust evidence base that exists for the aortic, visceral, and lower extremity arteries.

Class Descriptions

Class I: Treatment is beneficial, useful, and effective.

Class II: There is conflicting evidence and/or a divergence of opinion about the usefulness of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: A procedure or treatment is not useful/effective and may be harmful.

(Levels of Evidence are included in full-text Guidelines.)

Lower Extremity P.A.D.

Individuals at Risk for P.A.D.

- Age less than 50 years, with diabetes and one other atherosclerosis risk factor (smoking, dyslipidemia, hypertension, or hyperhomocysteinemia)
- Age 50 to 69 years and history of smoking or diabetes
- Age 70 years and older
- Leg symptoms with exertion (suggestive of claudication) or ischemic rest pain

- Abnormal lower extremity pulse examination
- Known atherosclerotic coronary, carotid, or renal artery disease

Noninvasive and Invasive Vascular Diagnostic Tools: Benefits and Limitations

Tools are listed in order from least to most invasive and from least to most costly. (CLI is critical limb ischemia.)

Diagnostic Tool	Benefits	Limitations
Ankle-Brachial Indices (ABI)	• A quick and cost-effective way to establish or refute the lower extremity P.A.D. diagnosis	• May not be accurate when systolic blood pressure cannot be abolished by inflation of an air-filled blood pressure cuff (noncompressible pedal arteries), as occurs in a small fraction of diabetic or very elderly individuals
Toe-brachial indices	• A quick and cost-effective way to establish or refute the lower extremity P.A.D. diagnosis • Can measure digital perfusion when small-vessel arterial occlusive disease is present • Useful in individuals with noncompressible posterior tibial or dorsalis pedis arteries	• Requires small cuffs and careful technique to preserve accuracy
Segmental pressure examination	• Useful to establish or refute the P.A.D. diagnosis • Useful to provide anatomic localization of lower extremity P.A.D. when these data are required to create a therapeutic plan • Can provide data to predict limb survival, wound healing, and patient survival • Useful to monitor the efficacy of therapeutic interventions	• May not be accurate when systolic blood pressure cannot be measured by inflation of an air-filled blood pressure cuff owing to noncompressible pedal arteries, as occurs in a small fraction of diabetic or very elderly individuals

Diagnostic Tool	Benefits	Limitations
Pulse volume recording	• Useful to establish the diagnosis of P.A.D. in vascular laboratories or office practice • Helpful in predicting the outcome in CLI and risk of amputation • Can be used to monitor limb perfusion after revascularization procedures • Usefulness maintained in patients with noncompressible vessels (ABI value greater than 1.3)	• Qualitative, not quantitative, measure of perfusion • May not be accurate in more distal segments • Less accurate than other noninvasive tests in providing arterial anatomic localization of P.A.D • May be abnormal in patients with low cardiac stroke volume
Continuous-wave Doppler ultrasound	• Useful to assess lower extremity P.A.D. anatomy, severity, and progression • Can provide localizing information in patients with poorly compressible arteries • Can provide quantitative data after successful lower extremity revascularization	• "Pulse normalization" downstream from stenosis can diminish test sensitivity • Test specificity greater for patent superficial femoral arteries than for aortoiliac occlusive disease • Does not provide visualization of arterial anatomy • Limited accuracy in tortuous, overlapping, or densely calcified arterial segments, and insensitive for iliac arteries (in context of obesity, bowel gas, and vessel tortuosity)
Duplex ultrasound	• Can establish the lower extremity P.A.D. diagnosis, establish anatomic localization, and define severity of focal lower extremity arterial stenoses • Can be useful to select candidates for endovascular or surgical revascularization • Useful tool to provide graft surveillance after femoral popliteal or femoral tibial or pedal surgical bypass with venous (but not prosthetic) conduit	• Accuracy is diminished in proximal aortoiliac arterial segments in some individuals (e.g., due to obesity or the presence of bowel gas) • Dense arterial calcification can limit diagnostic accuracy • Sensitivity is diminished for detecting stenosis downstream from a proximal stenosis • Diminished predictive value in surveillance of prosthetic bypass grafts
Toe-tip exercise testing, with pre-exercise and postexercise ABIs	• Useful to diagnose lower extremity P.A.D. when resting ABI values are normal • Can be performed in the absence of a treadmill, with increased convenience and low cost	• Provides qualitative (rather than quantitative) exercise diagnostic results • Lower workload may not elicit symptoms in all individuals with claudication

