Summary of the ESC Guidelines on Peripheral Artery Diseases

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Topics: Peripheral Arterial Diseases
Date: 21 Dec 2011

For the first time the European Society of Cardiology (ESC) issued guidelines on Peripheral Artery Diseases (PAD) in 2011.

The ESC PAD guidelines are unique in that they provide recommendations for all areas along the cardiovascular continuum, thereby presenting the current up-to-date data from evidence-based studies, under consideration of surgical revascularisation procedures and the increasing use of catheter-based revascularisation intervention for renal arterial stenoses documenting the atherosclerotic changes in the different vessel beds.

The guidelines give diagnostic approaches and therapeutic options by specialists in cardiology, vascular surgery, neurology and angiology. The guideline recommendations reflect a consensus of expert opinion after a review of clinical trials relevant to patient populations not only in Europe, identified through a broad-based process.

The guidelines regarded that new data supported the clinical equivalence of surgical and endovascular treatment. The major advantage of endovascular treatment is lower morbidity and mortality whereas surgical treatment is associated higher patency rates.

Risk factors

Risk factors for PAD are similar to those important in the aetiology of CAD and are the typical risk factors for atherosclerotic disease. These include the traditional risk factors: smoking, dyslipidaemia, diabetes mellitus, and hypertension. For private practice cardiologists three areas are important and are focused upon:

1. Extracranial carotid/vertebral artery disease
2. Renal artery disease
3. LEAD (lower extremity artery disease).

Extracranial carotid/ vertebral artery disease

In general, the risk factors for carotid stenosis are similar to those for LEAD, although smoking, while commonly associated with carotid disease, is not as dominant as it is with LEAD.

In the Western world, ischaemic stroke has a major public health impact as the first cause of long-term disability and the third leading cause of death. Stroke mortality ranges from 10% to 30%, and survivors remain at risk of recurrent neurological and cardiac ischaemic events. The risk of stroke and transient ischaemic attacks (TIAs), defined in most studies as transient neurological deficits usually lasting 1–2 h and no longer than 24 h, increases with age. Major risk factors for stroke include hypertension, hypercholesterolaemia, smoking, diabetes, cerebrovascular disease.

