9.6.2.3 Technical considerations for revascularization
See Web addenda 9.6.2.3.

Recommendations for treatment strategies for renal artery disease

Recommendations	Class[a]	Level[b]
Medical therapy		
ACEIs/ARBs are recommended for treatment of hypertension associated with unilateral RAS.[219–222,240]	I	B
Calcium channel blockers, beta-blockers and diuretics are recommended for treatment of hypertension associated with renal artery disease.	I	C
ACEIs/ARBs may be considered in bilateral severe RAS and in the case of stenosis in a single functioning kidney, if well-tolerated and under close monitoring.[219,221]	IIb	B
Revascularization		
Routine revascularization is not recommended in RAS secondary to atherosclerosis.[229,231,232]	III	A
In cases of hypertension and/or signs of renal impairment related to renal arterial fibromuscular dysplasia, balloon angioplasty with bailout stenting should be considered.[234–236]	IIa	B
Balloon angioplasty, with or without stenting, may be considered in selected patients with RAS and unexplained recurrent congestive heart failure or sudden pulmonary oedema.[229,237,238]	IIb	C
In the case of an indication for revascularization, surgical revascularization should be considered for patients with complex anatomy of the renal arteries, after a failed endovascular procedure or during open aortic surgery.[241–243]	IIa	B

ACEIs = angiotensin-converting enzyme inhibitor; ARBs = angiotensin-receptor blockers; RAS = renal artery stenosis.
[a]Class of recommendation.
[b]Level of evidence.

10. Lower extremity artery disease

Key messages

- Most patients with LEAD are asymptomatic. Walking capacity must be assessed to detect clinically masked LEAD.
- The clinical signs vary broadly. Atypical symptoms are frequent.
- Even asymptomatic patients with LEAD are at high risk of CV events and will benefit from most CV preventive strategies, especially strict control of risk factors.
- Antithrombotic therapies are indicated in patients with symptomatic LEAD. There is no proven benefit for their use in asymptomatic patients.
- Ankle-brachial index is indicated as a first-line test for screening and diagnosis of LEAD. DUS is the first imaging method.
- Data from anatomical imaging tests should always be analysed in conjunction with symptoms and haemodynamic tests prior to treatment decision.
- In patients with intermittent claudication, CV prevention and exercise training are the cornerstones of management. If daily life activity is severely compromised, revascularization can be proposed, along with exercise therapy.
- Chronic limb-threatening ischaemia specifies clinical patterns with a vulnerable limb viability related to several factors. The risk is stratified according to the severity of ischaemia, wounds and infection.
- Early recognition of tissue loss and/or infection and referral to a vascular specialist is mandatory for limb salvage by a multidisciplinary approach. Revascularization is indicated whenever feasible.
- Acute limb ischaemia with neurological deficit mandates urgent revascularization.

10.1. Clinical presentation and natural history

LEAD has several different presentations, categorized according to the Fontaine or Rutherford classifications (*Table 6*). Even with a similar extent and level of disease progression, symptoms and their intensity may vary from one patient to another. The current background information and detailed discussion of the data for the following section of these Guidelines can be found in ESC CardioMed.

Most patients are asymptomatic, detected either by a low ABI (<0.90) or pulse abolition. Among these, a subset may have severe disease without symptoms, which can be related to their incapacity to walk enough to reveal symptoms (e.g. heart failure) and/or reduced pain sensitivity (e.g. diabetic neuropathy). This subgroup should be qualified as 'masked LEAD'. In a study of 460 patients with LEAD, one-third of asymptomatic patients were unable to walk more than six blocks, corresponding to this concept.[244] These patients were older, more often women, with higher rates of neuropathy and multiple comorbidities. While all asymptomatic patients are at increased risk of CV events, the subgroup with masked LEAD is also at high risk of limb events. This situation explains how a subset of patients presents a specific path with 'asymptomatic' disease shifting rapidly to severe LEAD. A typical presentation is an elderly patient with several comorbidities who presents with toe necrosis after a trivial wound (e.g. after aggressive nail clipping). It is important to identify these patients to educate them about foot protection. Hence, prior to the estimation of pain when walking, a clinical assessment of walking ability is necessary, and clinical examination should also look for neuropathy. LEAD can also be clinically masked in one leg when the other one has more disabling disease.

In symptomatic patients, the most typical presentation is IC. The Edinburgh Claudication Questionnaire is a standardized method to screen and diagnose typical IC.[245]

CLTI is defined by the presence of ischaemic rest pain, with or without tissue loss (ulcers, gangrene) or infection. When present,

Table 6 Clinical stages of lower extremity artery disease

Fontaine classification				Rutherford classification		
Stage		Symptoms		Grade	Category	Symptoms
I		Asymptomatic	⇔	0	0	Asymptomatic
II	IIa	Non-disabling intermittent claudication	⇔	I	1	Mild claudication
				I	2	Moderate claudication
	IIb	Disabling intermittent claudication		I	3	Severe claudication
III		Ischaemic rest pain	⇔	II	4	Ischaemic rest pain
IV		Ulceration or gangrene	⇔	III	5	Minor tissue loss
				III	6	Major tissue loss

arterial ulcers are usually painful and are often complicated by local infection and inflammation. When pain is absent, peripheral neuropathy should be considered. While CLTI is a clinical diagnosis, it is often associated with an ankle pressure <50 mmHg or toe pressure <30 mmHg.[246] Investigation of the microcirculation [i.e. transcutaneous oxygen pressure ($TcPO_2$)] is helpful in some cases of medial calcinosis.

Regular clinical examination is important in elderly patients, especially diabetic patients.[247] Early recognition of tissue loss and referral to a vascular specialist is mandatory to improve limb salvage. Primary major amputation rates in patients unsuitable for revascularization are high (20–25%).[248] CLTI is also a marker for generalized, severe atherosclerosis, with a 3-fold increased risk of MI, stroke and vascular death as compared to patients with IC.[246,248]

Clinical examination is fundamental but the diagnosis must be confirmed by objective tests. Pulse palpation should be systematic. Abdominal and/or groin auscultation is poorly sensitive. In severe cases, inspection may show foot pallor in a resting leg, with extended recoloration time (>2 s) after finger pressure.

Regarding the natural history, in a recent meta-analysis,[249] most patients with IC present increased 5-year cumulative CV-related morbidity of 13% vs. 5% in the reference population. Regarding the limb risk, at 5 years, 21% progress to CLTI, of whom 4–27% have amputations.[246]

10.2 Diagnostic tests

10.2.1 Ankle-brachial index

The ABI is the first diagnostic step after clinical examination (see **chapter 4**). An ABI ≤0.90 has 75% sensitivity and 86% specificity to diagnose LEAD.[250] Its sensitivity is poorer in patients with diabetes or end-stage CKD because of medial calcification.[251] Patients with borderline ABI (0.90–1.00) need further diagnostic tests (*Table 3* and **chapter 4**). When clinically suspected, a normal ABI (>0.90) does not definitely rule out the diagnosis of LEAD; further post-exercise ABI and/or DUS are necessary. In case of a high ABI (>1.40) related to medial calcification, alternative tests such as toe pressure, toe-brachial index (TBI) or Doppler waveform analysis of ankle arteries are useful. Along with DUS, ABI can be used during patient follow-up. It is also a good tool for stratifying the CV risk (see **chapter 4**).[6]

Recommendations for ankle-brachial index measurement

Recommendations	Class[a]	Level[b]
Measurement of the ABI is indicated as a first-line non-invasive test for screening and diagnosis of LEAD.[250,251]	I	C
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 are indicated.[252]	I	C

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

10.2.2 Treadmill test

The treadmill test (usually using the Strandness protocol at a speed of 3 km/h and 10% slope) is an excellent tool for objective functional assessment and unmasking moderate stenosis, as well as for exercise rehabilitation follow-up. It is also helpful when the ischaemic origin of limb pain is uncertain. The test is stopped when the patient is unable to walk further because of pain, defining maximal walking distance (WD). A post-exercise ankle SBP decrease >30 mmHg or a post-exercise ABI decrease >20% are diagnostic for LEAD.[251]

10.2.3 Imaging methods

10.2.3.1 Ultrasound

DUS provides extensive information on arterial anatomy and haemodynamics. It must be combined with ABI measurement. It presents 85–90% sensitivity and >95% specificity to detect stenosis >50%.[253] A normal DUS at rest should be completed by a post-exercise test when iliac stenosis is suspected, because of lower sensitivity. DUS is operator dependent and good training is mandatory. DUS does not present as a roadmap the entire vasculature. Another imaging technique is usually required when revascularization is considered. DUS is also important to address vein quality for bypass substitutes. It is the method of choice for routine follow-up after revascularization.

10.2.3.2 Computed tomography angiography

In a meta-analysis, the reported sensitivity and specificity of CTA to detect aorto-iliac stenoses >50% were 96% and 98%, respectively, with similar sensitivity (97%) and specificity (94%) for the femoro-popliteal region.[254] The main advantages are visualization of calcifications, clips, stents, bypasses and concomitant aneurysms. Beyond general limitations (radiation, nephrotoxicity and allergies), pitfalls are severe calcifications (impeding the appreciation of stenosis, mostly in distal arteries).

10.2.3.3 Magnetic resonance angiography

The sensitivity and specificity of MRA are ~95% for diagnosing segmental stenosis and occlusion. However, MRA tends to overestimate the degree of stenosis.[255] It cannot visualize arterial calcifications, useful for the estimation of stenosis severity in highly calcified lesions. This is a limitation for selection of the anastomotic site of surgical bypass. The visualization of steel stents is poor. In expert centres, MRA has a higher diagnostic accuracy for tibial arteries than DUS and CTA.

10.2.3.4 Digital subtraction angiography

DSA is often required for guiding percutaneous peripheral interventional procedures or for the identification of patent arteries for distal bypass. It is also often needed for below-the-knee arteries, especially in patients with CLTI, because of the limitation of all other imaging tools to detect ankle/pedal segments suitable for distal bypass.

10.2.3.5 Cardiovascular screening in patients with LEAD

Patients with LEAD often have other concomitant arterial lesions, including other PADs and AAA. See Web addenda 10.2.3.5 and **chapter 11**.

10.2.4 Other tests

Toe systolic BP, TBI and $TcPO_2$ are useful in patients with medial calcinosis and incompressible arteries. For further details see Web addenda 10.2.4.

Recommendations on imaging in patients with lower extremity artery disease

Recommendations	Class[a]	Level[b]
DUS is indicated as a first-line imaging method to confirm LEAD lesions.[253]	I	C
DUS and/or CTA and/or MRA are indicated for anatomical characterization of LEAD lesions and guidance for optimal revascularization strategy.[254–257]	I	C
Data from an anatomical imaging test should always be analysed in conjunction with symptoms and haemodynamic tests prior to a treatment decision.[246]	I	C
DUS screening for AAA should be considered.[258,259]	IIa	C

AAA = abdominal aorta aneurysm; CTA = computed tomography angiography; DUS = duplex ultrasound; LEAD = lower extremity artery disease; MRA = magnetic resonance angiography.
[a]Class of recommendation.
[b]Level of evidence.

10.3 Medical treatment

The therapeutic options addressed here are those to improve limb symptoms or salvage. Treatments proposed to reduce other CV events and mortality are addressed in **chapter 4**.

General prevention strategies can improve limb events. Smoking cessation provides the most noticeable improvement in WD when combined with regular exercise, especially when lesions are located below the femoral arteries. In patients with IC, the natural history is deteriorated by ongoing tobacco use, with increased risk of amputation.[25,260]

Several studies have shown that statins significantly improve the CV prognosis of patients with IC or CLTI.[30,34] Additionally, several meta-analyses have shown a relevant improvement in pain-free and maximal WD with the use of statins.[30,261] It is suggested that statins could limit adverse limb events in patients with LEAD.[33]

In subjects with hypertension, calcium antagonists or ACEIs/ARBs should be preferred because of their potential in peripheral arterial dilatation. A meta-analysis[262] showed improved maximal and pain-free WD when using an ACEI over placebo; however, two of six RCT reports have been recently withdrawn because of unreliable data, and the meta-analysis of the remaining studies is inconclusive.[263] The benefit of verapamil in improving WD in LEAD has been shown in a randomized study.[264] Because of comorbidities such as heart failure, beta-blockers are indicated in some patients with LEAD. Studies have shown that beta-blockers, in particular nebivolol, are safe in patients with IC without negative effects on WD.[49] Metoprolol and nebivolol have been compared in a double-blind RCT including 128 beta-blocker-naive patients with IC and hypertension.[265] After a 48-week treatment period, both drugs were well tolerated and decreased BP equally. In both groups, maximal WD improved significantly. Nebivolol showed an advantage, with significant improvement in pain-free WD [+34% ($P < 0.003$) vs. +17% for metoprolol ($P < 0.12$)]. In a single-centre study of 1873 consecutive CLTI patients who received endovascular therapy, those treated with other beta-blockers did not have a poorer clinical outcome.[266] In a multicentre registry of 1273 patients hospitalized for severe LEAD (of whom 65% had CLTI and 28% were on beta-blocker therapy), death and amputation rates did not differ among those with vs. without beta-blocker.[267]

10.4 Revascularization options: general aspects

See Web addenda 10.4.

10.5 Management of intermittent claudication

10.5.1 Exercise therapy

In patients with IC, exercise therapy (ExT) is effective and improves symptoms and QOL and increases maximal WD. In 30 RCTs including 1816 patients with stable leg pain, ExT improved maximal WD on a treadmill by almost 5 min compared with usual care.[268] Pain-free and maximal WD were increased on average by 82 and 109 m, respectively. Improvement was observed up to 2 years. Moreover, ExT improved QOL. Exercise did not improve ABI. Whether ExT reduces CV events and improves life expectancy is still unclear. Supervised ExT is more effective than unsupervised ExT.[11,269]

In 14 trials with participants assigned to either supervised ExT or unsupervised ExT (1002 participants), lasting from 6 weeks to 12 months, maximal and pain-free WD increased by almost 180 m in favour of supervised ExT. These benefits remained at 1 year. Most studies use programmes of at least 3 months, with a minimum of 3 h/week, with walking to the maximal or submaximal distance. Long-term benefits of ExT are less clear and largely depend on patient compliance. Supervised ExT is safe and routine cardiac screening beforehand is not required.[270] It is also more cost effective than unsupervised ExT,[271] but it is not reimbursed or available everywhere. Although home-based walking ExT is not as effective as supervised ExT, it is a useful alternative, with positive effects on QOL and functional walking capacity vs. walking advice alone.[272,273] Alternative exercise modes (e.g. cycling, strength training and upper-arm ergometry) may be useful when walking exercise is not an option for patients, as these have also been shown to be effective.[274] ExT is impossible in patients with CLTI but can be considered after successful revascularization.[275,276]

10.5.2 Pharmacotherapy to decrease walking impairment

Some antihypertensive drugs (e.g. verapamil),[264] statins,[277,278] antiplatelet agents and prostanoids (prostaglandins I2 and E1)[279] have some favourable effects on WD and leg functioning (see above). Other pharmacological agents claim to increase WD in patients with IC without other effects on CV health. The drugs mostly studied are cilostazol, naftidrofuryl, pentoxifylline, buflomedil, carnitine and propionyl-L-carnitine.[261,280] However, objective documentation of such an effect is limited. The beneficial effects on WD, if any, are generally mild to moderate, with large variability.[261] Also, the incremental benefit of these treatments in addition to ExT and statins is unknown. For further details see Web addenda 10.5.2.

10.5.3 Revascularization for intermittent claudication

The anatomical location and extension of arterial lesions has an impact on revascularization options.

10.5.3.1 Aorto-iliac lesions

Isolated aorto-iliac lesions are a common cause of claudication. In the case of short stenosis/occlusion (<5 cm) of iliac arteries, endovascular therapy gives good long-term patency (≥90% over 5 years) with a low risk of complications.[281] In cases of ilio-femoral lesions, a hybrid procedure is indicated, usually endarterectomy or bypass at the femoral level combined with endovascular therapy of iliac arteries, even with long occlusions. If the occlusion extends to the infrarenal aorta, covered endovascular reconstruction of an aortic bifurcation can be considered. In a small series, 1- and 2-year primary patency was 87% and 82%, respectively.[282] If the occlusion comprises the aorta up to the renal arteries and iliac arteries, aorto-bifemoral bypass surgery is indicated in fit patients with severe life-limiting claudication.[283] In these extensive lesions, endovascular therapy may be an option, but it is not free of perioperative risk and long-term occlusion. In the absence of any other alternative, extra-anatomic bypass (e.g. axillary to femoral bypass) may be considered.

10.5.3.2 Femoro-popliteal lesions

Femoro-popliteal lesions are common in claudicants. If the circulation to the profunda femoral artery is normal, there is a good possibility that the claudication will be relieved with ExT and intervention is mostly unnecessary. If revascularization is needed, endovascular therapy is the first choice in stenosis/occlusions <25 cm. If the occlusion/stenosis is > 25 cm, endovascular recanalization is still possible, but better long-term patency is achieved with surgical bypass, especially when using the great saphenous vein (GSV). No head-to-head trials comparing endovascular therapy and surgery are yet available. In the Zilver-PTX trial, the 5-year primary patency with conventional and drug-eluting stents was 43% and 66%, respectively.[76] The 5-year patency after above-the-knee femoro-popliteal bypass is > 80% with GSV and 67% with prosthetic conduits.[284] The challenge of endovascular therapy is the long-term patency and durability of stents in the femoro-popliteal region, where the artery is very mobile. Several new endovascular solutions, such as atherectomy devices, drug-eluting balloons and new stent designs, have been shown to improve long-term patency.

10.5.4 Management strategy for intermittent claudication

Several studies have demonstrated the efficacy of endovascular therapy and open surgery on symptom relief, WD and QOL in claudicants. However, these interventions have limited durability and may be associated with mortality and morbidity. Thus they should be restricted to patients who do not respond favourably to ExT (e.g. after a 3-month period of ExT) or when disabling symptoms substantially alter daily life activities. A systematic review of 12 trials (1548 patients) comparing medical therapy, ExT, endovascular therapy and open surgery in claudicants showed that, compared with the former, each of the three other alternatives was associated with improved WD, claudication symptoms and QOL.[285] Compared with endovascular therapy, open surgery may be associated with longer hospital stays and higher complication rates but results in more durable patency. The Claudication: Exercise Versus Endoluminal Revascularization (CLEVER) trial randomized 111 patients with IC and aorto-iliac lesions to BMT alone or in combination with supervised ExT or stenting.[286] At 6 months, changes in maximal WD were greatest with supervised ExT, while stenting provided greater improvement in peak walking time than BMT alone. At 18 months the difference in terms of peak walking time was not statistically different between supervised EXT and stenting.[286] The management of patients with intermittent claudication is summarized in *Figure 5*.