Diagnostic Tool	Benefits	Limitations
Treadmill exercise testing, with and without pre-exercise and postexercise ABIs	• Helps differentiate claudication from pseudoclaudication in individuals with exertional leg symptoms • Useful to diagnose lower extremity P.A.D. when resting ABI values are normal • Objectively documents the magnitude of symptom limitation in patients with claudication, especially when used with a standardized treadmill protocol • Demonstrates the safety of exercise and provides data to individualize exercise prescriptions in individuals with claudication before initiation of a formal program of therapeutic exercise training • Useful to measure the objective functional response to claudication therapeutic interventions	• Requires use of a motorized treadmill, with or without continuous electrocardiogram monitoring, as well as staff familiar with exercise testing protocols
Magnetic resonance angiography (MRA)	• Useful to assess P.A.D. anatomy and presence of significant stenoses • Useful to select patients who are candidates for endovascular or surgical revascularization	• Tends to overestimate the degree of stenosis • May be inaccurate in arteries treated with metal stents • Cannot be used in patients with contraindications to the magnetic resonance technique (e.g., pacemakers, defibrillators, intracranial metallic stents, clips, coils, and other devices)

Diagnostic Tool	Benefits	Limitations
Computed tomographic angiography (CTA)	• Useful to assess P.A.D. anatomy and presence of significant stenoses • Useful to select patients who are candidates for endovascular or surgical revascularization • Helpful to provide associated soft tissue diagnostic information that may be associated with P.A.D. presentation (e.g., aneurysms, popliteal entrapment, and cystic adventitial disease) • Patients with contraindications to MRA (e.g., pacemakers or defibrillators) may be safely imaged • Metal clips, stents, and metallic prostheses do not cause significant CTA artifacts • Scan times are significantly faster than for MRA	• Single-detector computed tomography lacks accuracy for detection of stenosis • Spatial resolution lower than digital subtraction angiography • Venous opacification can obscure arterial filling • Asymmetrical opacification of the legs may obscure arterial phase in some vessels • Accuracy and effectiveness not as well determined as MRA • Treatment plans based on CTA have not been compared with those of catheter angiography • Requires iodinated contrast and ionizing radiation (although radiation exposure is less than with catheter angiography) • Because CTA requires administration of iodinated contrast, use is limited in individuals with established renal dysfunction
Contrast angiography	• Definitive method for anatomic evaluation of P.A.D. when revascularization is planned	• Invasive evaluation is associated with risk of bleeding, infection, vascular access complications (e.g., dissection or hematoma), atheroembolization, contrast allergy, and contrast nephropathy • May provide limited visualization of tibial-pedal vessels in patients with CLI with poor inflow to the leg • Below-knee vessels may be difficult to identify by digital subtraction angiography • Multiple projections may be necessary to visualize eccentric lesions

Typical Noninvasive Vascular Laboratory Tests for Lower Extremity P.A.D. Patients by Clinical Presentation

Clinical Presentation	Noninvasive Vascular Test
Asymptomatic lower extremity P.A.D.	ABI
Claudication	ABI, PVR, or segmental pressures Duplex ultrasound Exercise test with ABI to assess functional status
Possible pseudoclaudication	Exercise test with ABI
Postoperative vein graft follow-up	Duplex ultrasound
Femoral pseudoaneurysm; iliac or popliteal aneurysm	Duplex ultrasound
Suspected aortic aneurysm; serial AAA follow-up	Abdominal ultrasound, CTA, or MRA
Candidate for revascularization	Duplex ultrasound, MRA, or CTA

Adapted from Primary Cardiology, 2nd ed., Braunwald E, Goldman L, eds., "Recognition and management of peripheral arterial disease," Hirsch AT, 659–71, Philadelphia, PA: WB Saunders, Copyright 2003, with permission from Elsevier.