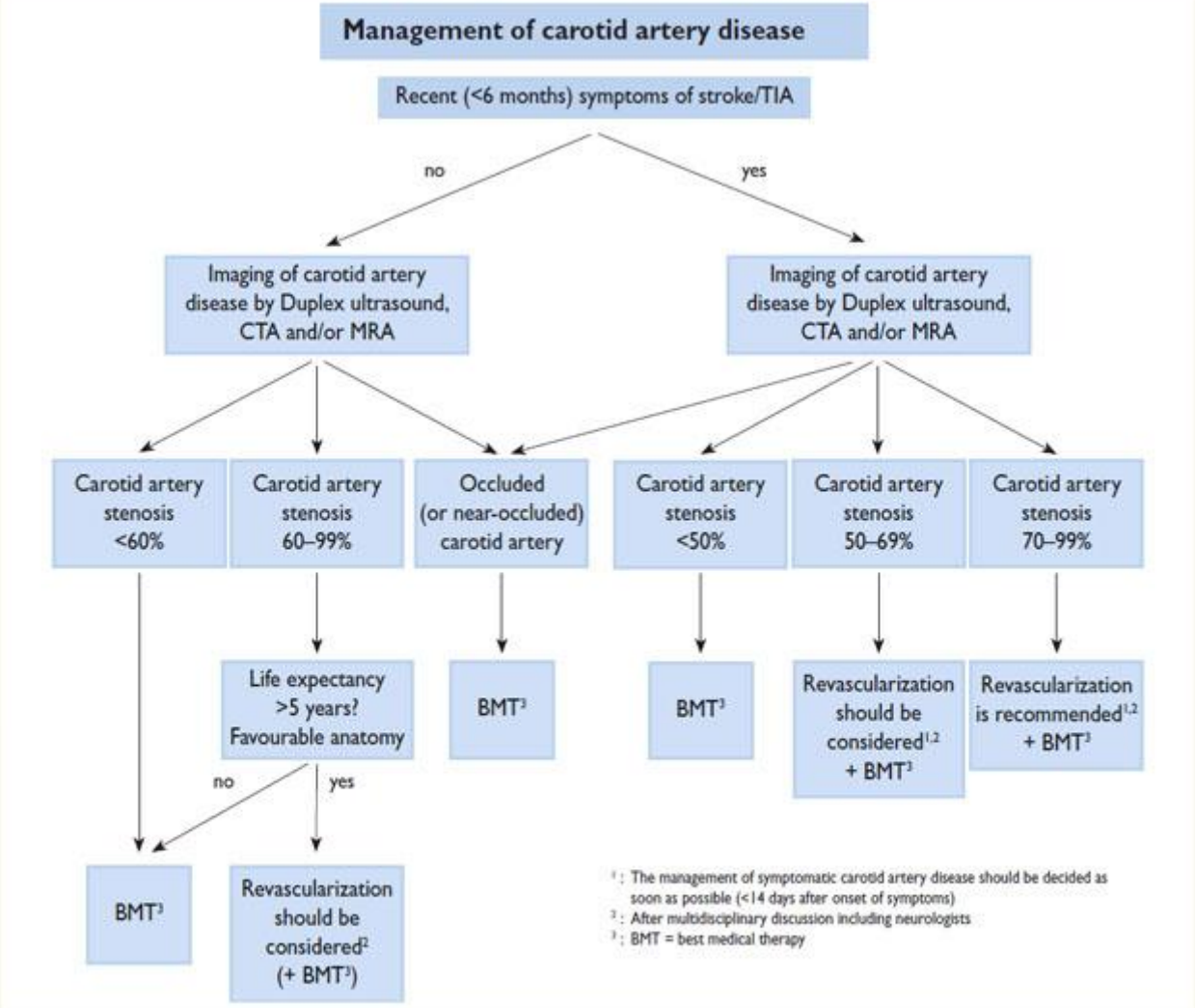


Figure 1 Algorithm for the management of extracranial carotid artery disease.
CTA = computed tomography angiography;
MRA = magnetic resonance angiography;
TIA = transient ischaemic attack.

Recommendations for management of asymptomatic carotid artery disease

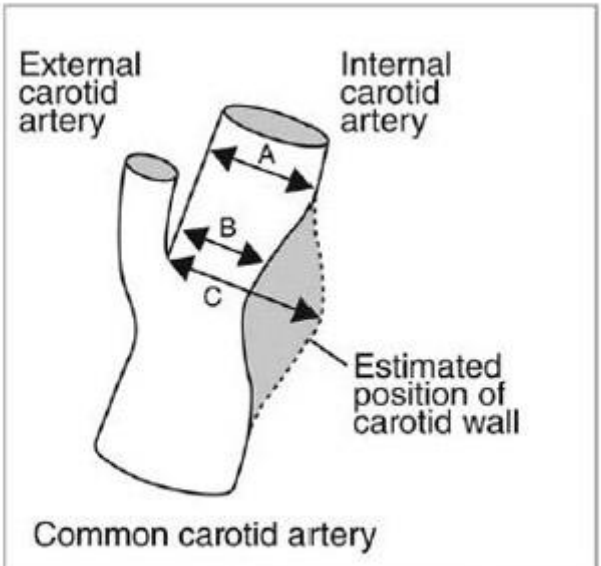
Recommendations	Class[a]	Level[b]	Ref[c]
All patients with asymptomatic carotid artery stenosis should be treated with long-term antiplatelet therapy.	I	B	52, 54, 66
All patients with asymptomatic carotid artery stenosis should be treated with long-term statin therapy.	I	C	-
In asymptomatic patients with carotid artery stenosis ≥60%, CEA should be considered as long as the perioperative stroke and death rate for procedures performed by the surgical team is <3% and the patient's life expectancy exceeds 5 years.	IIa	A	52, 54, 66
In asymptomatic patients with an indication for carotid revascularization, CAS may be considered as an alternative to CEA in high-volume centres with documented death or stroke rate <3%.	IIb	B	79, 99

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
CAS = carotid artery stenting; CEA = carotid endarterectomy.