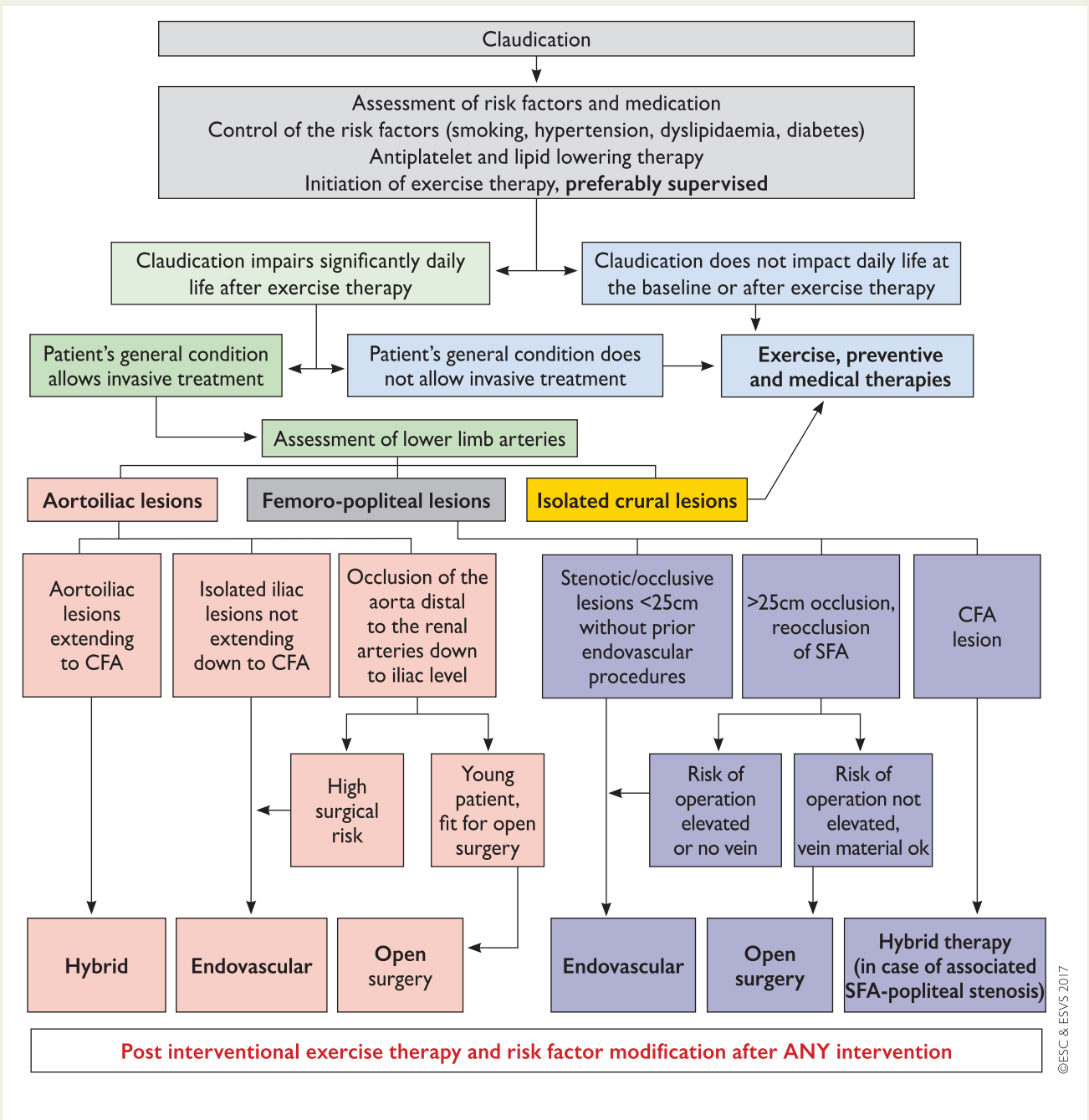

Figure 5 Management of patients with intermittent claudication[a]. CFA = common femoral artery; SFA = superficial femoral artery.
[a]Related to atherosclerotic lower extremity artery disease (LEAD).

Recommendations for the management of patients with intermittent claudication

Recommendations	Class[a]	Level[b]
On top of general prevention, statins are indicated to improve walking distance.[30,278]	I	A
In patients with intermittent claudication:		
• supervised exercise training is recommended[273,287–289]	I	A
• unsupervised exercise training is recommended when supervised exercise training is not feasible or available.	I	C
When daily life activities are compromised despite exercise therapy, revascularization should be considered.	IIa	C
When daily life activities are is severely compromised, revascularization should be considered in association with exercise therapy.[288,290]	IIa	B

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

Recommendations on revascularization of aorto-iliac occlusive lesions[c]

Recommendations	Class[a]	Level[b]
An endovascular-first strategy is recommended for short (i.e. <5 cm) occlusive lesions.[291]	I	C
In patients fit for surgery, aorto-(bi)femoral bypass should be considered in aorto-iliac occlusions.[281,292,293]	IIa	B
An endovascular-first strategy should be considered in long and/or bilateral lesions in patients with severe comorbidities.[288,294,295]	IIa	B
An endovascular-first strategy may be considered for aorto-iliac occlusive lesions if done by an experienced team and if it does not compromise subsequent surgical options.[76,281–283,286]	IIb	B
Primary stent implantation rather than provisional stenting should be considered.[294–296]	IIa	B
Open surgery should be considered in fit patients with an aortic occlusion extending up to the renal arteries.	IIa	C
In the case of ilio-femoral occlusive lesions, a hybrid procedure combining iliac stenting and femoral endarterectomy or bypass should be considered.[297–300]	IIa	C
Extra-anatomical bypass may be indicated for patients with no other alternatives for revascularization.[301]	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]These recommendations apply for patients with intermittent claudication and severe chronic limb ischaemia.

Recommendations on revascularization of femoro-popliteal occlusive lesions[c]

Recommendations	Class[a]	Level[b]
An endovascular-first strategy is recommended in short (i.e. <25 cm) lesions.[302,303]	I	C
Primary stent implantation should be considered in short (i.e. <25 cm) lesions.[304,305]	IIa	A
Drug-eluting balloons may be considered in short (i.e. <25 cm) lesions.[77,306–310]	IIb	A
Drug-eluting stents may be considered for short (i.e. <25 cm) lesions.[302,303,311]	IIb	B
Drug-eluting balloons may be considered for the treatment of in-stent restenosis.[312,313]	IIb	B
In patients who are not at high risk for surgery, bypass surgery is indicated for long (i.e. ≥25 cm) superficial femoral artery lesions when an autologous vein is available and life expectancy is > 2 years.[314]	I	B
The autologous saphenous vein is the conduit of choice for femoro-popliteal bypass.[284,315]	I	A
When above-the-knee bypass is indicated, the use of a prosthetic conduit should be considered in the absence of any autologous saphenous vein.[284]	IIa	A
In patients unfit for surgery, endovascular therapy may be considered in long (i.e. ≥25 cm) femoro-popliteal lesions.[312]	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]These recommendations apply for patients with intermittent claudication and severe chronic limb ischaemia.

10.6 Chronic limb-threatening ischaemia

This entity includes clinical patterns with a threatened limb viability related to several factors. In contrast to the former term 'critical limb ischaemia', severe ischaemia is not the only underlying cause. Three issues must be considered with the former terminology of critical limb ischaemia. First, 'critical' implies that treatment is urgent to avoid limb loss, while some patients can keep their legs for long periods of time even in the absence of revascularization.[316] Second, the increasing predominance of diabetes in these situations, present in 50–70% of cases, presents mostly as neuro-ischaemic diabetic foot ulcers. Third, the risk of amputation not only depends on the severity of ischaemia, but also the presence of a wound and infection. This explains why ankle or toe pressures, measured to address LEAD severity, are not a definition component of CLTI.

10.6.1 Chronic limb-threatening ischaemia severity and risk stratification: the WIfI classification

A new classification system (WIfI) has been proposed as the initial assessment of all patients with ischaemic rest pain or wounds.[317] The target population for this system includes any patient with

- ischaemic rest pain, typically in the forefoot with objectively confirmed haemodynamic studies (ABI <0.40, ankle pressure <50 mmHg, toe pressure <30 mmHg, $TcPO_2$ <30 mmHg),
- diabetic foot ulcer,
- non-healing lower limb or foot ulceration ≥2 weeks duration or
- gangrene involving any portion of the foot or lower limb.

The three primary factors that constitute and contribute to the risk of limb threat are wound (W), ischaemia (I) and foot infection (fI).

Each factor is graded into four categories (0 = none, 1 = mild, 2 = moderate, 3 = severe). *Table 7* shows the coding and clinical staging according to the WIfI classification. Web Figure 2 provides an estimation of the amputation risk according the WIfI classification. The management of patients with CLTI should consider the three components of this classification system. Revascularization should always be discussed, as its suitability is increased with more severe stages (except stage 5).

10.6.2 Management of patients with chronic limb-threatening ischaemia

The management of patients with CLTI is summarized in *Figure 6*. All patients with CLTI must have BMT with correction of risk factors (see **section 9.3**). In those with diabetes, glycaemic control is particularly important for improved limb-related outcomes, including lower rates of major amputation and increased patency after infrapopliteal revascularization.[318,319] Proper wound care must be started immediately, as well as the use of adapted footwear, treatment of concomitant infection and pain control.

10.6.2.1 Revascularization

Revascularization should be attempted as much as possible.[246,320–322] So far, only one randomized trial, the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial, has directly compared endovascular therapy to open surgery in CLTI patients.[323] At 2 years there was no significant difference between endovascular therapy and surgery regarding amputation-free survival. In survivors after 2 years, bypass surgery was associated with improved survival (on average 7 months, $P = 0.02$) and amputation-free survival (6 months,

Table 7 Assessment of the risk of amputation: the WIFI classification (for further details see Mills *et al*[317])

Component	Score	Description		
W (Wound)	0	No ulcer (ischaemic rest pain)		
	1	Small, shallow ulcer on distal leg or foot without gangrene		
	2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes		
	3	Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene		
I (Ischaemia)		ABI	Ankle pressure (mmHg)	Toe pressure or $TcPO_2$
	0	≥0.80	> 100	≥60
	1	0.60–0.79	70–100	40–59
	2	0.40–0.59	50–70	30–39
	3	<0.40	<50	<30
fI (foot Infection)	0	No symptoms/signs of infection		
	1	Local infection involving only skin and subcutaneous tissue		
	2	Local infection involving deeper than skin/subcutaneous tissue		
	3	Systemic inflammatory response syndrome		
Example: A 65-year-old male diabetic patient with gangrene of the big toe and a <2 cm rim of cellulitis at the base of the toe, without any clinical/biological sign of general infection/inflammation, whose toe pressure is at 30 mmHg would be classified as Wound 2, Ischaemia 2, foot Infection 1 (WIfI 2-2-1). The clinical stage would be 4 (high risk of amputation). The benefit of revascularization (if feasible) is high, also depending on infection control.				

ABI = ankle-brachial index; TcPO2 = transcutaneous oxygen pressure.

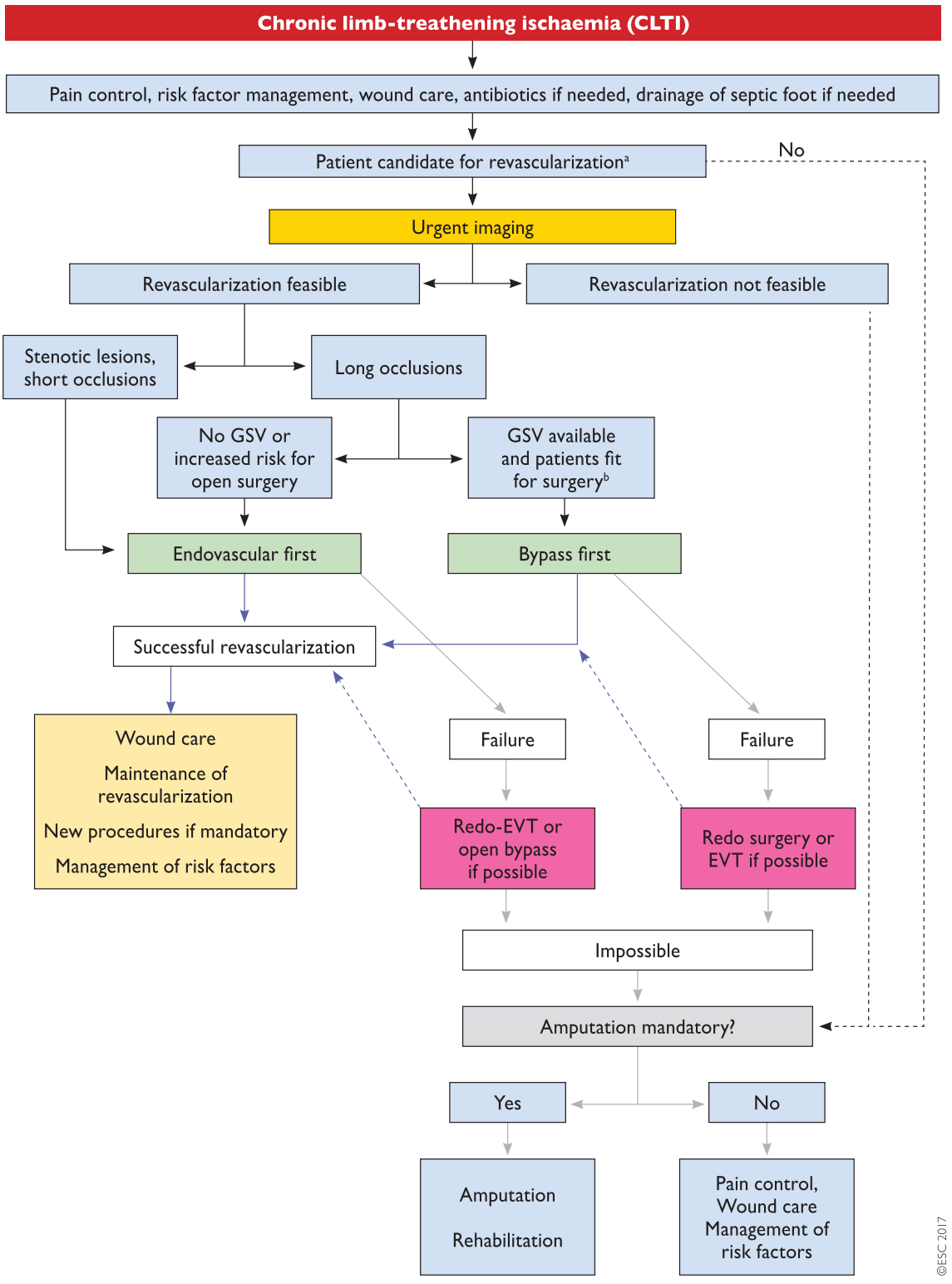

Figure 6 Management of patients with chronic limb-threatening ischaemia. EVT= endovascular therapy; GSV = great saphenous vein.
[a]In bedridden, demented and/or frail patients, primary amputation should be considered.
[b]In the absence of contra-indication for surgery and in the presence of adequate target for anastomosis/runoff.

$P = 0.06$).[314] These data are challenged by more recent endovascular therapy techniques. So far, drug-eluting balloons in below-the-knee disease have shown no superiority over plain balloon angioplasty.[324] The results of two ongoing RCTs, BASIL-2 and Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischaemia (BEST-CLI), are awaited.[325,326] Meanwhile, in each anatomical region, both revascularization options should be individually discussed.

10.6.2.1.1 Aorto-iliac disease. CLTI is almost never related to isolated aorto-iliac disease, and downstream lesions are often concomitant. In addition to CTA and/or MRA, complete DSA down to the plantar arches is required for proper arterial network assessment and procedure planning.[327] Hybrid procedures (e.g. aorto-iliac stenting and distal bypass) should be encouraged in a one-step modality when necessary.

10.6.2.1.2 Femoro-popliteal disease. CLTI is unlikely to be related to isolated SFA lesions; usually femoro-popliteal involvement combined with aorto-iliac or below-the-knee disease is found. In up to 40% of cases, inflow treatment is needed.[324] The revascularization strategy should be judged on lesion complexity. If endovascular therapy is chosen first, landing zones for potential bypass grafts should be preserved. When bypass surgery is decided, the bypass should be as short as possible, using the saphenous vein.

10.6.2.1.3 Infra-popliteal disease. Extended infra-popliteal artery disease is mainly seen in diabetic patients, often associated with SFA lesions (inflow disease). Full-leg DSA down to the plantar arches is mandatory to explore all revascularization options.[327] In stenotic lesions and short occlusions, endovascular therapy can be the first choice. In long occlusions of crural arteries, bypass with an autologous vein gives superior long-term patency and leg survival. If the patient has increased risk for surgery or does not have an autologous vein, endovascular therapy can be attempted. The decision of revascularization should also consider the angiosome concept, targeting the ischaemic tissues. For further details, see Web addenda 10.6.2.1.3.1.

Recommendations on revascularization of infra-popliteal occlusive lesions

Recommendations	Class[a]	Level[b]
In the case of CLTI, infra-popliteal revascularization is indicated for limb salvage.[320–326]	I	C
For revascularization of infra-popliteal arteries:		
• bypass using the great saphenous vein is indicated	I	A
• endovascular therapy should be considered.[320–326]	IIa	B

CLTI = chronic limb threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

10.6.3 Spinal cord stimulation

See Web addenda 10.6.3.

10.6.4 Stem cell and gene therapy

Angiogenic gene and stem cell therapy are still being investigated, with insufficient evidence in favour of these treatments.[328–330] For further details see Web addenda 10.6.4.

10.6.5 Amputation

10.6.5.1 Minor amputation

In case of CLTI, minor amputation (up to the forefoot level) is often necessary to remove necrotic tissues with minor consequences on patient's mobility. Revascularization is needed before amputation to improve wound healing. Foot $TcPO_2$ and toe pressure can be useful to delineate the amputation zone (see **section 10.2.4**).

10.6.5.2 Major amputation

Patients with extensive necrosis or infectious gangrene and those who are non-ambulatory with severe comorbidities may be best served with primary major amputation. This remains the last option to avoid or halt general complications of irreversible limb ischaemia, allowing in some cases patient recovery with rehabilitation and prosthesis. For a moribund patient, adequate analgesia and other supportive measures may also be an option.

Secondary amputation should be performed when revascularization has failed and re-intervention is no longer possible or when the limb continues to deteriorate because of infection or necrosis despite patent graft and optimal management. In any case, infragenicular amputation should be preferred, because the knee joint allows better mobility with a prosthesis. For bedridden patients, femoral amputation may be the best option.

Recommendations on the management of chronic limb-threatening ischaemia

Recommendations	Class[a]	Level[b]
Early recognition of tissue loss and/or infection and referral to the vascular team is mandatory to improve limb salvage.[317]	I	C
In patients with CLTI, assessment of the risk of amputation is indicated.[317]	I	C
In patients with CLTI and diabetes, optimal glycaemic control is recommended.[318,319]	I	C
For limb salvage, revascularization is indicated whenever feasible.[314]	I	B
In CLTI patients with below-the-knee lesions, angiography including foot runoff should be considered prior to revascularization.	IIa	C
In patients with CLTI, stem cell/gene therapy is not indicated.[328]	III	B

CLTI = chronic limb threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

10.7 Acute limb ischaemia

Acute limb ischaemia is caused by an abrupt decrease in arterial perfusion of the limb. Potential causes are artery disease progression, cardiac embolization, aortic dissection or embolization, graft thrombosis, thrombosis of a popliteal aneurysm or cyst, popliteal artery entrapment syndrome, trauma, phlegmasia cerulea dolens, ergotism, hypercoagulable states and iatrogenic complications related to vascular procedures. Limb viability is threatened and prompt management is needed for limb salvage.

Once the clinical diagnosis is established, treatment with unfractionated heparin should be given, along with appropriate analgesia.[246,331] The emergency level and the choice of therapeutic strategy depend on the clinical presentation, mainly the presence of neurological deficits. The clinical categories are presented in *Table 8*.