AAA abdominal aortic aneurysm; **ABI** ankle-brachial index; **CTA** computed tomographic angiography; **MRA** magnetic resonance angiography; **P.A.D.** peripheral arterial disease; **PVR** pulse volume recording.

ABI Interpretation Levels

>1.3	Noncompressible
1.00 – 1.29	Normal
0.91 – 0.99	Borderline (equivocal)
0.41 – 0.90	Mild-to-moderate P.A.D.
0.00 – 0.40	Severe P.A.D.

Lower Extremity P.A.D. Treatment—Cardiovascular Risk Reduction

A. LIPID-LOWERING DRUGS

Class I Recommendations

- Treatment with a hydroxymethyl glutaryl (HMG) coenzyme-A reductase inhibitor (statin) medication is indicated for all patients with P.A.D. to achieve a target low-density lipoprotein (LDL) cholesterol level of less than 100 mg/dL.

Class IIa Recommendations

- Treatment with an HMG coenzyme-A reductase inhibitor (statin) medication to achieve a target LDL cholesterol level of less than 70 mg/dL is reasonable for patients with lower extremity P.A.D. at very high risk of ischemic events.
- Treatment with a fibric acid derivative can be useful for patients with P.A.D. and low HDL cholesterol, normal LDL cholesterol, and elevated triglycerides.

B. ANTIHYPERTENSIVE DRUGS

Class I Recommendations

- Antihypertensive therapy should be administered to hypertensive patients with lower extremity P.A.D. to achieve a goal of less than 140 mm Hg systolic over 90 mm Hg diastolic (nondiabetics) or less than 130 mm Hg systolic over 80 mm Hg diastolic (diabetics and individuals with chronic renal disease) to reduce the risk of MI, stroke, congestive heart failure, and cardiovascular death.
- Beta-adrenergic blocking drugs are effective antihypertensive agents and are not contraindicated in patients with P.A.D.

Class IIa Recommendations

- The use of angiotensin-converting enzyme (ACE) inhibitors is reasonable for symptomatic patients with lower extremity P.A.D. to reduce the risk of adverse cardiovascular events.

Class IIb Recommendations

- ACE inhibitors may be considered for patients with asymptomatic lower extremity P.A.D. to reduce the risk of adverse cardiovascular events.

C. DIABETES THERAPIES

Class I Recommendations

- Proper foot care, including use of appropriate footwear, chiropody/podiatric medicine, daily foot inspection, skin cleansing, and use of topical moisturizing creams should be encouraged, and skin lesions and ulcerations should be addressed urgently in all diabetic patients with lower extremity P.A.D.

Class IIa Recommendations

- Treatment of diabetes in individuals with lower extremity P.A.D. by administration of glucose control therapies to reduce the hemoglobin A1C to less than 7% can be effective to reduce microvascular complications and potentially improve cardiovascular outcomes.

D. SMOKING CESSATION

Class I Recommendations

- Individuals with lower extremity P.A.D. who smoke cigarettes or use other forms of tobacco should be advised by each of their clinicians to stop smoking and should be offered comprehensive smoking cessation interventions, including behavior modification therapy, nicotine replacement therapy, or bupropion.

E. HOMOCYSTEINE-LOWERING DRUGS

Class IIb Recommendations

- The effectiveness of the therapeutic use of folic acid and B12 vitamin supplements in individuals with lower extremity P.A.D. and homocysteine levels greater than 14 micromoles per liter is not well established.

F. ANTIPLATELET AND ANTITHROMBOTIC DRUGS

Class I Recommendations

- Antiplatelet therapy is indicated to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic lower extremity P.A.D.
- Aspirin, in daily doses of 75 to 325 mg, is recommended as safe and effective antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic lower extremity P.A.D.
- Clopidogrel (75 mg per day) is recommended as an effective alternative antiplatelet therapy to aspirin to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic lower extremity P.A.D.