Recommendations for management of symptomatic carotid artery disease

Recommendations	Class[a]	Level[b]	Ref[c]
All patients with symptomatic carotid stenosis should receive long-term antiplatelet therapy.	I	A	37
All patients with symptomatic carotid stenosis should receive long-term statin therapy.	I	B	60, 61
In patients with symptomatic 70-99% stenosis of the internal carotid artery, CEA is recommended for the prevention of recurrent stroke.	I	A	50, 51, 91, 92
In patients with symptomatic 50-69% stenosis of the internal carotid artery, CEA should be considered for recurrent stroke prevention, depending on patient-specific factors.	IIa	A	50, 51, 91, 92
In symptomatic patients with indications for revascularization, the procedure should be performed as soon as possible, optimally within 2 weeks of the onset of symptoms.	I	B	93
In symptomatic patients at high surgical risk requiring revascularization, CAS should be considered as an alternative to CEA.	IIa	B	79, 99, 102

Duplex ultrasound / duplex ultrasonography (DUS) is commonly used as the first step to detect extracranial carotid artery stenosis and to assess its severity. The peak systolic velocity measured in the internal carotid artery is the primary variable used for this purpose; secondary variables include the end diastolic velocity in the internal carotid artery as well as the ratio of peak systolic velocity in the internal carotid artery to that in the common carotid artery.
Although DUS evaluation may be hampered by severe plaque calcifications, tortuous vessels, tandem lesions, and slow turbulent flow in subtotal stenoses, this imaging modality allows for a reliable estimation of the degree of the stenosis as well as for the assessment of plaque morphology in the hands of an experienced investigator.



NASCET $\frac{A-B}{A}$ ECST $\frac{C-B}{C}$

NASCET	ECST
30 40	65 70
50	75
60	80
70	85
80 90	91 97

Approximate equivalent degrees of internal carotid artery stenosis used in NASCET and ESCT according to recent comparisons

Figure 1 Differences between NASCET and ECST measurement trechniques of internal carotid artery stenosis. Reproduced with permission from Donnan GA *et al. Lancet* 1989;**351**:1372–1373.[15]

The advantages of computed tomography angiography (CTA) and magnetic resonance angiography (MRA) include the simultaneous imaging of the aortic arch, the complete common and internal carotid arteries, the intracranial circulation, as well as the brain parenchyma.
MRA is more time-consuming than CTA but does not expose patients to radiation, and the contrast agents used are far less nephrotoxic. CTA offers excellent sensitivity and specificity for the detection of carotid artery stenosis, however the presence of severe plaque calcification may lead to overestimation of the degree of stenosis. In a systematic review and meta-analysis, no major difference was found between DUS, MRA, and CTA for the detection of a significant carotid artery stenosis.

In order to improve the accuracy of the diagnosis, **the use of two imaging modalities prior to revascularization** is suggested. **Digital subtraction angiography** (DSA) may be required for diagnostic purposes only in selected cases (e.g. discordant non-invasive imaging results, additional intracranial vascular disease). In patients with severe asymptomatic carotid artery stenosis, imaging of the brain to detect asymptomatic embolic events and a transcranial Doppler for emboli detection, may be considered.

Recommendation for evaluation of carotid artery stenosis

Recommendations	Class[a]	Level[b]	Ref[c]
DUS, CTA, and/or MRA are indicated to evaluate carotid artery stenosis.	I	A	59

[a]Class of recommendation.
[b]Level of evidence.
[c]Reference.
CTA = computed tomography angiography; DUS = duplex ultrasonography; MRA = magnetic resonance angiography.

Recommendations for renal disease

Recommendations for diagnostic strategies for renal artery stenosis (RAS)

Table 4 Clinical situations where the diagnosis of RAS should be considered

Clinical presentation
• Onset of hypertension before the age of 30 years and after 55 years
• Hypertension with hypokalemia, in particular when receiving thiazide diuretics
• Hypertension and abdominal bruit
• Accelerated hypertension (sudden and persistent worsening of previously controlled hypertension)
• Resistant hypertension (failure of blood-pressure control despite full doses of an appropriate three-drug regimen including a diuretic)
• Malignant hypertension (hypertension with coexistent end-organ damage, i.e. acute renal failure, flash pulmonary oedema, hypertensive left ventricular failure, aortic dissection, new visual or neurological disturbance, and/or advanced retinopathy)
• New azotemia or worsening renal function after the administration of an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker
• Unexplained hypotrophic kidney
• Unexplained renal failure

RAS = renal artery stenosis.