In the case of neurological deficit, urgent revascularization is mandatory; imaging should not delay intervention. The imaging method depends on its immediate availability. DUS and DSA are mostly used in these situations.

Different revascularization modalities can be applied, including percutaneous catheter–directed thrombolytic therapy, percutaneous mechanical thrombus extraction or thrombo-aspiration (with or without thrombolytic therapy) and surgical thrombectomy, bypass and/or arterial repair. The strategy will depend on the presence of a neurological deficit, ischaemia duration, its localization, comorbidities, type of conduit (artery or graft) and therapy-related risks and outcomes. Owing to reduced morbidity and mortality, endovascular therapy is often preferred, especially in patients with severe comorbidities. Thrombus extraction, thrombo-aspiration and surgical thrombectomy are indicated in the case of neurological deficit, while catheter-directed thrombolytic therapy is more appropriate in less severe cases without neurological deficit. The modern concept of the combination of intra-arterial thrombolysis and catheter-based clot removal is associated with 6-month amputation rates of < 10%.[246] Systemic thrombolysis has no role in the treatment of patients with acute limb ischaemia.

Based on RCTs, there is no clear superiority of local thrombolysis vs. open surgery on 30-day mortality or limb salvage.[333] After thrombus removal, the pre-existing arterial lesion should be treated by endovascular therapy or open surgery. Lower extremity four-compartment fasciotomies should be performed in patients with long-lasting ischaemia to prevent a post-reperfusion compartment syndrome. The management of acute limb ischaemia is summarized in *Figure 7*.

Table 8 Clinical categories of acute limb ischaemia[332]

Grade	Category	Sensory loss	Motor deficit	Prognosis
I	Viable	None	None	No immediate threat
IIA	Marginally threatened	None or minimal (toes)	None	Salvageable if promptly treated
IIB	Immediately threatened	More than toes	Mild/ moderate	Salvageable if promptly revascularized
III	Irreversible	Profound, anaesthetic	Profound, paralysis (rigor)	Major tissue loss, permanent nerve damage inevitable

Recommendations for the management of patients presenting with acute limb ischaemia

Recommendations	Class[a]	Level[b]
In the case of neurological deficit, urgent revascularization is indicated.[246,331,c]	I	C
In the absence of neurological deficit, revascularization is indicated within hours after initial imaging in a case-by-case decision.[246,331]	I	C
Heparin and analgesics are indicated as soon as possible.[246,331]	I	C

[a]Class of recommendation.
[b]Level of evidence.
[c]In this case, imaging should not delay intervention.

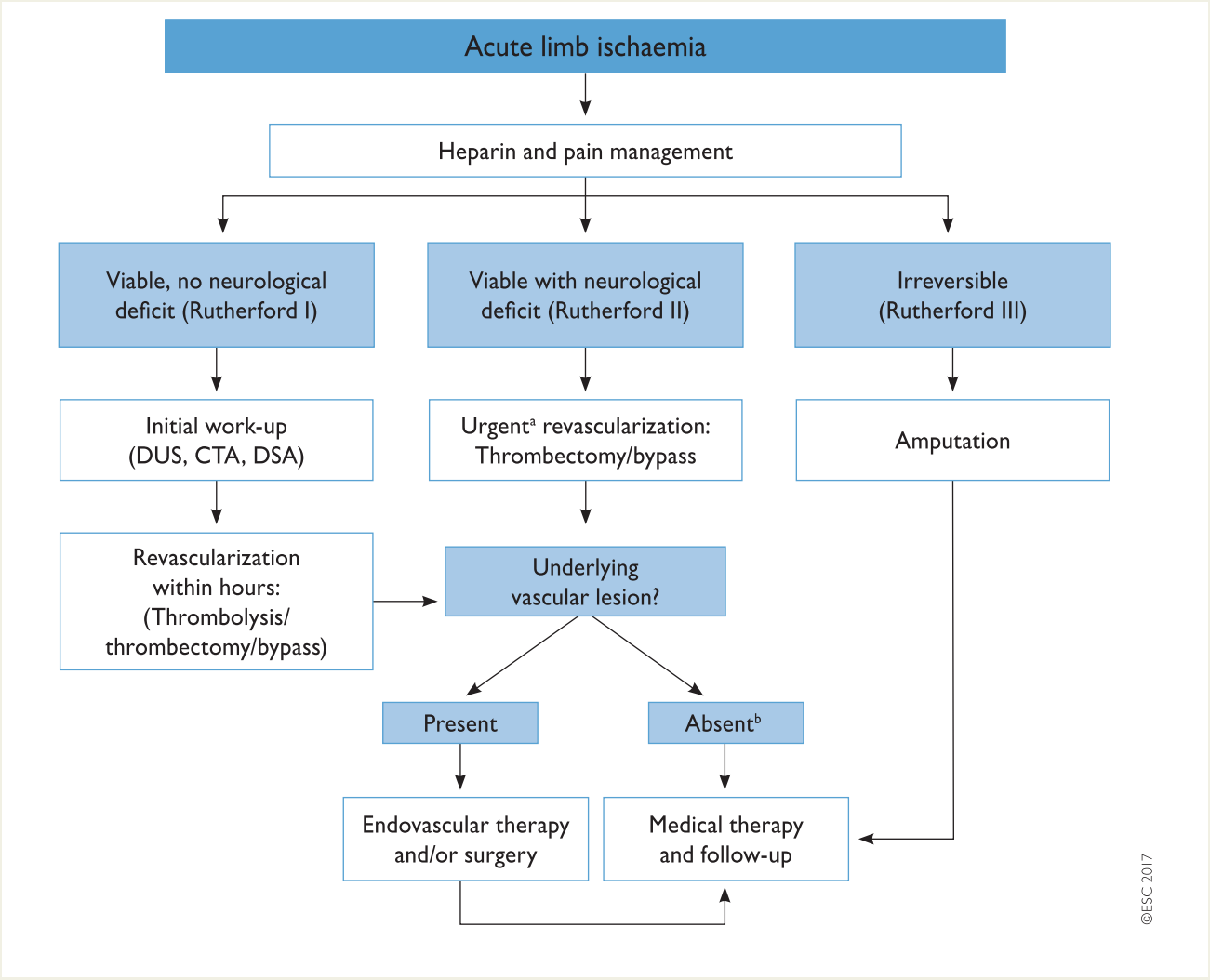

Figure 7 Management of acute limb ischaemia. CTA = computed tomography angiography; DSA = digital subtraction ultrasound; DUS = duplex ultrasound.
[a]Imaging should not delay revascularization.
[b]Specific etiological work-up is necessary (cardiac, aorta).

10.8 Blue toe syndrome

Another particular clinical presentation is blue toe syndrome. This is characterized by a sudden cyanotic discoloration of one or more toes. It is usually due to embolic atherosclerotic debris from the proximal arteries. For further details see Web addenda 10.8.

11. Multisite artery disease

Key messages

- Multisite artery disease (MSAD) is common in patients with atherosclerotic involvement in one vascular bed, ranging from 10 to 15% in patients with CAD to 60 to 70% in patients with severe carotid stenosis or LEAD.
- MSAD is invariably associated with worse clinical outcomes; however, screening for asymptomatic disease in additional vascular sites has not been proven to improve prognosis.
- In patients with any presentation of PADs, clinical assessment of symptoms and physical signs of other localizations and/or CAD is necessary, and in case of clinical suspicion, further tests may be planned.
- Systematic screening for asymptomatic MSAD is not indicated for any presentation of PADs, as it would not consistently lead to a modification of management strategy. It may be interesting in some cases for risk stratification (e.g. an antiplatelet therapy strategy beyond 1 year in patients who benefited from coronary stenting for ACS).
- In some situations the identification of asymptomatic lesions may affect patient management. This is the case for patients undergoing CABG, where ABI measurement may be considered,

especially when saphenous vein harvesting is planned, and carotid screening should be considered in a subset of patients at high risk of CAD.
- In patients scheduled for CABG with severe carotid stenoses, prophylactic carotid revascularization should be considered in recently symptomatic cases and may be considered in asymptomatic cases after multidisciplinary discussion.
- In patients planned for carotid artery revascularization for asymptomatic stenosis, preoperative coronary angiography for detection (and revascularization) of CAD may be considered.

Multisite artery disease (MSAD) is defined by the simultaneous presence of clinically relevant atherosclerotic lesions in at least two major vascular territories. Subclinical plaques are beyond the scope of this document. While patients with MSAD are regularly encountered in clinical practice, robust data on the management of these patients are scarce. For the management of these patients, clinical status and comorbidities should be considered, in addition to the lesion sites. Generally the treatment strategy should be decided case by case within a multidisciplinary team and should focus first on the symptomatic vascular site. The current background information and detailed discussion of the data for the following section of these Guidelines can be found in ESC CardioMed.

11.1 Multisite artery disease: epidemiology and impact prognosis

Among 3.6 million American volunteers for a systematic ultrasound screening for LEAD, CAD and AAA, the proportion of subjects with two or more localizations increased with age, from 0.04% at 40–50 years to 3.6% at 81–90 years.[334] *Figure 8* summarizes the prevalence of MSAD when atherosclerotic disease is diagnosed in one territory.

Although several studies have demonstrated that patients with MSAD have a significantly worse clinical outcome as compared with patients with single vascular site disease, the only RCT designed to assess the impact on prognosis of systematic screening for MSAD in patients with high-risk CAD (three-vessel CAD and/or with an ACS at age >75 years) failed to prove any significant benefit.[344] The Aggressive detection and Management of the Extension of atherothrombosis in high Risk coronary patients In comparison with standard of Care for coronary Atherosclerosis (AMERICA) trial randomized 521 patients to a proactive strategy (total-body DUS and ABI measurement associated with intensive medical therapy) or to conventional strategy (no screening for asymptomatic MSAD and standard medical therapy); at the 2-year follow-up, the primary composite endpoint, including death, any ischaemic event leading to rehospitalization or any evidence of organ failure, occurred in 47.4% and 46.9% of patients, respectively ($P > 0.2$).[344] Hence the clinical benefit of systematic screening for asymptomatic MSAD in patients with known atherosclerotic disease appears questionable.

11.2 Screening for and management of multisite artery disease

11.2.1 Peripheral arterial diseases in patients presenting with coronary artery disease

11.2.1.1 Carotid artery disease in patients scheduled for coronary artery bypass grafting

Web Table 11 details the epidemiology of CAD and the incidence of stroke among patients undergoing isolated CABG (without synchronous/staged CEA).[341] In another study, unilateral 50–99% carotid stenosis was found in 11% of patients, bilateral 50–99% stenosis in 5.6% and unilateral occlusion in 1.3%.[345]

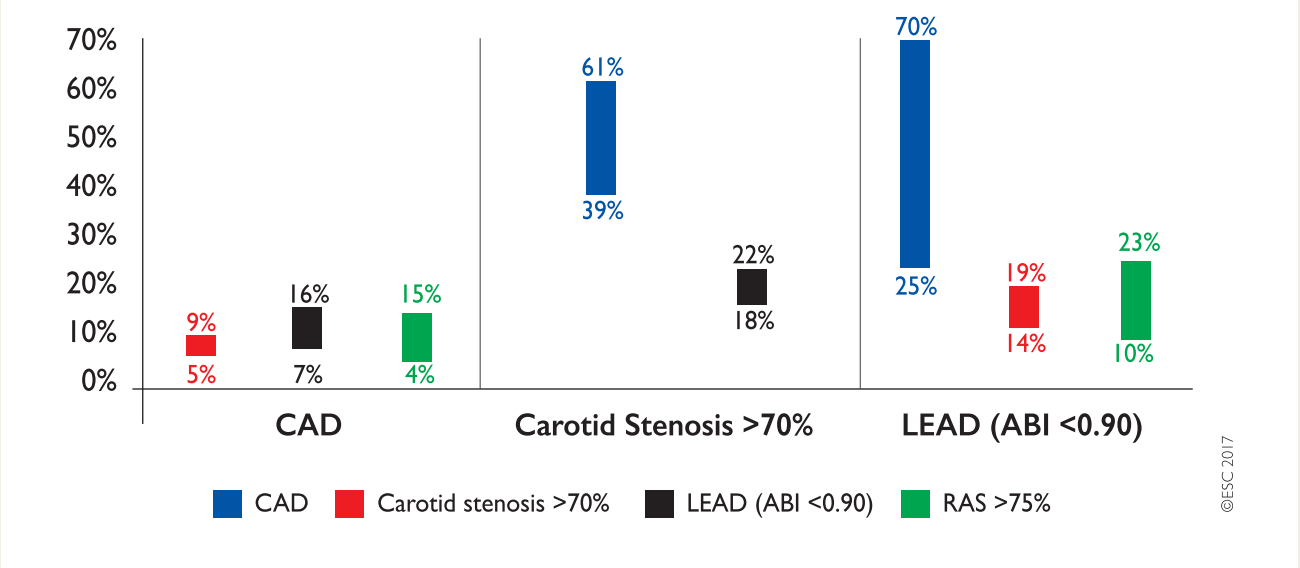

Figure 8 Reported rate ranges of other localizations of atherosclerosis in patients with a specific arterial disease.[51, 335–343] The graph reports the rates of concomitant arterial diseases in patients presenting an arterial disease in one territory (e.g. in patients with CAD, 5 - 9% of cases have concomitant carotid stenosis >70%). ABI = ankle-brachial index; CAD = coronary artery disease; LEAD = lower extremity artery disease; RAS = renal artery stenosis.

Ischaemic stroke after CABG is multifactorial, including aortic embolism during manipulation, cannulation/decannulation and graft anastomosis to the ascending aorta; platelet aggregation during cardiopulmonary bypass (CPB) and hypercoagulable states; carotid embolization; postoperative AF and haemodynamic instability, especially in patients with impaired cerebral vascular reserve.[346]

The impact of asymptomatic carotid stenosis on stroke risk after CABG is modest, except for bilateral stenoses or unilateral occlusion. In a systematic review, 86% of postoperative strokes were not attributed to carotid disease. Carotid stenosis appears as a marker of severe aortic atherosclerosis and stroke risk rather than the direct cause. Conversely, a history of prior stroke/TIA is a significant risk factor for post-CABG stroke.[341,347–349] Evidence of the benefits of prophylactic revascularization of asymptomatic carotid stenoses in all CABG candidates to reduce perioperative stroke is lacking. The decision to perform CEA/CAS in these patients should be made by a multidisciplinary team. It may be reasonable to restrict prophylactic carotid revascularization to patients at highest risk of postoperative stroke, i.e. patients with severe bilateral lesions or a history of prior stroke/TIA.[341,348–350]

The timing and the modality of carotid revascularization (CEA or CAS) are controversial and should be individualized based on clinical presentation, level of emergency and severity of carotid and coronary artery diseases. Web Table 12 details the results of meta-analyses evaluating outcomes following different scenarios. No specific strategy is clearly safer. A recent RCT did not report lower stroke rate for off-pump vs. on-pump surgery.[351]

The two-staged CEA strategies provide higher risk of periprocedural MI if the carotid artery is revascularized first and a trend towards increased cerebral risk if CABG is performed first. In a recent RCT in patients with unilateral asymptomatic carotid stenosis, CABG followed by CEA was the worst strategy, with a higher 90-day stroke and death rate compared with CABG with previous or synchronous CEA (8.8% vs. 1.0%; $P = 0.02$).[352]

The higher risk of cerebral embolization from aortic arch plaques may explain why CAS is not associated with lower procedural risks. If CAS is performed before elective CABG, the need for DAPT usually delays cardiac surgery for at least 4 weeks, exposing the patient to the risk of MI between the staged CAS and CABG (0–1.9%).[353,354] Some authors performed CAS immediately prior to CABG and reported low death/stroke rates.[355] Among 132 patients with same-day CAS plus cardiac surgery, the in-hospital stroke rate was 0.75%, while 5- and 10-year freedom from neurological events was 95% and 85%, respectively.[356] In a single-centre propensity-matched analysis of 350 patients undergoing carotid revascularization within 90 days before cardiac surgery, staged CAS plus cardiac surgery and combined CEA plus cardiac surgery had similar early outcomes (death/stroke/MI), whereas staged CEA plus cardiac surgery incurred the highest risk, driven by interstage MI. Beyond 1 year, patients with either staged or combined CEA plus cardiac surgery had a 3-fold higher rate of MACE compared with patients undergoing staged CAS plus cardiac surgery.[357] However, staged CAS plus cardiac surgery entails an increased bleeding risk during CABG (if performed within the DAPT period).

Two studies suggest that limiting DUS to patients with at least one risk factor (age >70 years, history of cerebrovascular disease, presence of a carotid bruit, multivessel CAD or LEAD) identifies all patients with carotid stenosis >70%, reducing the total number of scans by 40%.[338,358] However, a study comparing patients undergoing a preoperative carotid scan before cardiac surgery with those without screening reported no difference in perioperative mortality and stroke.[345] But only 12% of those with severe carotid stenosis underwent synchronous CABG plus CEA. Hence routine carotid DUS identifies only the minority of patients who will develop perioperative stoke, without clearly evidenced benefit of prophylactic carotid revascularization. Carotid DUS is indicated in patients with recent (<6 months) stroke/TIA. No carotid imaging is indicated when CABG is urgent, unless neurological symptoms occurred in the previous 6 months.

Recommendations on screening for carotid disease in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients undergoing CABG, DUS is recommended in patients with a recent (<6 months) history of TIA/stroke.[345,358]	I	B
In patients with no recent (<6 months) history of TIA/stroke, DUS may be considered in the following cases: age ≥70 years, multivessel coronary artery disease, concomitant LEAD or carotid bruit.[345,358]	IIb	B
Screening for carotid stenosis is not indicated in patients requiring urgent CABG with no recent stroke/TIA.	III	C

CABG = coronary artery bypass grafting; DUS = duplex ultrasound; LEAD = lower extremity artery disease; TIA = transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations on the management of carotid stenosis in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
It is recommended that the indication (and, if so, the method and timing) for carotid revascularization be individualized after discussion within a multidisciplinary team, including a neurologist.	I	C
In patients with a recent (<6 months) history of TIA/stroke who are scheduled for CABG:		
• Carotid revascularization should be considered in patients with 50–99% carotid stenosis.[359,360]	IIa	B
• Carotid revascularization with CEA should be considered as the first choice in patients with 50–99% carotid stenosis.[359,360]	IIa	B
• Carotid revascularization is not recommended in patients with carotid stenosis <50%.	III	C
In neurologically asymptomatic patients scheduled for CABG:		
• Routine prophylactic carotid revascularization in patients with a 70–99% carotid stenosis is not recommended.[350]	III	B
• Carotid revascularization may be considered in patients with bilateral 70–99% carotid stenoses or 70–99% carotid stenosis + contralateral occlusion.[350]	IIb	B
• Carotid revascularization may be considered in patients with a 70–99% carotid stenosis in the presence of one or more characteristics that may be associated with an increased risk of ipsilateral stroke[c] in order to reduce stroke risk beyond the perioperative period.	IIb	C

CABG = coronary artery bypass grafting; CAS = carotid artery stenting; CEA = carotid endarterectomy.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Table 4*.

11.2.1.2 Carotid artery stenosis in other coronary artery disease patients (without coronary artery bypass grafting)

The available data regarding the prevalence of carotid stenosis in these patients and the lack of evidence of any effect on outcome lead to the conclusion that carotid screening is not indicated in patients with CAD other than in candidates for CABG. For further details refer to Web addenda 11.2.1.2.