Class III Recommendations

- Oral anticoagulation therapy with warfarin is not indicated to reduce the risk of adverse cardiovascular ischemic events in individuals with atherosclerotic lower extremity P.A.D.

Lower Extremity P.A.D. Treatment—Claudication

Classic claudication symptoms include muscle fatigue, cramping, or pain that reproducibly begins during exercise and that promptly resolves with rest. A history of walking impairment and specific lifestyle limitations due to claudication should be obtained. A history of limb ischemic symptoms including leg pain at rest, non-healing wounds, and gangrene should also be documented.

A. EXERCISE AND LOWER EXTREMITY P.A.D. REHABILITATION

Class I Recommendations

- A program of supervised exercise training is recommended as an initial treatment modality for patients with intermittent claudication.
- Supervised exercise training should be performed for a minimum of 30 to 45 minutes, in sessions performed at least 3 times per week for a minimum of 12 weeks.

Class IIb Recommendations

- The usefulness of unsupervised exercise programs is not well established as an effective initial treatment modality for patients with intermittent claudication.

B. MEDICAL AND PHARMACOLOGICAL TREATMENT

Class I Recommendations

- Cilostazol (100 mg orally 2 times per day) is indicated as an effective therapy to improve symptoms and increase walking distance in patients with lower extremity P.A.D. and intermittent claudication (in the absence of heart failure).
- A therapeutic trial of cilostazol should be considered in all patients with lifestyle-limiting claudication (in the absence of heart failure).

Class IIb Recommendations

- Pentoxifylline (400 mg 3 times per day) may be considered as

second-line alternative therapy to cilostazol to improve walking distance in patients with intermittent claudication.

- The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established.

C. OTHER PROPOSED MEDICAL THERAPIES

See full-text Guidelines for coverage of L-arginine, propionyl-L-carnitine, and ginkgo biloba.

D. GRAFT SURVEILLANCE

Patients who have undergone angioplasty/stent or surgical revascularization procedures require careful long-term care and vascular follow-up to detect both the recurrence of disease at revascularized sites and the development of new arterial disease at remote sites. Early revascularization interventions for recurrent hemodynamic compromise are preferred, because delay in detection or treatment can lead to higher morbidity and poorer outcome. Participation in a follow-up surveillance program is imperative. Long-term patency of bypass grafts should be evaluated in a surveillance program, which should include an interval vascular history, resting ABIs, physical examination, and a duplex ultrasound at regular intervals.

Renal Arterial Disease

A. PREVALENCE AND NATURAL HISTORY

Renal artery stenosis (RAS) is both a common and progressive disease in patients with atherosclerosis and a relatively uncommon cause of hypertension. From a limited epidemiological database, it is estimated that atherosclerotic RAS may affect as many as 6.8% of people aged 65 years and older.

Clinical Clues to the Diagnosis of Renal Artery Stenosis

1. Onset of hypertension before the age of 30 years or severe hypertension after the age of 55 (Class I)
2. Accelerated, resistant, or malignant hypertension (Class I)
3. Development of new azotemia or worsening renal function after administration of an ACE inhibitor or ARB agent (Class I)
4. Unexplained atrophic kidney or size discrepancy between kidneys of greater than 1.5 cm (Class I)

5. Sudden, unexplained pulmonary edema (Class I)
6. Unexplained renal dysfunction, including individuals starting renal replacement therapy (Class IIa)
7. Multi-vessel coronary artery disease (Class IIb)
8. Unexplained congestive heart failure (Class IIb)
9. Refractory angina (Class IIb)

Treatment of Renovascular Disease: Renal Artery Stenosis

Treatment of renal arterial disease should serve to aid in the normalization of blood pressure and to preserve renal function, and thereby decrease cardiovascular ischemic events and avert the need for renal replacement therapies. Both medical (pharmacological) and revascularization strategies should be considered for patients with documented renal arterial disease. (See full-text version of Guidelines for complete Treatment Algorithms and Recommendations.)