Recommendations for diagnostic strategies for RAS

Recommendations	Class[a]	Level[b]	Ref[c]
DUS is recommended as the first-line imaging test to establish the diagnosis of RAS.	I	B	171, 172
CTA (in patients with creatinine clearance >60 mL/min) is recommended to establish the diagnosis of RAS.	I	B	151, 174
MRA (in patients with creatinine clearance >30 mL/min) is recommended to establish the diagnosis of RAS.	I	B	174
When the clinical index of suspicion is high and the results of non-invasive tests are inconclusive, DSA is recommended as a diagnostic test (prepared for intervention) to establish the diagnosis of RAS.	I	C	-
Captopril renal scintigraphy, selective renal vein renin measurements, plasma renin activity, and the captopril test are not recommended as useful screening tests to establish the diagnosis of RAS.	III	B	151, 178

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
CTA = computed tomography angiography; DSA = digital subtraction angiography; DUS = duplex ultrasonography; MRA = magnetic resonance angiography; RAS = renal artery stenosis.

Medical therapy for renal disease

All patients with atherosclerotic RAS should be treated according to the European Guidelines on Cardiovascular Disease Prevention.

Revascularization for renal disease

There are some new studies that support a more important role for renal revascularization. For example, the ASTRAL (Angioplasty and Stent for Renal Artery Lesions) study.

It is mentioned that ongoing studies such as the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trial will provide additional evidence relevant to these recommendations in the near future.

Recommendations: treatment strategies for RAS

Recommendations	Class[a]	Level[b]	Ref[c]
Medical therapy			
ACE inhibitors, angiotensin II receptor blockers, and calcium channel blockers are effective medications for treatment of hypertension associated with unilateral RAS.	I	B	166, 182, 183, 189, 192, 219
ACE inhibitors and angiotensin II receptor blockers are contraindicated in bilateral severe RAS and in the case of RAS in a single functional kidney.	III	B	151, 166, 182, 183, 189, 192
Endovascular therapy			
Angioplasty, preferably with stenting, may be considered in the case of >60% symptomatic RAS secondary to atherosclerosis.	IIb	A	151, 201-204
In the case of indication for angioplasty, stenting is recommended in ostial atherosclerotic RAS.	I	B	205, 220
Endovascular treatment of RAS may be considered in patients with impaired renal function.	IIb	B	193, 206, 221-223
Treatment of RAS, by balloon angioplasty with or without stenting, may be considered for patients with RAS and unexplained recurrent congestive heart failure or sudden pulmonary oedema and preserved systolic left ventricular function.	IIb	C	-
Surgical therapy			
Surgical revascularization may be considered for patients undergoing surgical repair of the aorta, patients with complex anatomy of the renal arteries, or after a failed endovascular procedure.	IIb	C	-

Management of lower extremity artery disease (LEAD)

All patients with LEAD are at increased risk of further CVD events and general secondary prevention is mandatory to improve prognosis.

In LEAD, **cigarette smoking** has consistently been shown in several epidemiological studies to be an important risk factor and to be dose-dependent.

Diabetes mellitus is the other risk factor especially important in the development of LEAD. This is certainly true for severe disease, notably gangrene and ulceration, but for intermittent claudication the strength of the association with diabetes may be comparable with that for coronary heart disease. The association of diabetes with LEAD is inconsistent on multivariable analysis, which includes other risk factors, but it appears that the duration and severity of diabetes affect the level of risk.

Ankle–brachial (ABI) index is the primary non-invasive test for the diagnosis of LEAD.

Recommendations for ABI measurement

Recommendations	Class[a]	Level[b]	Ref[c]
Measurement of the ABI is indicated as a first-line non-invasive test for screening and diagnosis of LEAD.	I	B	226
In the case of incompressible ankle arteries or ABI >1.40, alternative methods such as the toe-brachial index, Doppler waveform analysis or pulse volume recording should be used.	I	B	231

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
ABI = ankle–brachial index; LEAD = lower extremity artery disease.

In healthy persons, the ABI is 1.0. Usually an ABI 0.90 is used to define LEAD. The actual sensitivity and specificity have been estimated to be 79% and 96% respectively.

For diagnosis in primary care an ABI of 0.8 or the mean of three ABIs of 0.90 had a positive predictive value of ?95%.

An ABI of 1.10 or the mean of three ABIs of 1.00 had a negative predictive value of ?99%. The level of ABI also correlates with LEAD severity, with high risk of amputation when the ABI is 0.50.

An ABI change of 0.15 is generally required to consider worsening of limb perfusion over time, or improving after revascularization.
For its measurement (Figure 2), a 10–12 cm sphygmomanometer cuff placed just above the ankle and a (handheld) Doppler instrument (5–10 MHz), to measure the pressure of the posterior and anterior tibial arteries of each foot, are required.