11.2.1.3. Renal artery disease in patients presenting with coronary artery disease

In the absence of any proof of benefit, systematic screening for RAS in patients with CAD cannot be recommended. For further details refer to Web addenda 11.2.1.3. As in other patients, the indications for imaging renal arteries are presented in *Table 5*.

11.2.1.4 Lower extremity artery disease in patients with coronary artery disease

LEAD often coexists with CAD (*Figure 8*). It is often asymptomatic or masked by limiting angina and/or dyspnoea. LEAD (ABI < 0.90) is present in 13–16% of patients who have CAD at coronary angiography.[361,362] Left main coronary artery stenosis and multivessel CAD were independent predictors. Patients with LEAD exhibit more extensive, calcified and progressive coronary atherosclerosis.[363]

The coexistence of LEAD in CAD patients has been consistently associated with worse outcome, although it is unclear whether LEAD is a marker or a cause of cardiac adverse events.[364,365] In the 3-year follow-up of the PEGASUS trial, patients with concomitant LEAD had adjusted 2-fold increased rates of all-cause death, CV death, stroke and MACE.[81] In ACS registries, in-hospital mortality, acute heart failure and recurrent ischaemia rates were significantly higher (up to 5-fold) in subjects with LEAD.[340,343] In a pooled analysis of 19 867 patients enrolled in RCTs on PCI, 8% had clinical LEAD, identified as an independent predictor of mortality at 30 days (HR 1.67), 6 months (HR 1.76) and 1 year (HR 1.46).[366] Concomitant LEAD (clinical or subclinical) is also associated with worse outcome in patients undergoing CABG.[367,368]

In patients with CAD who have concomitant LEAD, strict risk factor control is mandatory, although no specific recommendations exist, as compared with CAD patients without MSAD. In a post hoc analysis of the CHARISMA trial, DAPT with aspirin and clopidogrel was associated with a significant decrease in non-fatal MI compared with aspirin alone,[65] at a cost of increased minor bleeding. The potential benefits of DAPT in these patients need further confirmation.

In LEAD patients requiring coronary revascularization, the treatment of CAD is usually prioritized, except in the case of CLTI. Whether PCI or CABG should be favoured to treat CAD in patients with LEAD is controversial.[369,370] In the case of PCI, radial artery access should be favoured. If the femoral approach is necessary, pre-interventional assessment of the iliac and common femoral arteries should be performed to minimize the risk of ischaemia/embolization and to identify the best location for arterial puncture, since access site complications are more frequent in these patients, particularly when closure devices are used.[371] In patients undergoing CABG with advanced LEAD, the GSV should be spared whenever possible; later success of peripheral arterial revascularization is strongly dependent on the availability of sufficient autologous venous segments.[372] Also, saphenous vein harvesting may be associated with wound healing delays in severe LEAD. This justifies the screening for LEAD prior to use of the saphenous vein as bypass material, at least by clinical examination and/or ABI. CPB during CABG causes a mean arterial pressure drop and loss of pulsatile flow, entailing the risk of worsening CLTI. When off-pump CABG is not feasible, maintaining an adequate mean arterial pressure and monitoring peripheral oxygen

saturation in CLTI patients are strongly advisable during CPB. Postoperatively, active clinical surveillance is needed to diagnose in a timely fashion the compartment syndrome potentially caused by ischaemia–reperfusion injury during CPB. The coexistence of LEAD, even asymptomatic, may upset cardiac rehabilitation.[373]

Screening for LEAD by means of ABI could represent a non-invasive and inexpensive method for prognostic stratification of patients. However, the AMERICA trial failed to demonstrate the benefit of a proactive strategy of MSAD screening in patients.[344] However, the trial was small, with some limitations. It does not exclude a role for screening for asymptomatic LEAD in CAD patients for prognostic stratification. Importantly, in patients with severe CAD, the presence of symptomatic or asymptomatic LEAD is associated with a high probability (almost 20%) of carotid stenosis.[374]

Recommendations for screening and management of concomitant lower extremity artery disease and coronary artery disease

	Class[a]	Level[b]
In patients with LEAD, radial artery access is recommended as the first option for coronary angiography/intervention.[365]	I	C
In patients with LEAD undergoing CABG, sparing the autologous great saphenous vein for potential future use for surgical peripheral revascularization should be considered.	IIa	C
In patients undergoing CABG and requiring saphenous vein harvesting, screening for LEAD should be considered.	IIa	C
In patients with CAD, screening for LEAD by ABI measurement may be considered for risk stratification.[340,343,344,366–368,375–379]	IIb	B

ABI = ankle-brachial index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; LEAD = lower extremity artery disease; TIA = transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.

11.2.2. Coronary artery disease in patients presenting with peripheral arterial diseases

11.2.2.1. Coronary artery disease in patients with carotid artery stenosis

In a study including 276 patients with non-cardioembolic ischaemic stroke/TIA, coronary CTA detected coronary stenosis (>50%) in 18% of cases. The prevalence was 4-fold higher in the case of carotid stenosis >50%.[380] In a prospective investigation of 390 patients undergoing elective CAS, systematic coronary angiography found coronary artery stenosis ≥70% in 61% of cases.[381]

In the case of severe carotid artery stenosis, the presence of associated CAD requires prioritization of revascularization according to the patient's clinical status and to the severity of carotid and coronary disease. Carotid revascularization should be performed first only in the case of unstable neurological symptoms; asymptomatic carotid stenosis should be treated, whenever appropriate, following CAD revascularization.

In an RCT, 426 patients planned for CEA and without a history of CAD and normal electrocardiogram (ECG) and cardiac ultrasound were randomized to either systematic coronary angiography (with subsequent revascularization) or no coronary angiography.[382] Significant CAD was found (and treated) before CEA in 39% of those randomized to angiography, with no postoperative MI, vs. 2.9% in the no-angiography group ($P = 0.01$). Importantly, PCI delayed CEA by a median of 4 days (range 1–8 days), without neurological events and without bleeding complications in patients on DAPT. At 6 years, patients allocated to systematic coronary angiography had a lower rate of MI (1.4% vs. 15.7%; $P < 0.01$) and improved survival (95% vs. 90%; $P < 0.01$).[383] Hence routine preoperative coronary angiography may be considered in patients undergoing elective CEA.

Recommendation on screening for coronary artery disease in patients with carotid disease

	Class[a]	Level[b]
In patients undergoing elective CEA, preoperative CAD screening, including coronary angiography, may be considered.[382,383]	IIb	B

CAD = coronary artery disease; CEA = carotid endarterectomy.
[a]Class of recommendation.
[b]Level of evidence.

11.2.2.2 Coronary artery disease in patients undergoing vascular surgery of lower limbs

In patients undergoing surgery for LEAD, the probability of significant concomitant CAD at coronary angiography is ~50–60%.[384–386] For the management of these patients, aortic and major vascular surgery are classified as 'high risk' for cardiac complications, with an expected 30-day MACE rate (cardiac death and MI) >5%.[387] The management of CAD in patients requiring vascular surgery should be based on the 2014 ESC/ESA Guidelines on non-cardiac surgery.[387]

11.2.2.3 Coronary artery disease in patients with lower extremity artery disease not undergoing vascular surgery

At least one-third of patients with LEAD have a history and/or ECG signs of CAD, while two-thirds have an abnormal stress test and up to 70% present at least single-vessel disease at coronary angiography.[69,388] The prevalence of CAD is 2- to 4-fold higher in patients with LEAD vs. those without. In the Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter (CONFIRM) registry, among 7590 patients with LEAD without a history and symptoms of heart disease, the prevalence of obstructive CAD at coronary CTA was 25%.[389] In the REACH registry, 57% of the participants with LEAD also suffered from CAD.[390] The severity of LEAD is related to the prevalence of associated CAD; up to 90% of patients presenting with CLTI also have CAD.

There is no evidence that the presence of CAD directly influences limb outcomes in LEAD patients; however, in the CONFIRM registry, obstructive CAD was associated with an annual mortality rate of 1.6% vs. 0.7% in the absence of severe CAD.[389]

Table 9 Indication for screening of associated atherosclerotic disease in additional vascular territories

Leading disease \ Screened disease	CAD	LEAD	Carotid	Renal
CAD				
Scheduled for CABG		IIa[a]	I[b] / IIb[c]	U
Not scheduled for CABG		IIb	NR	U
LEAD				
Scheduled for CABG	I[d]		NR	U
Not scheduled for CABG	NR		NR	U
Carotid stenosis				
Scheduled for CEA/CAS	IIb	NR		U
Not scheduled for CEA/CAS	NR	NR		U

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CAS: carotid artery stenting; CEA = coronary endarterectomy; CKD = chronic kidney disease; ECG = electrocardiogram; LEAD = lower extremity artery disease; NR = no recommendation (not enough evidence to support systematic screening); TIA = transient ischaemic attack; U = uncertain.

[a]Especially when venous harvesting is planned for bypass.

[b]In patients with symptomatic cerebrovascular disease.

[c]In patients with asymptomatic carotid disease and: age ≥ 70 years, multivessel CAD, associated LEAD or carotid bruit.

[d]Screening with ECG is recommended in all patients and with imaging stress testing in patients with poor functional capacity and more than two of the following: history of CAD, heart failure, stroke or TIA, CKD, diabetes mellitus requiring insulin therapy.

The presence of CAD in patients with LEAD may require coronary revascularization, depending on the severity and urgency of LEAD symptoms. Risk factor modification and medical treatment recommended for CAD also apply to LEAD.[391] Screening for CAD in LEAD patients may be useful for risk stratification, as morbidity and mortality are mainly cardiac. Non-invasive screening can be performed by stress testing or coronary CTA, but there is no evidence of improved outcomes in LEAD patients with systematic screening for CAD.

11.2.3 Other peripheral localizations in patients with peripheral arterial diseases

11.2.3.1 Carotid artery stenosis in patients with lower extremity artery disease

Carotid stenosis is frequent in patients with LEAD (*Figure 8*), but there is no evidence that the presence of CAS would influence lower limb outcomes. The presence of CAD is a marker of worse CV prognosis.[392] For more details see Web addenda 11.2.3.1.

11.2.3.2 Renal artery disease in patients with lower extremity artery disease

While RAS is frequently discovered incidentally during imaging for LEAD, it requires specific intervention. Opinions on whether atherosclerotic RAD could be a marker of worse CV prognosis in LEAD patients are conflicting.[335,393] The only report looking also at limb outcome found no prognostic alteration in the case of concomitant RAS.[335] Systematic screening for RAS in patients with LEAD cannot be recommended, as the therapeutic value of renal artery stenting is questionable (see **chapter 9**).

For more details see Web addenda 11.2.3.2.

12. Cardiac conditions in peripheral arterial diseases

Key messages

- Cardiac conditions other than CAD are frequent in patients with PADs. This is especially the case for heart failure and atrial fibrillation in patients with LEAD.
- In patients with symptomatic PADs, screening for heart failure should be considered.
- In patients with heart failure, screening for LEAD may be considered. Full vascular assessment is indicated in patients planned for heart transplantation or a cardiac assist device.
- In patients with stable PADs who have AF, anticoagulation is the priority and suffices in most cases. In the case of recent endovascular revascularization, a period of combination therapy (anticoagulant + antiplatelet therapies) should be considered according to the bleeding and thrombotic risks. The period of combination therapy should be as brief as possible.
- In patients undergoing transcatheter aortic valve implantation or other structural interventions, screening for LEAD and UEAD is indicated.

12.1 Introduction

Cardiac diseases are frequent in patients with PADs. The simultaneous presence of PADs and CAD is addressed in **chapter 11**. Here we address the most important issues related to PADs patients with coexisting heart failure, AF and valvular heart disease (VHD). Such coexistence may carry important prognostic and

therapeutic implications and often needs a multidisciplinary approach. The current background information and detailed discussion of the data for the following section of these Guidelines can be found in ESC CardioMed.

12.2 Heart failure and peripheral arterial diseases

There are multiple pathways linking LEAD and heart failure (Web Figure 3). Together with diabetes, smoking and other risk factors, inflammation may be one of the common factors leading to the development of heart failure in PADs patients.[394] Data on the coexistence of the two conditions are generally limited to subjects with heart failure and LEAD.

LEAD is associated with increased risk for incident heart failure. It is often associated with overt atherosclerosis involving CAD, which may cause subsequent heart failure.[53] Also, elevated aortic stiffness increases left ventricular (LV) afterload and high pulse pressure impairs coronary blood flow, resulting in hypertension, LV hypertrophy, diastolic dysfunction and ultimately heart failure.[395,396] Importantly, skeletal muscle involvement and deconditioning in LEAD may affect heart failure severity.[397,398] On the other hand, functional limitation due to heart failure is likely to mask symptoms of LEAD, causing underestimation of the number of patients with both conditions.

12.2.1 Epidemiology

Overall, LV dysfunction and heart failure are more frequent in patients with PADs. The evidence is mostly presented in patients with LEAD. See Web addenda 12.2.1.

12.2.2. Heart failure in patients with peripheral arterial diseases

Despite the high prevalence and incidence of heart failure in patients with PADs, outcome data for this group are very limited. It is most likely, however, that this combination is associated with increased CV morbidity and mortality. Evaluation of LV function in PADs may be of value for better risk stratification for future CV events and comprehensive management of patients' CV diseases.[399] This is particularly important when an intermediate- or high-risk vascular intervention is planned.[387] The primary assessment should include medical history, physical examination and resting ECG. In case of any abnormalities suggestive of heart failure, transthoracic echocardiography (TTE) or measurement of natriuretic peptides should be undertaken.[400] Natriuretic peptides are particularly useful in patients with a poor echocardiographic window and in those with diastolic dysfunction.[401] In patients with LEAD, heart failure may be associated with reduced patency after endovascular therapy.[402] TTE and natriuretic peptides can also be proposed in patients with claudication, even if no revascularization is planned.

12.2.3 Peripheral arterial diseases in patients with heart failure

Observational studies and meta-analyses consistently show that the presence of LEAD in heart failure patients is an independent predictor of hospitalizations and mortality.[376–379,403] In the Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study, LEAD was reported in ~7% of patients with heart failure and LV ejection fraction <35% and was associated with an increased risk of all-cause hospitalization and mortality (HR 1.31, P = 0.011).[376] Other studies reported an increased risk for progressive heart failure (HR 1.35, P = 0.03), all-cause mortality (HR 1.36, P < 0.001)[404] and CV mortality (HR 1.31, P = 0.02).[405] Among hospitalized patients with heart failure, the prevalence of subclinical (ABI ≤0.90) and symptomatic LEAD was 19% and 7%, respectively, and was associated with increased cardiac and all-cause mortality.[378] Therefore, in heart failure patients, screening for PADs may be considered.

Finally, flash pulmonary oedema may be due to severe RAS (see **section 9.2**). Therefore, in patients with this condition, testing for RAS may be considered.

12.3 Peripheral arterial diseases and atrial fibrillation

12.3.1 General considerations

Ageing is a strong risk factor for AF[406] and PADs, thus a frequent coexistence of the two conditions is expected. In an analysis from the Cardiovascular Health Study, LEAD was associated with a higher risk of AF (HR 1.52, P < 0.01).[407]

Despite a considerable variability in BP due to the beat-to-beat variability in stroke volume, ABI appears to be a reliable method to detect unknown LEAD in patients with AF.[408] In patients with AF receiving anticoagulant treatment, abnormal ABI was an independent predictor of all-cause death and major bleeding complications.[409]

Among 41 882 patients hospitalized for LEAD, the prevalence of AF was 13%.[406] Those with AF tend to be older, more often hypertensive, female and with diabetes, CKD, CAD and/or heart failure than patients in sinus rhythm. LEAD was overall more severe in patients with AF as assessed by the Rutherford classification. In-hospital complications, including renal failure, MI, stroke, infections and death, occurred more frequently in the presence of AF. In other studies, AF associated with LEAD was an independent predictor of stroke, amputation and death.[410,411] In the REACH registry, AF was present in 10% of patients with LEAD.[84] Compared with patients without AF, the two-year CV and all-cause mortality was higher, 7.7% and 5.6% vs. 2.5% and 1.6%, respectively (P < 0.001 for both). Those with AF also had higher incidences of heart failure, unstable angina and severe bleeding.

12.3.2 Antithrombotic treatment in patients with atrial fibrillation

Except for recent stenting, patients with PADs and AF should mostly be on OACs alone. See **section 5.3**.

12.4 Peripheral arterial diseases and valvular heart disease

PADs are common among patients with VHD, especially among the elderly with symptomatic aortic stenosis. The presence of LEAD is captured within the scores used to predict outcome after cardiac surgery.[412] Among patients with symptomatic aortic stenosis not eligible for surgical aortic valve replacement, the prevalence of LEAD is as high as 40%.[413–415] It often coexists with other manifestations of systemic atherosclerosis, including CAD and cerebrovascular disease. This has an impact on patient care with respect to the timing of coronary revascularization, if needed,[366] and the vascular access site for transcatheter aortic

valve implantation (TAVI).[416] Systematic CT scan imaging of the aorta, including all major peripheral arteries, has become the standard of care in patients eligible for TAVI.

12.5 Peripheral arterial diseases and vascular access site for cardiac interventions

Patient evaluation for the presence of LEAD and UEAD is pivotal for access site choice in patients eligible for TAVI and their diagnosis has a great impact on clinical outcome after TAVI because of the increased rate of peri- and post-procedural complications.[417,418] The presence of LEAD or UEAD is an independent predictor of mortality following TAVI with both percutaneous and surgical access, independent of the occurrence of vascular complications.[417,419] The use of low-profile devices for TAVI and alternative access sites, such as direct aortic, carotid or subclavian, may also reduce vascular complications.

Acute limb ischaemia is a complication of intra-aortic balloon pump insertion in the setting of cardiogenic shock or in the prophylaxis of low output syndrome. LEAD is a major risk factor for this complication and preliminary iliac artery stenting with the use of an unsheathed device may avoid such complications.[420] These complications are also common in LV assist device recipients, where sheaths are usually larger, resulting in higher 30-day mortality in patients with LEAD.[421] The added risk of underlying LEAD is not clearly established in that particular setting and deserves additional investigations. These patients often need lower limb revascularization and surgical vascular closure when weaned off LV assist devices.

Recommendations on the management of cardiac conditions associated with peripheral arterial diseases

Recommendations	Class[a]	Level[b]
PADs and heart failure		
Full vascular assessment is indicated in all patients considered for heart transplantation or cardiac assist device implantation.	I	C
In patients with symptomatic PADs, screening for heart failure with TTE and/or natriuretic peptides assessment should be considered.	IIa	C
Screening for LEAD may be considered in patients with heart failure.	IIb	C
Testing for renal artery disease may be considered in patients with flash pulmonary oedema.	IIb	C
PADs and atrial fibrillation[c]		
In patients with LEAD and atrial fibrillation, oral anticoagulation:[83]		
• is recommended with a CHA_2DS_2-VASc score ≥2	I	A
• should be considered in all other patients.	IIa	B
PADs and valvular heart disease		
Screening for LEAD and UEAD is indicated in patients undergoing TAVI or other structural interventions requiring an arterial approach.	I	C

CHA_2DS_2VASC = Congestive heart failure, Hypertension, Age ≥75 (2 points), Diabetes mellitus, Stroke or TIA (2 points), Vascular disease, Age 65–74 years, Sex category; LEAD = lower extremity artery disease; PADs = peripheral arterial diseases; TAVI = transcatheter aortic valve implantation; TTE = transthoracic echocardiography; UEAD = upper extremity artery disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]For more detail please refer to **chapter 5**.