Mesenteric Arterial Disease

Regardless of cause, intestinal ischemia is rare, and there are no randomized or controlled trials of diagnosis or therapy for intestinal ischemia. Largely retrospective clinical reviews form the basis for our knowledge of and recommendations for treatment of intestinal ischemia.

Acute Intestinal Ischemia

Acute Intestinal Ischemia Caused by Arterial Obstruction

Acute obstructive intestinal ischemia occurs when the intestinal arteries are suddenly blocked to such a degree that all or part of the intestine has insufficient perfusion for viability. The many possible causes include embolism from cardiac or proximal arterial sources and arterial thrombosis. Regardless of the cause, patients with acute intestinal ischemia present with severe abdominal pain that is initially out of proportion to any physical findings that may be present.

Acute Nonocclusive Intestinal Ischemia

Acute intestinal ischemia sufficient to produce infarction also occurs in the absence of fixed arterial obstruction. The most frequent setting is severe systemic illness with systemic shock, usually as a result of reduced cardiac output. In this situation, the intestinal ischemia has been shown to be the result of severe and prolonged intestinal arterial vasospasm.

Chronic Intestinal Ischemia

Although atherosclerotic disease of the celiac and mesenteric vessels is common, the clinical presentation of chronic intestinal ischemia is rare. It is nearly uniformly caused by atherosclerosis. Classic clinical approaches to the diagnosis of intestinal ischemia have often suggested that this syndrome requires occlusion or stenosis of at least 2 of the 3 intestinal arteries; however, this is not entirely true. Well-documented cases of intestinal ischemia occur as a result of single-vessel disease, virtually always of the superior mesenteric artery. Patients in whom some of the normal collateral intestinal arterial connections have been interrupted by previous surgery are especially vulnerable to single-vessel occlusions.

Patients with chronic intestinal ischemia are most often female (70%) and classically complain of severe abdominal pain induced by eating. The pattern of pain is quite variable, however, and the relationship to food is not always clear, at least by history. What is clear is that patients voluntarily vastly reduce their food intake, so that weight loss occurs, and this may be profound. Vomiting, diarrhea, and constipation are present in a minority of patients. A majority have a history of cardiovascular disease, and 30% to 50% have had previous operations for atherosclerotic disease, most frequently coronary and lower extremity bypass.
(See full-text version of Guidelines for complete ischemia Treatment Recommendations.)

Aneurysms of the Abdominal Aorta, Its Branch Vessels, and the Lower Extremities

Definition

There is abundant information concerning normal diameters of the abdominal aorta and its branches in healthy adults that indicates enlargement with age and body size and larger diameters in men than in women. Generally, an abdominal aortic aneurysm (AAA) is considered to be present when the minimum anteroposterior diameter of the aorta reaches 3.0 cm.

Abdominal Aortic and Iliac Aneurysms

HEREDITARY RISK FACTORS

A family history of AAAs is particularly relevant for male siblings of male probands, in whom the relative risk for AAA is as high as 18%, which suggests a single dominant gene effect. First-degree male relatives of patients with AAA have 2 to 4 times the normal risk for AAA. Female first-degree relatives appear to be at similar risk, but the data are less certain.

ATHEROSCLEROTIC RISK FACTORS

Class I Recommendations

- In patients with AAAs, blood pressure and fasting serum lipid values should be monitored and controlled as recommended for patients with atherosclerotic disease.
- Patients with aneurysms or a family history of aneurysms should be advised to stop smoking and be offered smoking cessation interventions, including behavior modification, nicotine replacement, or bupropion.

AORTIC ANEURYSM RUPTURE

Class I Recommendations

- Patients with infrarenal or juxtarenal AAAs measuring 5.5 cm or larger should undergo repair to eliminate the risk of rupture.
- Patients with infrarenal or juxtarenal AAAs measuring 4.0 to 5.4 cm in diameter should be monitored by ultrasound or CT scans every 6 to 12 months to detect expansion.