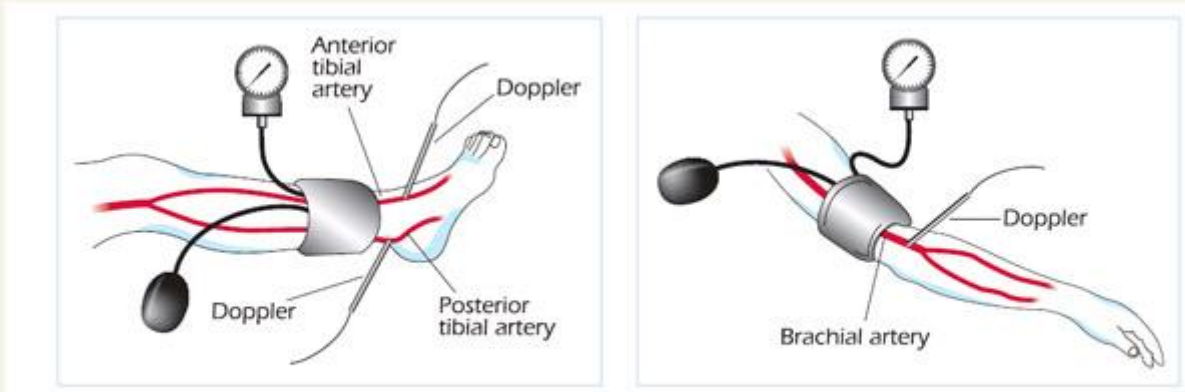


Figure 2 Measurement of the ankle–brachial index (ABI), calculated by dividing the ankle systolic blood pressure by the arm systolic blood pressure.

Usually the highest ankle systolic pressure is divided by the highest brachial systolic pressure, resulting in an ABI per leg.
Recently some papers reported higher sensitivity to detect LEAD if the ABI numerator is the lowest pressure in the arteries of both ankles. Patients with asymptomatic LEAD have no indication for prophylactic revascularization.

The recommendations for patients with intermittent claudication are shown here.

Recommendations for patients with intermittent claudication

Recommendations	Class[a]	Level[b]	Ref[c]
Supervised exercise therapy is indicated.	I	A	255
Non-supervised exercise therapy is indicated when supervised exercise therapy is not feasible or available.	I	C	-
In patients with intermittent claudication with symptoms affecting daily life activity, drug therapy may be considered.	IIb	A	260-265, 269
In the case of intermittent claudication with poor improvement after conservative therapy, revascularization should be considered.	IIa	C	-
In patients with disabling intermittent claudication that impacts their activities of daily living, with culprit lesions located at the aorta/ iliac arteries, revascularization (endovascular or surgical) should be considered as first-choice therapeutic option, along with the risk factor management.	IIa	C	-
Stem cell/gene therapy is not indicated.	III	C	-

[a]Class of recommendation.
[b]Level of evidence.
[c]References.

Critical limb ischaemia (CLI) is the most severe clinical manifestation of LEAD, defined as the presence of ischaemic rest pain, and ischaemic lesions or gangrene objectively attributable to arterial occlusive disease. An ankle pressure of 50 mmHg is usually recommended as a diagnostic criterion because it includes most patients for whom rest pain or ischaemic lesions do not improve spontaneously without

intervention. For patients with ischaemic lesions or gangrene, CLI is suggested by an ankle pressure of 70 mmHg. Toe pressure of 30 mmHg replaces the ankle pressure criteria in the case of medial calcinosis.

The investigation of the microcirculation (i.e. transcutaneous oxygen pressure) is also helpful in some cases, not only for diagnostic and prognostic purpose, but also sometimes to determine the level of amputation.

CLI is also a marker for generalized,severe atherosclerosis, with a three-fold risk excess of future myocardial infarction, stroke, and vascular death compared with patients with intermittent claudication.

The therapeutic strategies are described in ESC Guidelines on the diagnosis and treatment of peripheral artery diseases chapter 4.5.3

Recommendations for the management of critical limb ischaemia

Recommendations	Class[a]	Level[b]	Ref[c]
For limb salvage, revascularization is indicated whenever technically feasible.	I	A	302, 331, 336
When technically feasible, endovascular therapy may be considered as the first-line option.	IIb	B	302, 331
If revascularization is impossible, prostanoids may be considered.	IIb	B	338, 339

[a]Class of recommendation.
[b]Level of evidence.
[c]References.