13. Gaps in evidence

Rapid changes in therapeutic techniques create the situation in which clinical practice tends to follow technical developments without evidence from RCTs. In addition, RCTs often yield conflicting results because of technical evolution. Moreover, PADs may involve multiple sites, creating a large number of clinical scenarios to investigate. All these contribute to the broad spectrum of gaps in evidence, of which the most relevant are listed in *Table 10*. The current background information and detailed discussion of the data for the following section of these Guidelines can be found in ESC CardioMed.

Table 10 Main gaps in evidence in the management of patients with peripheral arterial diseases

Epidemiology
Data on epidemiology of PADs in Europe are scarce.
Important challenges are associated with PADs in women. This group has classically been underrepresented in research studies. Therefore, several sex-related challenges regarding diagnosis and management issues should be acknowledged.
Carotid artery disease
The benefits of new antiplatelet drugs for the management of asymptomatic carotid artery disease should be assessed by RCTs.
A multifactorial and standardized score is necessary to stratify the risk of stroke in patients with asymptomatic carotid artery stenosis, to determine the subgroup who may benefit from revascularization, in addition to best medical therapy.
The efficacy of embolic protection devices during CAS has not been studied in adequately powered RCTs, and the available evidence is conflicting.
The optimal duration of dual antiplatelet therapy after CAS is not well established.
The timing of carotid revascularization in the acute phase of stroke after intra-cerebral thrombolysis/thrombectomy is not yet defined and should be investigated.
Vertebral artery disease
Almost no data are available on the comparison between surgical and endovascular revascularization in symptomatic patients.
Upper extremity artery disease
Little is known about the natural course in upper extremity artery disease.
Almost no data are available on the long-term clinical benefit of revascularization (and the optimal mode) of symptomatic subclavian artery stenosis/occlusion.
Optimal duration for DAPT after subclavian artery stenting is unknown.
Mesenteric artery disease
The potential benefits of prophylactic revascularization for asymptomatic mesenteric artery disease involving multiple vessels needs investigations.
In case of symptomatic mesenteric artery disease, no data are available on the potential benefit of covered vs. bare stents.
Optimal duration for DAPT after mesenteric stenting is unknown.
Renal artery disease
The role of renal artery stenting for patients with pulmonary flash oedema remains to be demonstrated by RCT.
Appropriate treatment of in-stent renal artery restenosis is not yet defined.
Risk stratification would be necessary to clarify whether a subgroup of patients with RAS may benefit from renal revascularization. In case of renal stenting, optimal duration for DAPT is unknown.
Lower extremity artery disease
The role of drug-eluting stents and drug-eluting balloons in superficial femoral artery and below-the-popliteal artery interventions has to be established.
Optimal treatment for popliteal artery stenosis needs to be addressed.
Clinical studies on self-expanding stents, drug-coated balloons and drug-eluting stents for below-the-knee interventions in patients with CLTI should include amputation-free survival, wound healing and quality of life in addition to standard-patency outcomes.
Optimal duration of DAPT after stenting, as well as the potential benefit of its long-term use in patients with CLTI, should be further investigated.
The rationale of the angiosome concept to decide on modality of revascularization in patients with CLTI remains to be demonstrated.
There is a need to develop European registries for patients with LEAD in order to provide "real world" assessment of clinical outcomes and practices.
There is a need to validate improved classification systems for CLTI that incorporate wound, ischaemia and foot infection such as the WIfI classification.
Multisite artery disease
Whether the screening for other sites of atherosclerosis (e.g. CAD) in patients with PADs may improve their outcome needs further investigation.
Cardiac conditions in patients with PADs
The impact of heart failure screening and treatment and its impact on outcome of patients with PADs requires further investigations.
The optimal strategy of antithrombotic treatment in patients with atrial fibrillation and PADs requires specific RCTs.

CAD = coronary artery disease; CAS = carotid artery stenting; CLTI = chronic limb-threatening ischaemia; DAPT= dual antiplatelet therapy; LEAD = lower extremity artery disease; PADs = peripheral arterial diseases; RAS = renal artery stenosis; RCT = randomized clinical trial.

14. To do and not to do messages from the Guidelines

Recommendations	Class[a]	Level[b]
General recommendations on the management of patients with PADs		
In healthcare centres, it is recommended to set up a multidisciplinary Vascular Team to make decisions for the management of patients with PADs.	I	C
It is recommended to implement and support initiatives to improve medical and public awareness of PADs, especially cerebrovascular and lower extremity artery diseases.	I	C
Recommendations in patients with PADs: best medical therapy		
Smoking cessation is recommended in all patients with PADs.	I	B
A healthy diet and physical activity are recommended for all patients with PADs.	I	C
Statins are recommended in all patients with PADs.	I	A
In patients with PADs, it is recommended to reduce LDL-C to < 1.8 mmol/L (70 mg/dL) or decrease it by ≥ 50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).	I	C
In diabetic patients with PADs, strict glycaemic control is recommended.	I	C
Antiplatelet therapy is recommended in patients with symptomatic PADs.	I	C[c]
In patients with PADs and hypertension, it is recommended to control blood pressure at < 140/90 mmHg.	I	A
Recommendations on antithrombotic therapy in patients with PADs		
In patients with symptomatic carotid stenosis, long-term SAPT is recommended.	I	A
Dual antiplatelet therapy with aspirin and clopidogrel is recommended for at least 1 month after CAS.	I	B
Long-term SAPT is recommended in symptomatic patients.	I	A
Long-term SAPT is recommended in all patients who have undergone revascularization.	I	C
SAPT is recommended after infra-inguinal bypass surgery.	I	A
Because of the lack of proven benefit, antiplatelet therapy is not routinely indicated in patients with isolated[d] asymptomatic LEAD.	III	A
In patients with PADs and AF, OAC is recommended when the CHA_2DS_2-VASc score is ≥ 2	I	A
Recommendations for imaging of extracranial carotid arteries		
DUS (as first-line), CTA and/or MRA are recommended for evaluating the extent and severity of extracranial carotid stenoses.	I	B
When CAS is being considered, it is recommended that any DUS study be followed either by MRA or CTA to evaluate the aortic arch, as well as the extra- and intracranial circulation.	I	B
When CEA is considered, it is recommended that the DUS stenosis estimation be corroborated either by MRA or CTA (or by a repeat DUS study performed in an expert vascular laboratory).	I	B
Recommendations on revascularization in patients with symptomatic carotid disease[e]		
CEA is recommended in symptomatic patients with 70–99% carotid stenoses, provided the documented procedural death/stroke rate is < 6%.	I	A
When decided, it is recommended to perform revascularization of symptomatic 50–99% carotid stenoses as soon as possible, preferably within 14 days of symptom onset.	I	A
Revascularization is not recommended in patients with a < 50% carotid stenosis.	III	A

Continued

Recommendations for management of vertebral artery stenoses		
Revascularization of asymptomatic vertebral artery stenosis is not indicated, irrespective of the degree of severity.	III	C
Recommendations on the management of acute mesenteric ischaemia		
In patients with suspected acute mesenteric ischaemia, urgent CTA is recommended.	I	C
Recommendations for management of chronic mesenteric artery disease		
In patients with suspected CMI, DUS is recommended as the first-line examination.	I	C
In patients with symptomatic multivessel CMI, revascularization is recommended.	I	C
In patients with symptomatic multivessel CMI, it is not recommended to delay revascularization in order to improve the nutritional status.	III	C
Recommendations for diagnostic strategies for RAD		
DUS (as first-line), CTA[f] and MRA[g] are recommended imaging modalities to establish a diagnosis of RAD.	I	B
Renal scintigraphy, plasma renin measurements before and after ACEI provocation and vein renin measurements are not recommended for screening of atherosclerotic RAD.	III	C
Recommendations for treatment strategies for RAD		
ACEIs/ARBs are recommended for treatment of hypertension associated with unilateral renal artery stenosis.	I	B
Calcium channel blockers, beta-blockers and diuretics are recommended for treatment of hypertension associated with RAD.	I	C
Routine revascularization is not recommended in renal artery stenosis secondary to atherosclerosis.	III	A
Recommendations for ABI measurement		
Measurement of the ABI is indicated as a first-line non-invasive test for screening and diagnosis of LEAD.	I	C
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 are indicated.	I	C
Recommendations on imaging in patients with LEAD		
DUS is indicated as a first-line imaging method to confirm LEAD lesions.	I	C
DUS and/or CTA and/or MRA are indicated for anatomical characterization of LEAD lesions and guidance for optimal revascularization strategy.	I	C
The data from an anatomical imaging test should always be analysed in conjunction with symptoms and haemodynamic tests prior to a treatment decision.	I	C
Recommendations for the management of patients with intermittent claudication		
On top of general prevention, statins are indicated to improve walking distance.	I	A
In patients with intermittent claudication, supervised exercise training is recommended.	I	A
In patients with intermittent claudication, non-supervised exercise training is recommended when supervised exercise training is not feasible or available.	I	C
Recommendations on revascularization of aorto-iliac occlusive lesions[h]		
An endovascular-first strategy is recommended for short (i.e. <5 cm) occlusive lesions.	I	C
Recommendations on revascularization of femoro-popliteal occlusive lesions[g]		
An endovascular-first strategy is recommended in short (i.e. <25 cm) lesions.	I	C
In patients who are not at high risk for surgery, bypass surgery is indicated for long (i.e. ≥25 cm) superficial femoral artery lesions when an autologous vein is available and life expectancy is > 2 years.	I	B
The autologous saphenous vein is the conduit of choice for femoro-popliteal bypass.	I	A

Continued

Recommendations on revascularization of infra-popliteal occlusive lesions		
In the case of CLTI, infra-popliteal revascularization is indicated for limb salvage.	I	C
For revascularization of infra-popliteal arteries, bypass using the great saphenous vein is indicated.	I	A
Recommendations on the management of CLTI		
Early recognition of tissue loss and/or infection and referral to the vascular team is mandatory to improve limb salvage.	I	C
In patients with CLTI, assessment of the risk of amputation is indicated.	I	C
In patients with CLTI and diabetes, optimal glycaemic control is recommended.	I	C
For limb salvage, revascularization is indicated whenever feasible.	I	B
In patients with CLTI, stem cell/gene therapy is not indicated.	III	B
Recommendations for the management of patients presenting with acute limb ischaemia		
In the case of neurological deficit, urgent revascularization is indicated.[i]	I	C
In the absence of neurological deficit, revascularization is indicated within hours after initial imaging in a case-by-case decision.	I	C
Heparin and analgesics are indicated as soon as possible.	I	C
Recommendations on screening for carotid disease in patients undergoing CABG surgery		
In patients undergoing CABG, DUS is recommended in patients with a recent (<6 months) history of TIA/stroke.	I	B
Screening for carotid stenosis is not indicated in patients requiring urgent CABG with no recent stroke/TIA.	III	C
Recommendations on the management of carotid stenosis in patients undergoing CABG surgery		
It is recommended that the indication (and, if so, the method and timing) for carotid revascularization be individualized after discussion within a multidisciplinary team, including a neurologist.	I	C
In patients scheduled for CABG, with a recent (<6 months) history of TIA/stroke, carotid revascularization is not recommended in those with carotid stenosis <50%.	III	C
In neurologically asymptomatic patients scheduled for CABG, routine prophylactic carotid revascularization in patients with a 70–99% carotid stenosis is not recommended.	III	B
Recommendations for screening and management of concomitant LEAD and CAD		
In patients with LEAD, radial artery access is recommended as the first option for coronary angiography/intervention.	I	C
Recommendations on the management of cardiac conditions associated with PADs		
Full vascular assessment is indicated in all patients considered for heart transplantation or cardiac assist device implantation.	I	C
In patients with LEAD and atrial fibrillation, OAC is recommended with a CHA_2DS_2-VASc score ≥2.	I	A
Screening for LEAD and UEAD is indicated in patients undergoing TAVI or other structural interventions requiring an arterial approach.	I	C

ABI = ankle-brachial index; ACEI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin-receptor blocker; CABG = coronary artery bypass grafting; CAS = carotid artery stenting; CEA = carotid endarterectomy; CLTI = chronic limb-threatening ischaemia; CMI = chronic mesenteric ischaemia; CTA = computed tomography angiography; DUS = duplex ultrasound; eGFR = estimated glomerular filtration rate; LDL-C = low-density lipoprotein cholesterol; LEAD = lower extremity artery disease; MRA = magnetic resonance angiography; OAC = oral anticoagulation; PADs = peripheral arterial diseases; RAD = renal artery disease; SAPT = single antiplatelet therapy; TAVI = transcatheter aortic valve implantation; TIA = transient ischaemic attack; UEAD = upper extremity artery disease. CHA_2DS_2-VASc score is calculated as follows: congestive heart failure history (1 point), hypertension (1 point), age >75 years (2 points), diabetes mellitus (1 point), stroke/TIA or arterial thromboembolic history (1 point), vascular disease history (1 point), age 65–74 years (1 point), sex category (1 point if female).

[a]Class of recommendation.

[b]Level of evidence.

[c]Evidence is not available for all sites. When evidence is available, recommendations specific for the vascular site are presented in corresponding sections.

[d]Without any other clinical cardiovascular condition requiring antiplatelet therapy (e.g. coronary artery disease or other multisite artery diseases).

[e]Stroke or TIA occurring within 6 months.

[f]When eGFR is ≥ 60 mL/min.

[g]When eGFR is ≥ 30 mL/min.

[h]These recommendations apply for patients with intermittent claudication and severe chronic limb ischaemia.

[i]In this case, imaging should not delay intervention.

15. Web addenda and companion document

All Web figures and Web tables are available at the European Heart Journal online and also via the ESC Web site at: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Peripheral-Artery-Diseases-Diagnosis-and-Treatment-of

The questions and answers companion document for these guidelines is available via this same link.

16. Appendix

ESC Committee for Practice Guidelines (CPG): Stephan Windecker (Chairperson) (Switzerland), Victor Aboyans (France), Stefan Agewall (Norway), Emanuele Barbato (Italy), Héctor Bueno (Spain), Antonio Coca (Spain), Jean-Philippe Collet (France), Ioan Mircea Coman (Romania), Veronica Dean (France), Victoria Delgado (The Netherlands), Donna Fitzsimons (UK), Oliver Gaemperli (Switzerland), Gerhard Hindricks (Germany), Bernard Iung (France), Peter Juni (Canada), Hugo A. Katus (Germany), Juhani Knuuti (Finland), Patrizio Lancellotti (Belgium), Christophe Leclercq (France), Theresa McDonagh (UK), Massimo Francesco Piepoli (Italy), Piotr Ponikowski (Poland), Dimitrios J. Richter (Greece), Marco Roffi (Switzerland), Evgeny Shlyakhto (Russia), Iain A. Simpson (UK), Jose Luis Zamorano (Spain).

ESC National Cardiac Societies actively involved in the review process of the 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases: Armenia: Armenian Cardiologists Association, Parounak H. Zelveian; Austria: Austrian Society of Cardiology, Markus Haumer; Belarus: Belorussian Scientific Society of Cardiologists, Dzmitry Isachkin; Belgium: Belgian Society of Cardiology, Tine De Backer; Bosnia and Herzegovina: Association of Cardiologists of Bosnia and Herzegovina, Mirza Dilic; Bulgaria: Bulgarian Society of Cardiology, Ivo Petrov; Croatia: Croatian Cardiac Society, Majda Vrkic Kirhmajer; Czech Republic: Czech Society of Cardiology, Debora Karetova; Denmark: Danish Society of Cardiology, Eva Prescott; Egypt: Egyptian Society of Cardiology, Hamdy Soliman; Estonia: Estonian Society of Cardiology, Ants Paapstel; Finland: Finnish Cardiac Society, Kimmo Makinen; The Former Yugoslav Republic of Macedonia: Macedonian FYR Society of Cardiology, Slavco Tosev; France: French Society of Cardiology, Emmanuel Messas; Georgia: Georgian Society of Cardiology, Zurab Pagava; Germany: German Cardiac Society, Oliver J. Müller; Greece: Hellenic Society of Cardiology, Katerina K. Naka; Hungary: Hungarian Society of Cardiology, Zoltán Járai; Iceland: Icelandic Society of Cardiology, Thorbjorn Gudjonsson; Israel: Israel Heart Society, Michael Jonas; Italy: Italian Federation of Cardiology, Salvatore Novo; Kosovo: Kosovo Society of Cardiology, Pranvera Ibrahimi; Kyrgyzstan: Kyrgyz Society of Cardiology, Olga Lunegova; Latvia: Latvian Society of Cardiology, Vilnis Dzerve; Lithuania: Lithuanian Society of Cardiology, Nerijus Misonis; Luxembourg: Luxembourg Society of Cardiology, Jean Beissel; Malta: Maltese Cardiac Society, Elton Pllaha; Morocco: Moroccan Society of Cardiology, Mustapha Taberkant; Norway: Norwegian Society of Cardiology, Torbjørn Bakken; Portugal: Portuguese Society of Cardiology, Rui Teles; Romania: Romanian Society of Cardiology, Daniel Lighezan; Russian Federation: Russian Society of Cardiology, Alexandra Konradi; San Marino: San Marino Society of Cardiology, Marco Zavatta; Slovakia: Slovak Society of Cardiology, Juraj Madaric; Slovenia: Slovenian Society of Cardiology, Zlatko Fras; Spain: Spanish Society of Cardiology, Lorenzo Silva Melchor; Sweden: Swedish Society of Cardiology, Ulf Näslund; Switzerland: Swiss Society of Cardiology, Beatrice Amann-Vesti; United Kingdom: British Cardiovascular Society, Agu Obiekezie.

17. References

1. Tendera M, Aboyans V, Bartelink ML, Baumgartner I, Clement D, Collet JP, Cremonesi A, De Carlo M, Erbel R, Fowkes FG, Heras M, Kownator S, Minar E, Ostergren J, Poldermans D, Riambau V, Roffi M, Rother J, Sievert H, van Sambeek M, Zeller T. ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2011;**32**:2851–2906.
2. Fowkes FG, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, Norman PE, Sampson UK, Williams LJ, Mensah GA, Criqui MH. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 2013;**382**:1329–1340.
3. Belcaro G, Nicolaides AN, Ramaswami G, Cesarone MR, De Sanctis M, Incandela L, Ferrari P, Geroulakos G, Barsotti A, Griffin M, Dhanjil S, Sabetai M, Bucci M, Martines G. Carotid and femoral ultrasound morphology screening and cardiovascular events in low risk subjects: a 10-year follow-up study (the CAFES-CAVE study). *Atherosclerosis* 2001;**156**:379–387.
4. Giannopoulos A, Kakkos S, Abbott A, Naylor AR, Richards T, Mikhailidis DP, Geroulakos G, Nicolaides AN. Long-term mortality in patients with asymptomatic carotid stenosis: implications for statin therapy. *Eur J Vasc Endovasc Surg* 2015;**50**:573–582.
5. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res* 2015;**116**:1509–1526.
6. Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, deBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Fowkes FG, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodriguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronek A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, McDermott MM. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA* 2008;**300**:197–208.
7. Weitz JI, Byrne J, Clagett GP, Farkouh ME, Porter JM, Sackett DL, Strandness DE Jr, Taylor LM. Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. *Circulation* 1996;**94**:3026–3049.
8. Valentine RJ, Guerra R, Stephan P, Scoggins E, Clagett GP, Cohen J. Family history is a major determinant of subclinical peripheral arterial disease in young adults. *J Vasc Surg* 2004;**39**:351–356.
9. Wassel CL, Loomba R, Ix JH, Allison MA, Denenberg JO, Criqui MH. Family history of peripheral artery disease is associated with prevalence and severity of peripheral artery disease: the San Diego population study. *J Am Coll Cardiol* 2011;**58**:1386–1392.
10. Khaleghi M, Isseh IN, Bailey KR, Kullo IJ. Family history as a risk factor for peripheral arterial disease. *Am J Cardiol* 2014;**114**:928–932.
11. Corra U, Piepoli MF, Carre F, Heuschmann P, Hoffmann U, Verschuren M, Halcox J, Giannuzzi P, Saner H, Wood D, Piepoli MF, Corra U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, McGee H, Mendes M, Niebauer J, Zwisler AD, Schmid JP. Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur Heart J* 2010;**31**:1967–1974.
12. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;**35**:1381–1395.

13. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol* 1993;**46**:153–162.
14. Pickett CA, Jackson JL, Hemann BA, Atwood JE. Carotid bruits as a prognostic indicator of cardiovascular death and myocardial infarction: a meta-analysis. *Lancet* 2008;**371**:1587–1594.
15. Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet* 2012;**379**:905–914.
16. Cournot M, Taraszkiewicz D, Cambou JP, Galinier M, Boccalon H, Hanaire-Broutin H, Chamontin B, Carrie D, Ferrieres J. Additional prognostic value of physical examination, exercise testing, and arterial ultrasonography for coronary risk assessment in primary prevention. *Am Heart J* 2009;**158**:845–851.
17. Vlachopoulos C, Xaplanteris P, Aboyans V, Brodmann M, Cifkova R, Cosentino F, De Carlo M, Gallino A, Landmesser U, Laurent S, Lekakis J, Mikhailidis DP, Naka KK, Protogerou AD, Rizzoni D, Schmidt-Trucksass A, Van Bortel L, Weber T, Yamashina A, Zimlichman R, Boutouyrie P, Cockcroft J, O'Rourke M, Park JB, Schillaci G, Sillesen H, Townsend RR. The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Group on peripheral circulation: endorsed by the Association for Research into Arterial Structure and Physiology (ARTERY) Society. *Atherosclerosis* 2015;**241**:507–532.
18. Criqui MH, McClelland RL, McDermott MM, Allison MA, Blumenthal RS, Aboyans V, Ix JH, Burke GL, Liu K, Shea S. The ankle-brachial index and incident cardiovascular events in the MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* 2010;**56**:1506–1512.
19. Wu MY, Hsiang HF, Wong CS, Yao MS, Li YW, Hsiang CY, Bai CH, Hsu YH, Lin YF, Tam KW. The effectiveness of N-acetylcysteine in preventing contrast-induced nephropathy in patients undergoing contrast-enhanced computed tomography: a meta-analysis of randomized controlled trials. *Int Urol Nephrol* 2013;**45**:1309–1318.
20. O'Sullivan S, Healy DA, Moloney MC, Grace PA, Walsh SR. The role of N-acetylcysteine in the prevention of contrast-induced nephropathy in patients undergoing peripheral angiography: a structured review and meta-analysis. *Angiology* 2013;**64**:576–582.
21. Merten GJ, Burgess WP, Gray LV, Holleman JH, Roush TS, Kowalchuk GJ, Bersin RM, Van Moore A, Simonton CA 3rd, Rittase RA, Norton HJ, Kennedy TP. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. *JAMA* 2004;**291**:2328–2334.
22. Akyuz S, Yaylak B, Altay S, Kasikcioglu H, Cam N. The role of statins in preventing contrast-induced acute kidney injury: a narrative review. *Angiology* 2015;**66**:701–707.
23. Ramalho J, Semelka RC, Ramalho M, Nunes RH, AlObaidy M, Castillo M. Gadolinium-based contrast agent accumulation and toxicity: an update. *AJNR Am J Neuroradiol* 2016;**37**:1192–1198.
24. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, Dallongeville J, De Backer G, Ebrahim S, Gjelsvik B, Herrmann-Lingen C, Hoes A, Humphries S, Knapton M, Perk J, Priori SG, Pyorala K, Reiner Z, Ruilope L, Sans-Menendez S, Scholte op Reimer W, Weissberg P, Wood D, Yarnell J, Zamorano JL, Walma E, Fitzgerald T, Cooney MT, Dudina A. European guidelines on cardiovascular disease prevention in clinical practice: executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J* 2007;**28**:2375–2414.
25. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FD, Lochen ML, Lollgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WM. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;**37**:2315–2381.
26. Ryden L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, Deaton C, Escaned J, Hammes HP, Huikuri H, Marre M, Marx N, Mellbin L, Ostergren J, Patrono C, Seferovic P, Uva MS, Taskinen MR, Tendera M, Tuomilehto J, Valensi P, Zamorano JL, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, De Backer G, Sirnes PA, Ezquerra EA, Avogaro A, Badimon L, Baranova E, Baumgartner H, Betteridge J, Ceriello A, Fagard R, Funck-Brentano C, Gulba DC, Hasdai D, Hoes AW, Kjekshus JK, Knuuti J, Kolh P, Lev E, Mueller C, Neyses L, Nilsson PM, Perk J, Ponikowski P, Reiner Z, Sattar N, Schachinger V, Scheen A, Schirmer H, Stromberg A, Sudzhaeva S, Tamargo JL, Viigimaa M, Vlachopoulos C, Xuereb RG. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2013;**34**:3035–3087.
27. Bullen C. Impact of tobacco smoking and smoking cessation on cardiovascular risk and disease. *Expert Rev Cardiovasc Ther* 2008;**6**:883–895.
28. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, Amann M, Anderson HR, Andrews KG, Aryee M, Atkinson C, Bacchus LJ, Bahalim AN, Balakrishnan K, Balmes J, Barker-Collo S, Baxter A, Bell ML, Blore JD, Blyth F, Bonner C, Borges G, Bourne R, Boussinesq M, Brauer M, Brooks P, Bruce NG, Brunekreef B, Bryan-Hancock C, Bucello C, Buchbinder R, Bull F, Burnett RT, Byers TE, Calabria B, Carapetis J, Carnahan E, Chafe Z, Charlson F, Chen H, Chen JS, Cheng AT, Child JC, Cohen A, Colson KE, Cowie BC, Darby S, Darling S, Davis A, Degenhardt L, Dentener F, Des Jarlais DC, Devries K, Dherani M, Ding EL, Dorsey ER, Driscoll T, Edmond K, Ali SE, Engell RE, Erwin PJ, Fahimi S, Falder G, Farzadfar F, Ferrari A, Finucane MM, Flaxman S, Fowkes FG, Freedman G, Freeman MK, Gakidou E, Ghosh S, Giovannucci E, Gmel G, Graham K, Grainger R, Grant B, Gunnell D, Gutierrez HR, Hall W, Hoek HW, Hogan A, Hosgood HD 3rd, Hoy D, Hu H, Hubbell BJ, Hutchings SJ, Ibeanusi SE, Jacklyn GL, Jasrasaria R, Jonas JB, Kan H, Kanis JA, Kassebaum N, Kawakami N, Khang YH, Khatibzadeh S, Khoo JP, Kok C, Laden F, Lalloo R, Lan Q, Lathlean T, Leasher JL, Leigh J, Li Y, Lin JK, Lipshultz SE, London S, Lozano R, Lu Y, Mak J, Malekzadeh R, Mallinger L, Marcenes W, March L, Marks R, Martin R, McGale P, McGrath J, Mehta S, Mensah GA, Merriman TR, Micha R, Michaud C, Mishra V, Mohd Hanafiah K, Mokdad AA, Morawska L, Mozaffarian D, Murphy T, Naghavi M, Neal B, Nelson PK, Nolla JM, Norman R, Olives C, Omer SB, Orchard J, Osborne R, Ostro B, Page A, Pandey KD, Parry CD, Passmore E, Patra J, Pearce N, Pelizzari PM, Petzold M, Phillips MR, Pope D, Pope CA 3rd, Powles J, Rao M, Razavi H, Rehfuess EA, Rehm JT, Ritz B, Rivara FP, Roberts T, Robinson C, Rodriguez-Portales JA, Romieu I, Room R, Rosenfeld LC, Roy A, Rushton L, Salomon JA, Sampson U, Sanchez-Riera L, Sanman E, Sapkota A, Seedat S, Shi P, Shield K, Shivakoti R, Singh GM, Sleet DA, Smith E, Smith KR, Stapelberg NJ, Steenland K, Stockl H, Stovner LJ, Straif K, Straney L, Thurston GD, Tran JH, Van Dingenen R, van Donkelaar A, Veerman JL, Vijayakumar L, Weintraub R, Weissman MM, White RA, Whiteford H, Wiersma ST, Wilkinson JD, Williams HC, Williams W, Wilson N, Woolf AD, Yip P, Zielinski JM, Lopez AD, Murray CJ, Ezzati M, AlMazroa MA, Memish ZA. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2224–2260.
29. Morris PB, Ference BA, Jahangir E, Feldman DN, Ryan JJ, Bahrami H, El-Chami MF, Bhakta S, Winchester DE, Al-Mallah MH, Sanchez Shields M, Deedwania P, Mehta LS, Phan BA, Benowitz NL. Cardiovascular effects of exposure to cigarette smoke and electronic cigarettes: clinical perspectives from the Prevention of Cardiovascular Disease Section Leadership Council and Early Career Councils of the American College of Cardiology. *J Am Coll Cardiol* 2015;**66**:1378–1391.
30. Aung PP, Maxwell HG, Jepson RG, Price JF, Leng GC. Lipid-lowering for peripheral arterial disease of the lower limb. *Cochrane Database Syst Rev* 2007;**4**;CD000123.
31. Antoniou GA, Fisher RK, Georgiadis GS, Antoniou SA, Torella F. Statin therapy in lower limb peripheral arterial disease: systematic review and meta-analysis. *Vascul Pharmacol* 2014;**63**:79–87.
32. Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg* 2007;**45**:645–654.
33. Kumbhani DJ, Steg PG, Cannon CP, Eagle KA, Smith SC Jr, Goto S, Ohman EM, Elbez Y, Sritara P, Baumgartner I, Banerjee S, Creager MA, Bhatt DL. Statin therapy and long-term adverse limb outcomes in patients with peripheral artery disease: insights from the REACH registry. *Eur Heart J* 2014;**35**:2864–2872.
34. Westin GG, Armstrong EJ, Bang H, Yeo KK, Anderson D, Dawson DL, Pevec WC, Amsterdam EA, Laird JR. Association between statin medications and mortality, major adverse cardiovascular event, and amputation-free survival in patients with critical limb ischemia. *J Am Coll Cardiol* 2014;**63**:682–690.
35. Murphy SA, Cannon CP, Blazing MA, Giugliano RP, White JA, Lokhnygina Y, Reist C, Im K, Bohula EA, Isaza D, Lopez-Sendon J, Dellborg M, Kher U, Tershakovec AM, Braunwald E. Reduction in total cardiovascular events with ezetimibe/simvastatin post-acute coronary syndrome: the IMPROVE-IT Trial. *J Am Coll Cardiol* 2016;**67**:353–361.
36. Meade T, Zuhrie R, Cook C, Cooper J. Bezafibrate in men with lower extremity arterial disease: randomised controlled trial. *BMJ* 2002;**325**:1139.

37. Amarenco P, Labreuche J, Lavallee P, Touboul PJ. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. *Stroke* 2004;**35**:2902–2909.
38. Huang Y, Li W, Dong L, Li R, Wu Y. Effect of statin therapy on the progression of common carotid artery intima-media thickness: an updated systematic review and meta-analysis of randomized controlled trials. *J Atheroscler Thromb* 2013;**20**:108–121.
39. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS, Pedersen TR. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;**376**:1713–1722.
40. Staessen JA, Thijs L, Gasowski J, Cells H, Fagard RH. Treatment of isolated systolic hypertension in the elderly: further evidence from the systolic hypertension in Europe (Syst-Eur) trial. *Am J Cardiol* 1998;**82**:20R–22R.
41. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013;**31**:1281–12357.
42. Bavry AA, Anderson RD, Gong Y, Denardo SJ, Cooper-Dehoff RM, Handberg EM, Pepine CJ. Outcomes among hypertensive patients with concomitant peripheral and coronary artery disease: findings from the INternational VErapamil-SR/Trandolapril STudy. *Hypertension* 2010;**55**:48–53.
43. Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC Jr, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;**373**:2103–2116.
44. Cushman WC, Whelton PK, Fine LJ, Wright JT Jr, Reboussin DM, Johnson KC, Oparil S. SPRINT trial results: latest news in hypertension management. *Hypertension* 2016;**67**:263–265.
45. World Health Organization. *Guideline: sodium intake for adults and children*. Geneva: World Health Organization, 2012 (reprinted 2014).
46. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;**342**:145–153.
47. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008;**358**:1547–1559.
48. Armstrong EJ, Chen DC, Singh GD, Amsterdam EA, Laird JR. Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use is associated with reduced major adverse cardiovascular events among patients with critical limb ischemia. *Vasc Med* 2015;**20**:237–244.
49. Paravastu SC, Mendonca DA, Da Silva A. Beta blockers for peripheral arterial disease. *Cochrane Database Syst Rev* 2013;**9**:CD005508.
50. Aronow WS, Ahn C. Effect of beta blockers on incidence of new coronary events in older persons with prior myocardial infarction and symptomatic peripheral arterial disease. *Am J Cardiol* 2001;**87**:1284–1286.
51. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;**348**:1329–1339.
52. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009;**338**:b1665.
53. Ostergren J, Sleight P, Dagenais G, Danisa K, Bosch J, Qilong Y, Yusuf S. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J* 2004;**25**:17–24.
54. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;**324**:71–86.
55. Sacco RL, Diener HC, Yusuf S, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlof B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, Pais P, Roberts R, Skvortsova V, Teal P, Toni D, Vandermaelen C, Voigt T, Weber M, Yoon BW. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med* 2008;**359**:1238–1251.
56. Bhatt DL, Flather MD, Hacke W, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Hamm CW, Hankey GJ, Johnston SC, Mak KH, Mas JL, Montalescot G, Pearson TA, Steg PG, Steinhubl SR, Weber MA, Fabry-Ribaudo L, Hu T, Topol EJ, Fox KA. Patients with prior myocardial infarction, stroke, or symptomatic peripheral arterial disease in the CHARISMA trial. *J Am Coll Cardiol* 2007;**49**:1982–1988.
57. Markus HS, Droste DW, Kaps M, Larrue V, Lees KR, Siebler M, Ringelstein EB. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using Doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. *Circulation* 2005;**111**:2233–2240.
58. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, Wang C, Li H, Meng X, Cui L, Jia J, Dong Q, Xu A, Zeng J, Li Y, Wang Z, Xia H, Johnston SC. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med* 2013;**369**:11–19.
59. Dalainas I, Nano G, Bianchi P, Stegher S, Malacrida G, Tealdi DG. Dual antiplatelet regime versus acetyl-acetic acid for carotid artery stenting. *Cardiovasc Intervent Radiol* 2006;**29**:519–521.
60. McKevitt FM, Randall MS, Cleveland TJ, Gaines PA, Tan KT, Venables GS. The benefits of combined anti-platelet treatment in carotid artery stenting. *Eur J Vasc Endovasc Surg* 2005;**29**:522–527.
61. Gensicke H, van der Worp HB, Nederkoorn PJ, Macdonald S, Gaines PA, van der Lugt A, Mali WP, Lyrer PA, Peters N, Featherstone RL, de Borst GJ, Engelter ST, Brown MM, Bonati LH. Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk. *J Am Coll Cardiol* 2015;**65**:521–529.
62. Udell JA, Bonaca MP, Collet JP, Lincoff AM, Kereiakes DJ, Costa F, Lee CW, Mauri L, Valgimigli M, Park SJ, Montalescot G, Sabatine MS, Braunwald E, Bhatt DL. Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials. *Eur Heart J* 2016;**37**:390–399.
63. Schmit K, Dolor RJ, Jones WS, Vemulapalli S, Hasselblad V, Subherwal S, Heidenfelder B, Patel MR. Comparative effectiveness review of antiplatelet agents in peripheral artery disease. *J Am Heart Assoc* 2014;**3**:e001330.
64. Belch JJ, Dormandy J, Biasi GM, Cairols M, Diehm C, Eikelboom B, Golledge J, Jawien A, Lepantalo M, Norgren L, Hiatt WR, Becquemin JP, Bergqvist D, Clement D, Baumgartner I, Minar E, Stonebridge P, Vermassen F, Matyas L, Leizorovicz A. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. *J Vasc Surg* 2010;**52**:825–833.
65. Cacoub PP, Bhatt DL, Steg PG, Topol EJ, Creager MA. Patients with peripheral arterial disease in the CHARISMA trial. *Eur Heart J* 2009;**30**:192–201.
66. Fowkes FG, Price JF, Stewart MC, Butcher I, Leng GC, Pell AC, Sandercock PA, Fox KA, Lowe GD, Murray GD. Aspirin for prevention of cardiovascular events in a general population screened for a low ankle brachial index: a randomized controlled trial. *JAMA* 2010;**303**:841–848.
67. Belch J, MacCuish A, Campbell I, Cobbe S, Taylor R, Prescott R, Lee R, Bancroft J, MacEwan S, Shepherd J, Macfarlane P, Morris A, Jung R, Kelly C, Connacher A, Peden N, Jamieson A, Matthews D, Leese G, McKnight J, O'Brien I, Semple C, Petrie J, Gordon D, Pringle S, MacWalter R. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ* 2008;**337**:a1840.
68. Berger JS, Krantz MJ, Kittelson JM, Hiatt WR. Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease: a meta-analysis of randomized trials. *JAMA* 2009;**301**:1909–1919.
69. Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, Katona BG, Mahaffey KW, Norgren L, Jones WS, Blomster J, Millegard M, Reist C, Patel MR. Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. *N Engl J Med* 2017;**376**:32–40.
70. Bonaca MP, Scirica BM, Creager MA, Olin J, Bounameaux H, Dellborg M, Lamp JM, Murphy SA, Braunwald E, Morrow DA. Vorapaxar in patients with peripheral artery disease: results from TRA2°P-TIMI 50. *Circulation* 2013;**127**:1522–1529.
71. Bonaca MP, Gutierrez JA, Creager MA, Scirica BM, Olin J, Murphy SA, Braunwald E, Morrow DA. Acute limb ischemia and outcomes with vorapaxar in patients with peripheral artery disease: results from the Trial to Assess the Effects of Vorapaxar in Preventing Heart Attack and Stroke in Patients With Atherosclerosis-Thrombolysis in Myocardial Infarction 50 (TRA2°P-TIMI 50). *Circulation* 2016;**133**:997–1005.
72. Bedenis R, Lethaby A, Maxwell H, Acosta S, Prins MH. Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery. *Cochrane Database Syst Rev* 2015;**2**:CD000535.
73. Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch Bypass Oral Anticoagulants or Aspirin Study): a randomised trial. *Lancet* 2000;**355**:346–351.
74. Johnson WC, Williford WO. Benefits, morbidity, and mortality associated with long-term administration of oral anticoagulant therapy to patients with peripheral arterial bypass procedures: a prospective randomized study. *J Vasc Surg* 2002;**35**:413–421.