SCREENING HIGH-RISK POPULATIONS

Class I Recommendations

- Men 60 years of age or older who are either the siblings or offspring of patients with AAAs should undergo physical examination and ultrasound screening for detection of aortic aneurysms.

Class IIa Recommendations

- Men who are 65 to 75 years of age who have ever smoked should undergo a physical examination and 1-time ultrasound screening for detection of AAAs.

POPLITEAL AND FEMORAL ARTERY ANEURYSMS

Popliteal aneurysms account for 70% of all aneurysms in the lower extremities and have an estimated incidence of 0.1% to 2.8%. Femoral

artery aneurysms may be discovered incidentally as a pulsatile mass in the thigh, or they may present with distal ischemia, and even more rarely, with rupture and bleeding.

Class I Recommendations

- Patients with a palpable popliteal mass should undergo an ultrasound examination to exclude popliteal aneurysm.
- Patients with popliteal aneurysms 2.0 cm in diameter or larger should undergo repair to reduce the risk of thromboembolic complications and limb loss.
- Patients with anastomotic pseudoaneurysms or symptomatic femoral artery aneurysms should undergo repair.

Class IIa Recommendations

- Surveillance by annual ultrasound imaging is suggested for patients with asymptomatic femoral artery true aneurysms smaller than 3.0 cm in diameter.
- In patients with acute ischemia and popliteal artery aneurysms and absent runoff, catheter-directed thrombolysis or mechanical thrombectomy (or both) is suggested to restore distal runoff and resolve emboli.
- In patients with asymptomatic enlargement of the popliteal arteries twice the normal diameter for age and gender, annual ultrasound monitoring is reasonable.
- In patients with femoral or popliteal artery aneurysms, administration of antiplatelet medication may be beneficial.

References:

ACC/AHA Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic): A Collaborative Report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) http://www.americanheart.org/presenter.jhtml?identifier=3036229

The Five Major P.A.D. Clinical Syndromes

Syndrome	Description
Asymptomatic (20–50%)	The absence of classic leg claudication symptoms
Atypical (40–50%)	Lower extremity discomfort that is exertional, but that does not consistently resolve with rest, consistently limit exercise at a reproducible distance, or meet all "Rose questionnaire" criteria
Classic claudication (10–35%)	Fatigue, discomfort, or frank pain that occurs in specific limb muscle groups during effort due to exercise-induced ischemia
Acute limb ischemia (<1%)	A rapid or sudden decrease in limb perfusion that threatens tissue viability
Critical limb ischemia (1–2%)	Limb pain that occurs at rest or impending limb loss that is caused by severe compromise of blood flow to the affected extremity

The American Heart Association
www.americanheart.org

The P.A.D. Coalition
www.padcoalition.org

Guidelines Writing Committee Members
Alan T. Hirsch, MD, FACC, FAHA, *Chair*; Ziv J. Haskal, MD, FAHA, FSIR, *Co-Chair*; Norman R. Hertzer, MD, FACS, *Co-Chair*

Curtis W. Bakal, MD, MPH, FAHA; Mark A. Creager, MD, FACC, FAHA; Jonathan L. Halperin, MD, FACC, FAHA†; Loren F. Hiratzka, MD, FACC, FAHA, FACS; William R.C. Murphy, MD, FACC, FACS; Jeffrey W. Olin, DO, FACC; Jules B. Puschett, MD, FAHA; Kenneth A. Rosenfield, MD, FACC; David Sacks, MD, FACR, FSIR§; James C. Stanley, MD, FACS, FACR, FSIR‡; Lloyd M. Taylor, Jr., MD, FACS‡; Christopher J. White, MD, FACC, FAHA, FESC, FSCAI¶; John White, MD, FACS‡; Rodney A. White, MD, FACS‡

†Society for Vascular Medicine and Biology official representative
‡Society for Vascular Surgery official representative
§Society of Interventional Radiology official representative
¶Society for Cardiovascular Angiography and Interventions official representative

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Supported through unrestricted educational grants from the Bristol-Myers Squibb/ Sanofi-Aventis partnership and Cordis®, a Johnson & Johnson company.