75. Monaco M, Di Tommaso L, Pinna GB, Lillo S, Schiavone V, Stassano P. Combination therapy with warfarin plus clopidogrel improves outcomes in femoropopliteal bypass surgery patients. *J Vasc Surg* 2012;**56**:96–105.
76. Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, Machan LS, Snyder SA, O'Leary EE, Ragheb AO, Zeller T. Durable clinical effectiveness with paclitaxel-eluting stents in the femoropopliteal artery: 5-year results of the Zilver PTX randomized trial. *Circulation* 2016;**133**:1472–1483.
77. Laird JR, Schneider PA, Tepe G, Brodmann M, Zeller T, Metzger C, Krishnan P, Scheinert D, Micari A, Cohen DJ, Wang H, Hasenbank MS, Jaff MR. Durability of treatment effect using a drug-coated balloon for femoropopliteal lesions: 24-month results of IN.PACT SFA. *J Am Coll Cardiol* 2015;**66**:2329–2338.
78. Dagher NN, Modrall JG. Pharmacotherapy before and after revascularization: anticoagulation, antiplatelet agents, and statins. *Semin Vasc Surg* 2007;**20**:10–14.
79. Franzone A, Piccolo R, Gargiulo G, Ariotti S, Marino M, Santucci A, Baldo A, Magnani G, Moschovitis A, Windecker S, Valgimigli M. Prolonged vs short duration of dual antiplatelet therapy after percutaneous coronary intervention in patients with or without peripheral arterial disease: a subgroup analysis of the PRODIGY randomized clinical trial. *JAMA Cardiol* 2016;**1**:795–803.
80. Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Oude Ophuis T, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS. Long-term use of ticagrelor in patients with prior myocardial infarction. *N Engl J Med* 2015;**372**:1791–1800.
81. Bonaca MP, Bhatt DL, Storey RF, Steg PG, Cohen M, Kuder J, Goodrich E, Nicolau JC, Parkhomenko A, Lopez-Sendon J, Dellborg M, Dalby A, Spinar J, Aylward P, Corbalan R, Abola MT, Jensen EC, Held P, Braunwald E, Sabatine MS. Ticagrelor for prevention of ischemic events after myocardial infarction in patients with peripheral artery disease. *J Am Coll Cardiol* 2016;**67**:2719–2728.
82. 2017 Guidelines for DAPT (citation pending).
83. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G, Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;**37**:2893–2962.
84. Winkel TA, Hoeks SE, Schouten O, Zeymer U, Limbourg T, Baumgartner I, Bhatt DL, Steg PG, Goto S, Rother J, Cacoub PP, Verhagen HJ, Bax JJ, Poldermans D. Prognosis of atrial fibrillation in patients with symptomatic peripheral arterial disease: data from the REduction of Atherothrombosis for Continued Health (REACH) Registry. *Eur J Vasc Endovasc Surg* 2010;**40**:9–16.
85. Jones WS, Hellkamp AS, Halperin J, Piccini JP, Breithardt G, Singer DE, Fox KA, Hankey GJ, Mahaffey KW, Califf RM, Patel MR. Efficacy and safety of rivaroxaban compared with warfarin in patients with peripheral artery disease and non-valvular atrial fibrillation: insights from ROCKET AF. *Eur Heart J* 2014;**35**:242–249.
86. Heidbuchel H, Verhamme P, Alings M, Antz M, Diener HC, Hacke W, Oldgren J, Sinnaeve P, Camm AJ, Kirchhof P. Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. *Europace* 2015;**17**:1467–1507.
87. Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, Buring J, Hennekens C, Kearney P, Meade T, Patrono C, Roncaglioni MC, Zanchetti A. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009;**373**:1849–1860.
88. Donaldson DR, Kester RC, Rajah SM, Hall TJ, Sreeharan N, Crow MJ. The influence of platelet inhibition on the patency of femoro-popliteal Dacron bypass grafts. *Vasc Endovasc Surg* 1985;**19**:224–230.
89. McCollum C, Alexander C, Kenchington G, Franks PJ, Greenhalgh R. Antiplatelet drugs in femoropopliteal vein bypasses: a multicenter trial. *J Vasc Surg* 1991;**13**:150–161.
90. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;**146**:857–867.
91. Lamberts M, Lip GY, Ruwald MH, Hansen ML, Ozcan C, Kristensen SL, Kober L, Torp-Pedersen C, Gislason GH. Antithrombotic treatment in patients with heart failure and associated atrial fibrillation and vascular disease: a nationwide cohort study. *J Am Coll Cardiol* 2014;**63**:2689–2698.
92. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MS, George MG, Hamdan AD, Higashida RT, Hoh BL, Janis LS, Kase CS, Kleindorfer DO, Lee JM, Moseley ME, Peterson ED, Turan TN, Valderrama AL, Vinters HV. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;**44**:2064–2089.
93. Donnan GA, Davis SM, Chambers BR, Gates PC. Surgery for prevention of stroke. *Lancet* 1998;**351**:1372–1373.
94. Sprynger M, RF, Moonen M, Aboyans V, Edvardsen T, Alcantara M, Brodmann M, Naka K, Kownaator S, Vlachopoulos C, Wautrecht JC, Lancellotti P. EACVI recommendations on echovascular imaging assessment of arterial diseases: Partim I. (in preparation), 2017.
95. Esposito-Bauer L, Saam T, Ghodrati I, Pelisek J, Heider P, Bauer M, Wolf P, Bockelbrink A, Feurer R, Sepp D, Winkler C, Zepper P, Boeckh-Behrens T, Riemenschneider M, Hemmer B, Poppert H. MRI plaque imaging detects carotid plaques with a high risk for future cerebrovascular events in asymptomatic patients. *PLoS One* 2013;**8**:e67927.
96. Gupta A, Kesavabhotla K, Baradaran H, Kamel H, Pandya A, Giambrone AE, Wright D, Pain KJ, Mtui EE, Suri JS, Sanelli PC, Mushlin AI. Plaque echolucency and stroke risk in asymptomatic carotid stenosis: a systematic review and meta-analysis. *Stroke* 2015;**46**:91–97.
97. Naylor AR, Schroeder TV, Sillesen H. Clinical and imaging features associated with an increased risk of late stroke in patients with asymptomatic carotid disease. *Eur J Vasc Endovasc Surg* 2014;**48**:633–640.
98. Sloan MA, Alexandrov AV, Tegeler CH, Spencer MP, Caplan LR, Feldmann E, Wechsler LR, Newell DW, Gomez CR, Babikian VL, Lefkowitz D, Goldman RS, Armon C, Hsu CY, Goodin DS. Assessment: transcranial Doppler ultrasonography: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2004;**62**:1468–1481.
99. Wardlaw JM, Chappell FM, Stevenson M, De Nigris E, Thomas S, Gillard J, Berry E, Young G, Rothwell P, Roditi G, Gough M, Brennan A, Bamford J, Best J. Accurate, practical and cost-effective assessment of carotid stenosis in the UK. *Health Technol Assess* 2006;**10**:iii–iv, ix–x, 1 - 182.
100. Blackshear JL, Cutlip DE, Roubin GS, Hill MD, Leimgruber PP, Begg RJ, Cohen DJ, Eidt JF, Narins CR, Prineas RJ, Glasser SP, Voeks JH, Brott TG. Myocardial infarction after carotid stenting and endarterectomy: results from the carotid revascularization endarterectomy versus stenting trial. *Circulation* 2011;**123**:2571–2578.
101. Giannakopoulos TG, Moulakakis K, Sfyroeras GS, Avgerinos ED, Antonopoulos CN, Kakisis JD, Karakitsos P, Brountzos EN, Liapis CD. Association between plaque echogenicity and embolic material captured in filter during protected carotid angioplasty and stenting. *Eur J Vasc Endovasc Surg* 2012;**43**:627–631.
102. Akkaya E, Vuruskan E, Gul ZB, Yildirim A, Pusuroglu H, Surgit O, Kalkan AK, Akgul O, Akgul GP, Gul M. Cerebral microemboli and neurocognitive change after carotid artery stenting with different embolic protection devices. *Int J Cardiol* 2014;**176**:478–483.
103. Bijuklic K, Wandler A, Hazizi F, Schofer J. The PROFI study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting): a prospective randomized trial. *J Am Coll Cardiol* 2012;**59**:1383–1389.
104. Cano MN, Kambara AM, de Cano SJ, Pezzi Portela LA, Paes AT, Costa JR Jr, Abizaid AA, Moreira SM, Sousa AG, Sousa JE. Randomized comparison of distal and proximal cerebral protection during carotid artery stenting. *JACC Cardiovasc Interv* 2013;**6**:1203–1209.
105. Montorsi P, Caputi L, Galli S, Ciceri E, Ballerini G, Agrifoglio M, Ravagnani P, Trabattoni D, Pontone G, Fabbiocchi F, Loaldi A, Parati E, Andreini D, Veglia F, Bartorelli AL. Microembolization during carotid artery stenting in patients with high-risk, lipid-rich plaque. A randomized trial of proximal versus distal cerebral protection. *J Am Coll Cardiol* 2011;**58**:1656–1663.
106. Stabile E, Esposito G. Operator's experience is the most efficient embolic protection device for carotid artery stenting. *Circ Cardiovasc Interv* 2013;**6**:496–497.
107. Garg N, Karagiorgos N, Pisimisis GT, Sohal DP, Longo GM, Johanning JM, Lynch TG, Pipinos, II. Cerebral protection devices reduce periprocedural strokes during carotid angioplasty and stenting: a systematic review of the current literature. *J Endovasc Ther* 2009;**16**:412–427.
108. Touze E, Trinquart L, Chatellier G, Mas JL. Systematic review of the perioperative risks of stroke or death after carotid angioplasty and stenting. *Stroke* 2009;**40**:e683–e693.
109. Zahn R, Ischinger T, Hochadel M, Zeymer U, Schmalz W, Treese N, Hauptmann KE, Seggewiss H, Janicke I, Haase H, Mudra H, Senges J. Carotid artery stenting in octogenarians: results from the ALKK Carotid Artery Stent (CAS) Registry. *Eur Heart J* 2007;**28**:370–375.
110. Rosenfield K, Matsumura JS, Chaturvedi S, Riles T, Ansel GM, Metzger DC, Wechsler L, Jaff MR, Gray W. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med* 2016;**374**:1011–1020.
111. Jansen O, Fiehler J, Hartmann M, Bruckmann H. Protection or nonprotection in carotid stent angioplasty: the influence of interventional techniques on outcome data from the SPACE Trial. *Stroke* 2009;**40**:841–846.
112. Gray WA, Rosenfield KA, Jaff MR, Chaturvedi S, Peng L, Verta P. Influence of site and operator characteristics on carotid artery stent outcomes: analysis of

the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) clinical study. *JACC Cardiovasc Interv* 2011;**4**:235–246.
113. Nallamothu BK, Gurm HS, Ting HH, Goodney PP, Rogers MA, Curtis JP, Dimick JB, Bates ER, Krumholz HM, Birkmeyer JD. Operator experience and carotid stenting outcomes in Medicare beneficiaries. *JAMA* 2011;**306**:1338–1343.
114. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 1995;**273**:1421–1428.
115. Halliday A, Harrison M, Hayter E, Kong X, Mansfield A, Marro J, Pan H, Peto R, Potter J, Rahimi K, Rau A, Robertson S, Streifler J, Thomas D. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. *Lancet* 2010;**376**:1074–1084.
116. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, Thomas D. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004;**363**:1491–1502.
117. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ. Sex difference in the effect of time from symptoms to surgery on benefit from carotid endarterectomy for transient ischemic attack and nondisabling stroke. *Stroke* 2004;**35**:2855–2861.
118. Hadar N, Raman G, Moorthy D, O'Donnell TF, Thaler DE, Feldmann E, Lau J, Kitsios GD, Dahabreh IJ. Asymptomatic carotid artery stenosis treated with medical therapy alone: temporal trends and implications for risk assessment and the design of future studies. *Cerebrovasc Dis* 2014;**38**:163–173.
119. Naylor AR, Gaines PA, Rothwell PM. Who benefits most from intervention for asymptomatic carotid stenosis: patients or professionals? *Eur J Vasc Endovasc Surg* 2009;**37**:625–632.
120. Baker WH, Howard VJ, Howard G, Toole JF. Effect of contralateral occlusion on long-term efficacy of endarterectomy in the Asymptomatic Carotid Atherosclerosis Study (ACAS). ACAS Investigators. *Stroke* 2000;**31**:2330–2334.
121. Nicolaides AN, Kakkos SK, Griffin M, Sabetai M, Dhanjil S, Tegos T, Thomas DJ, Giannoukas A, Geroulakos G, Georgiou N, Francis S, Ioannidou E, Dore CJ. Severity of asymptomatic carotid stenosis and risk of ipsilateral hemispheric ischaemic events: results from the ACSRS study. *Eur J Vasc Endovasc Surg* 2005;**30**:275–284.
122. Kakkos SK, Sabetai M, Tegos T, Stevens J, Thomas D, Griffin M, Geroulakos G, Nicolaides AN. Silent embolic infarcts on computed tomography brain scans and risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis. *J Vasc Surg* 2009;**49**:902–909.
123. Kakkos SK, Nicolaides AN, Charalambous I, Thomas D, Giannopoulos A, Naylor AR, Geroulakos G, Abbott AL. Predictors and clinical significance of progression or regression of asymptomatic carotid stenosis. *J Vasc Surg* 2014;**59**:956–967.
124. Markus HS, King A, Shipley M, Topakian R, Cullinane M, Reihill S, Bornstein NM, Schaafsma A. Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. *Lancet Neurol* 2010;**9**:663–671.
125. King A, Serena J, Bornstein NM, Markus HS. Does impaired cerebrovascular reactivity predict stroke risk in asymptomatic carotid stenosis? A prospective substudy of the asymptomatic carotid emboli study. *Stroke* 2011;**42**:1550–1555.
126. Nicolaides AN, Kakkos SK, Kyriacou E, Griffin M, Sabetai M, Thomas DJ, Tegos T, Geroulakos G, Labropoulos N, Dore CJ, Morris TP, Naylor R, Abbott AL. Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification. *J Vasc Surg* 2010;**52**:1486–1496.
127. Kakkos SK, Griffin MB, Nicolaides AN, Kyriacou E, Sabetai MM, Tegos T, Makris GC, Thomas DJ, Geroulakos G. The size of juxtaluminal hypoechoic area in ultrasound images of asymptomatic carotid plaques predicts the occurrence of stroke. *J Vasc Surg* 2013;**57**:609–618.
128. Gupta A, Baradaran H, Schweitzer AD, Kamel H, Pandya A, Delgado D, Dunning A, Mushlin AI, Sanelli PC. Carotid plaque MRI and stroke risk: a systematic review and meta-analysis. *Stroke* 2013;**44**:3071–3077.
129. Hawkins BM, Kennedy KF, Aronow HD, Nguyen LL, White CJ, Rosenfield K, Normand SL, Spertus JA, Yeh RW. Hospital variation in carotid stenting outcomes. *JACC Cardiovasc Interv* 2015;**6**:858–863.
130. Kallmayer MA, Tsantilas P, Knappich C, Haller B, Storck M, Stadlbauer T, Kuhnl A, Zimmermann A, Eckstein HH. Patient characteristics and outcomes of carotid endarterectomy and carotid artery stenting: analysis of the German mandatory national quality assurance registry – 2003 to 2014. *J Cardiovasc Surg (Torino)* 2015;**56**:827–836.
131. Werner N, Zeymer U, Hochadel M, Hauptmann KE, Jung J, Janicke I, Haase H, Leschke M, Mudra H, Zahn R. Fifteen-year experience with carotid artery stenting (from the carotid artery stenting-registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausarzte). *Am J Cardiol* 2015;**115**:360–366.
132. Paraskevas KI, Kalmykov EL, Naylor AR. Stroke/death rates following carotid artery stenting and carotid endarterectomy in contemporary administrative dataset registries: a systematic review. *Eur J Vasc Endovasc Surg* 2016;**51**:3–12.
133. Choi JC, Johnston SC, Kim AS. Early outcomes after carotid artery stenting compared with endarterectomy for asymptomatic carotid stenosis. *Stroke* 2015;**46**:120–125.
134. Dua A, Romanelli M, Upchurch GR Jr, Pan J, Hood D, Hodgson KJ, Desai SS. Predictors of poor outcome after carotid intervention. *J Vasc Surg* 2016;**64**:663–670.
135. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;**351**:1493–1501.
136. Gurm HS, Yadav JS, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Ansel G, Strickman NE, Wang H, Cohen SA, Massaro JM, Cutlip DE. Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2008;**358**:1572–1579.
137. Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, Goldstein LB, Meschia JF, Ferguson RD, Moore WS, Howard G, Brott TG. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke* 2011;**42**:675–680.
138. Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, Warlow CP, Barnett HJ. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet* 2003;**361**:107–116.
139. Naylor AR, Sillesen H, Schroeder TV. Clinical and imaging features associated with an increased risk of early and late stroke in patients with symptomatic carotid disease. *Eur J Vasc Endovasc Surg* 2015;**49**:513–523.
140. Stromberg S, Gelin J, Osterberg T, Bergstrom GM, Karlstrom L, Osterberg K. Very urgent carotid endarterectomy confers increased procedural risk. *Stroke* 2012;**43**:1331–1335.
141. Loftus IM, Paraskevas KI, Johal A, Waton S, Heikkila K, Naylor AR, Cromwell DA. Delays to surgery and procedural risks following carotid endarterectomy in the UK National Vascular Registry. *Eur J Vasc Endovasc Surg* 2016;**52**:438–443.
142. Tsantilas P, Kuehnl A, Konig T, Breitkreuz T, Kallmayer M, Knappich C, Schmid S, Storck M, Zimmermann A, Eckstein HH. Short time interval between neurologic event and carotid surgery is not associated with an increased procedural risk. *Stroke* 2016;**47**:2783–2790.
143. Bush CK, Kurimella D, Cross LJ, Conner KR, Martin-Schild S, He J, Li C, Chen J, Kelly T. Endovascular treatment with stent-retriever devices for acute ischemic stroke: a meta-analysis of randomized controlled trials. *PLoS One* 2016;**11**:e0147287.
144. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, van Walderveen MA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama a Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PL, van Rooij WJ, van den Berg JS, van Hasselt BA, Aerden LA, Dallinga RJ, Visser MC, Bot JC, Vroomen PC, Eshghi O, Schreuder TH, Heijboer RJ, Keizer K, Tielbeek AV, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers ME, Jenniskens SF, Beenen LF, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Majoie CB, Dippel DW. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;**372**:11–20.
145. Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, Mackey A, Hill MD, Leimgruber PP, Sheffet AJ, Howard VJ, Moore WS, Voeks JH, Hopkins LN, Cutlip DE, Cohen DJ, Popma JJ, Ferguson RD, Cohen SN, Blackshear JL, Silver FL, Mohr JP, Lal BK, Meschia JF. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;**363**:11–23.
146. Hill MD, Brooks W, Mackey A, Clark WM, Meschia JF, Morrish WF, Mohr JP, Rhodes JD, Popma JJ, Lal BK, Longbottom ME, Voeks JH, Howard G, Brott TG. Stroke after carotid stenting and endarterectomy in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *Circulation* 2012;**126**:3054–3061.
147. Economopoulos KP, Sergentanis TN, Tsivgoulis G, Mariolis AD, Stefanadis C. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. *Stroke* 2011;**42**:687–692.
148. Bonati LH, Lyrer P, Ederle J, Featherstone R, Brown MM. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *Cochrane Database Syst Rev* 2012;**9**:CD000515.
149. Rantner B, Goebel G, Bonati LH, Ringleb PA, Mas JL, Fraedrich G. The risk of carotid artery stenting compared with carotid endarterectomy is greatest in patients treated within 7 days of symptoms. *J Vasc Surg* 2013;**57**:619–626.
150. Meschia JF, Hopkins LN, Altafullah I, Wechsler LR, Stotts G, Gonzales NR, Voeks JH, Howard G, Brott TG. Time from symptoms to carotid endarterectomy or stenting and perioperative risk. *Stroke* 2015;**46**:3540–3542.
151. Howard G, Roubin GS, Jansen O, Hendrikse J, Halliday A, Fraedrich G, Eckstein HH, Calvet D, Bulbulia R, Bonati LH, Becquemin JP, Algra A, Brown MM, Ringleb PA, Brott TG, Mas JL. Association between age and risk of stroke or

death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. *Lancet* 2016;**387**:1305–1311.
152. Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, Mali WP, Beard JD, Cleveland T, Engelter ST, Lyrer PA, Ford GA, Dorman PJ, Brown MM. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet* 2015;**385**:529–538.
153. Brott TG, Howard G, Roubin GS, Meschia JF, Mackey A, Brooks W, Moore WS, Hill MD, Mantese VA, Clark WM, Timaran CH, Heck D, Leimgruber PP, Sheffet AJ, Howard VJ, Chaturvedi S, Lal BK, Voeks JH, Hobson RW 2nd. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med* 2016;**374**:1021–1031.
154. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;**351**:1379–1387.
155. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, Rankin RN, Clagett GP, Hachinski VC, Sackett DL, Thorpe KE, Meldrum HE, Spence JD. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1998;**339**:1415–1425.
156. Borhani Haghighi A, Edgell RC, Cruz-Flores S, Zaidat OO. Vertebral artery origin stenosis and its treatment. *J Stroke Cerebrovasc Dis* 2011;**20**:369–376.
157. Khan S, Cloud GC, Kerry S, Markus HS. Imaging of vertebral artery stenosis: a systematic review. *J Neurol Neurosurg Psychiatry* 2007;**78**:1218–1225.
158. Kumar Dundamadappa S, Cauley K. Vertebral artery ostial stenosis: prevalence by digital subtraction angiography, MR angiography, and CT angiography. *J Neuroimaging* 2013;**23**:360–367.
159. Berguer R, Flynn LM, Kline RA, Caplan L. Surgical reconstruction of the extracranial vertebral artery: management and outcome. *J Vasc Surg* 2000;**31**:9–18.
160. Kieffer E, Praquin B, Chiche L, Koskas F, Bahnini A. Distal vertebral artery reconstruction: long-term outcome. *J Vasc Surg* 2002;**36**:549–554.
161. Stayman AN, Nogueira RG, Gupta R. A systematic review of stenting and angioplasty of symptomatic extracranial vertebral artery stenosis. *Stroke* 2011;**42**:2212–2216.
162. Compter A, van der Worp HB, Schonewille WJ, Vos JA, Boiten J, Nederkoorn PJ, Uyttenboogaart M, Lo RT, Algra A, Kappelle LJ. Stenting versus medical treatment in patients with symptomatic vertebral artery stenosis: a randomised open-label phase 2 trial. *Lancet Neurol* 2015;**14**:606–614.
163. Aboyans V, Criqui MH, McDermott MM, Allison MA, Denenberg JO, Shadman R, Fronek A. The vital prognosis of subclavian stenosis. *J Am Coll Cardiol* 2007;**49**:1540–1545.
164. Klitfod L, Jensen LP. Treatment of chronic upper limb ischaemia is safe and results are good. *Dan Med J* 2014;**61**:A4859.
165. Daniel VT, Madenci AL, Nguyen LL, Eslami MH, Kalish JA, Farber A, McPhee JT. Contemporary comparison of supra-aortic trunk surgical reconstructions for occlusive disease. *J Vasc Surg* 2014;**59**:1577–1582.
166. Duran M, Grotemeyer D, Danch MA, Grabitz K, Schelzig H, Sagban TA. Subclavian carotid transposition: immediate and long-term outcomes of 126 surgical reconstructions. *Ann Vasc Surg* 2015;**29**:397–403.
167. Burihan E, Soma F, lared W. Angioplasty versus stenting for subclavian artery stenosis. *Cochrane Database Syst Rev* 2011;**10**:CD008461.
168. Chatterjee S, Nerella N, Chakravarty S, Shani J. Angioplasty alone versus angioplasty and stenting for subclavian artery stenosis—a systematic review and meta-analysis. *Am J Ther* 2013;**20**:520–523.
169. Huttl K, Nemes B, Simonffy A, Entz L, Berczi V. Angioplasty of the innominate artery in 89 patients: experience over 19 years. *Cardiovasc Intervent Radiol* 2002;**25**:109–114.
170. van de Weijer MA, Vonken EJ, de Vries JP, Moll FL, Vos JA, de Borst GJ. Technical and clinical success and long-term durability of endovascular treatment for atherosclerotic aortic arch branch origin obstruction: evaluation of 144 procedures. *Eur J Vasc Endovasc Surg* 2015;**50**:13–20.
171. Modarai B, Ali T, Dourado R, Reidy JF, Taylor PR, Burnand KG. Comparison of extra-anatomic bypass grafting with angioplasty for atherosclerotic disease of the supra-aortic trunks. *Br J Surg* 2004;**91**:1453–1457.
172. Owens LV, Tinsley EA Jr, Criado E, Burnham SJ, Keagy BA. Extrathoracic reconstruction of arterial occlusive disease involving the supraaortic trunks. *J Vasc Surg* 1995;**22**:217–221.
173. Song L, Zhang J, Li J, Gu Y, Yu H, Chen B, Guo L, Wang Z. Endovascular stenting vs. extrathoracic surgical bypass for symptomatic subclavian steal syndrome. *J Endovasc Ther* 2012;**19**:44–51.
174. Lee AD, Agarwal S, Sadhu D. A 7-year experience with thoracoscopic sympathectomy for critical upper limb ischemia. *World J Surg* 2006;**30**:1644–1647.
175. Björck M, Koelemay M, Acosta S, Bastos Goncalves F, Kölbel T, Kolkman JJ, Lees T, Lefevre JH, Menyhei G, Oderich G, ESVS Guidelines Committee, Kolh P, de Borst GJ, Chakfe N, Debus S, Hinchliffe R, Kakkos S, Koncar I, Sanddal Lindholt J, Vega de Ceniga M, Vermassen F, Verzini F, Document Reviewers, Geelkerken B, Gloviczki P, Huber T, Naylor R. Management of the diseases of mesenteric arteries and veins: clinical practice guidelines of the European Society of Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2017;**53**:460–510.
176. Acosta S, Nilsson TK, Bjorck M. D-dimer testing in patients with suspected acute thromboembolic occlusion of the superior mesenteric artery. *Br J Surg* 2004;**91**:991–994.
177. Block T, Nilsson TK, Bjorck M, Acosta S. Diagnostic accuracy of plasma biomarkers for intestinal ischaemia. *Scand J Clin Lab Invest* 2008;**68**:242–248.
178. Matsumoto S, Sekine K, Funaoka H, Yamazaki M, Shimizu M, Hayashida K, Kitano M. Diagnostic performance of plasma biomarkers in patients with acute intestinal ischaemia. *Br J Surg* 2014;**101**:232–238.
179. Cudnik MT, Darbha S, Jones J, Macedo J, Stockton SW, Hiestand BC. The diagnosis of acute mesenteric ischemia: a systematic review and meta-analysis. *Acad Emerg Med* 2013;**20**:1087–1100.
180. Lehtimaki TT, Karkkainen JM, Saari P, Manninen H, Paajanen H, Vanninen R. Detecting acute mesenteric ischemia in CT of the acute abdomen is dependent on clinical suspicion: review of 95 consecutive patients. *Eur J Radiol* 2015;**84**:2444–2453.
181. Jrvinen O, Laurikka J, Salenius JP, Tarkka M. Acute intestinal ischaemia. A review of 214 cases. *Ann Chir Gynaecol* 1994;**83**:22–25.
182. Beaulieu RJ, Arnaoutakis KD, Abularrage CJ, Efron DT, Schneider E, Black JH 3rd. Comparison of open and endovascular treatment of acute mesenteric ischemia. *J Vasc Surg* 2014;**59**:159–164.
183. Bjorck M, Orr N, Endean ED. Debate: Whether an endovascular-first strategy is the optimal approach for treating acute mesenteric ischemia. *J Vasc Surg* 2015;**62**:767–772.
184. Block TA, Acosta S, Bjorck M. Endovascular and open surgery for acute occlusion of the superior mesenteric artery. *J Vasc Surg* 2010;**52**:959–966.
185. Kalra M, Ryer EJ, Oderich GS, Duncan AA, Bower TC, Gloviczki P. Contemporary results of treatment of acute arterial mesenteric thrombosis: has endovascular treatment improved outcomes? *Perspect Vasc Surg Endovasc Ther* 2012;**24**:171–176.
186. Wyers MC, Powell RJ, Nolan BW, Cronenwett JL. Retrograde mesenteric stenting during laparotomy for acute occlusive mesenteric ischemia. *J Vasc Surg* 2007;**45**:269–275.
187. Arthurs ZM, Titus J, Bannazadeh M, Eagleton MJ, Srivastava S, Sarac TP, Clair DG. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. *J Vasc Surg* 2011;**53**:698–704.
188. Schermerhorn ML, Giles KA, Hamdan AD, Wyers MC, Pomposelli FB. Mesenteric revascularization: management and outcomes in the United States, 1988–2006. *J Vasc Surg* 2009;**50**:341–348.
189. Rotondo MF, Schwab CW, McGonigal MD, Phillips GR 3rd, Fruchterman TM, Kauder DR, Latenser BA, Angood PA. 'Damage control': an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993;**35**:375–382.
190. Bjorck M, Acosta S, Lindberg F, Troeng T, Bergqvist D. Revascularization of the superior mesenteric artery after acute thromboembolic occlusion. *Br J Surg* 2002;**89**:923–927.
191. Bjornsson S, Bjorck M, Block T, Resch T, Acosta S. Thrombolysis for acute occlusion of the superior mesenteric artery. *J Vasc Surg* 2011;**54**:1734–1742.
192. Thomas JH, Blake K, Pierce GE, Hermreck AS, Seigel E. The clinical course of asymptomatic mesenteric arterial stenosis. *J Vasc Surg* 1998;**27**:840–844.
193. van Petersen AS, Meerwaldt R, Kolkman JJ, Huisman AB, van der Palen J, van Bockel JH, Zeebregts CJ, Geelkerken RH. The influence of respiration on criteria for transabdominal duplex examination of the splanchnic arteries in patients with suspected chronic splanchnic ischemia. *J Vasc Surg* 2013;**57**:1603–1611.
194. Zwolak RM, Fillinger MF, Walsh DB, LaBombard FE, Musson A, Darling CE, Cronenwett JL. Mesenteric and celiac duplex scanning: a validation study. *J Vasc Surg* 1998;**27**:1078–1087.
195. Rheudasil JM, Stewart MT, Schellack JV, Smith RB 3rd, Salam AA, Perdue GD. Surgical treatment of chronic mesenteric arterial insufficiency. *J Vasc Surg* 1988;**8**:495–500.
196. Moghadamyeghaneh Z, Carmichael JC, Mills SD, Dolich MO, Pigazzi A, Fujitani RM, Stamos MJ. Early outcome of treatment of chronic mesenteric ischemia. *Am Surg* 2015;**81**:1149–1156.
197. Rawat N, Gibbons CP. Surgical or endovascular treatment for chronic mesenteric ischemia: a multicenter study. *Ann Vasc Surg* 2010;**24**:935–945.
198. Peck MA, Conrad MF, Kwolek CJ, LaMuraglia GM, Paruchuri V, Cambria RP. Intermediate-term outcomes of endovascular treatment for symptomatic chronic mesenteric ischemia. *J Vasc Surg* 2010;**51**:140–147.
199. Silva JA, White CJ, Collins TJ, Jenkins JS, Andry ME, Reilly JP, Ramee SR. Endovascular therapy for chronic mesenteric ischemia. *J Am Coll Cardiol* 2006;**47**:944–950.
200. Malgor RD, Oderich GS, McKusick MA, Misra S, Kalra M, Duncan AA, Bower TC, Gloviczki P. Results of single- and two-vessel mesenteric artery stents for chronic mesenteric ischemia. *Ann Vasc Surg* 2010;**24**:1094–1101.

201. Oderich GS, Erdoes LS, Lesar C, Mendes BC, Gloviczki P, Cha S, Duncan AA, Bower TC. Comparison of covered stents versus bare metal stents for treatment of chronic atherosclerotic mesenteric arterial disease. *J Vasc Surg* 2013;**58**:1316–1323.
202. Menke J, Luthje L, Kastrup A, Larsen J. Thromboembolism in atrial fibrillation. *Am J Cardiol* 2010;**105**:502–510.
203. Mensink PB, van Petersen AS, Geelkerken RH, Otte JA, Huisman AB, Kolkman JJ. Clinical significance of splanchnic artery stenosis. *Br J Surg* 2006;**93**:1377–1382.
204. Safian RD, Textor SC. Renal-artery stenosis. *N Engl J Med* 2001;**344**:431–442.
205. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B. ACC/AHA 2005 Practice 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): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006;**113**:e463–e654.
206. Persu A, Giavarini A, Touze E, Januszewicz A, Sapoval M, Azizi M, Barral X, Jeunemaitre X, Morganti A, Plouin PF, de Leeuw P. European consensus on the diagnosis and management of fibromuscular dysplasia. *J Hypertens* 2014;**32**:1367–1378.
207. Tafur-Soto JD, White CJ. Renal artery stenosis. *Cardiol Clin* 2015;**33**:59–73.
208. Messerli FH, Bangalore S, Makani H, Rimoldi SF, Allemann Y, White CJ, Textor S, Sleight P. Flash pulmonary oedema and bilateral renal artery stenosis: the Pickering syndrome. *Eur Heart J* 2011;**32**:2231–2235.
209. Jennings CG, Houston JG, Severn A, Bell S, Mackenzie IS, Macdonald TM. Renal artery stenosis-when to screen, what to stent? *Curr Atheroscler Rep* 2014;**16**:416.
210. Zeller T, Bonvini RF, Sixt S. Color-coded duplex ultrasound for diagnosis of renal artery stenosis and as follow-up examination after revascularization. *Catheter Cardiovasc Interv* 2008;**71**:995–999.
211. Williams GJ, Macaskill P, Chan SF, Karplus TE, Yung W, Hodson EM, Craig JC. Comparative accuracy of renal duplex sonographic parameters in the diagnosis of renal artery stenosis: paired and unpaired analysis. *AJR Am J Roentgenol* 2007;**188**:798–811.
212. AbuRahma AF, Yacoub M. Renal imaging: duplex ultrasound, computed tomography angiography, magnetic resonance angiography, and angiography. *Semin Vasc Surg* 2013;**26**:134–143.
213. Tan KT, van Beek EJ, Brown PW, van Delden OM, Tijssen J, Ramsay LE. Magnetic resonance angiography for the diagnosis of renal artery stenosis: a meta-analysis. *Clin Radiol* 2002;**57**:617–624.
214. De Bruyne B, Manoharan G, Pijls NH, Verhamme K, Madaric J, Bartunek J, Vanderheyden M, Heyndrickx GR. Assessment of renal artery stenosis severity by pressure gradient measurements. *J Am Coll Cardiol* 2006;**48**:1851–1855.
215. Drieghe B, Madaric J, Sarno G, Manoharan G, Bartunek J, Heyndrickx GR, Pijls NH, De Bruyne B. Assessment of renal artery stenosis: side-by-side comparison of angiography and duplex ultrasound with pressure gradient measurements. *Eur Heart J* 2008;**29**:517–524.
216. Conlon PJ, Little MA, Pieper K, Mark DB. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. *Kidney Int* 2001;**60**:1490–1497.
217. Mailloux LU, Napolitano B, Bellucci AG, Vernace M, Wilkes BM, Mossey RT. Renal vascular disease causing end-stage renal disease, incidence, clinical correlates, and outcomes: a 20-year clinical experience. *Am J Kidney Dis* 1994;**24**:622–629.
218. Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, Hoes AW, Jennings CS, Landmesser U, Pedersen TR, Reiner Z, Riccardi G, Taskinen MR, Tokgozoglu L, Verschuren WM, Vlachopoulos C, Wood DA, Zamorano JL. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias: the Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;**37**:2999–3058.
219. Evans KL, Tuttle KR, Folt DA, Dawson T, Haller ST, Brewster PS, He W, Jamerson K, Dworkin LD, Cutlip DE, Murphy TP, D'Agostino RB Sr, Henrich W, Cooper CJ. Use of renin-angiotensin inhibitors in people with renal artery stenosis. *Clin J Am Soc Nephrol* 2014;**9**:1199–1206.
220. Hackam DG, Duong-Hua ML, Mamdani M, Li P, Tobe SW, Spence JD, Garg AX. Angiotensin inhibition in renovascular disease: a population-based cohort study. *Am Heart J* 2008;**156**:549–555.
221. Chrysochou C, Foley RN, Young JF, Khavandi K, Cheung CM, Kalra PA. Dispelling the myth: the use of renin-angiotensin blockade in atheromatous renovascular disease. *Nephrol Dial Transplant* 2012;**27**:1403–1409.
222. Losito A, Errico R, Santirosi P, Lupattelli T, Scalera GB, Lupattelli L. Long-term follow-up of atherosclerotic renovascular disease. Beneficial effect of ACE inhibition. *Nephrol Dial Transplant* 2005;**20**:1604–1609.
223. Hackam DG, Wu F, Li P, Austin PC, Tobe SW, Mamdani MM, Garg AX. Statins and renovascular disease in the elderly: a population-based cohort study. *Eur Heart J* 2011;**32**:598–610.
224. Vashist A, Heller EN, Brown EJ Jr, Alhaddad IA. Renal artery stenosis: a cardiovascular perspective. *Am Heart J* 2002;**143**:559–564.
225. Chrysant GS, Bates MC, Sullivan TM, Bachinsky WB, Popma JJ, Peng L, Omran HL, Jaff MR. Proper patient selection yields significant and sustained reduction in systolic blood pressure following renal artery stenting in patients with uncontrolled hypertension: long-term results from the HERCULES trial. *J Clin Hypertens (Greenwich)* 2014;**16**:497–503.
226. Jaff MR, Bates M, Sullivan T, Popma J, Gao X, Zaugg M, Verta P. Significant reduction in systolic blood pressure following renal artery stenting in patients with uncontrolled hypertension: results from the HERCULES trial. *Catheter Cardiovasc Interv* 2012;**80**:343–350.
227. Nordmann AJ, Woo K, Parkes R, Logan AG. Balloon angioplasty or medical therapy for hypertensive patients with atherosclerotic renal artery stenosis? A meta-analysis of randomized controlled trials. *Am J Med* 2003;**114**:44–50.
228. Bavry AA, Kapadia SR, Bhatt DL, Kumbhani DJ. Renal artery revascularization: updated meta-analysis with the CORAL trial. *JAMA Intern Med* 2014;**174**:1849–1851.
229. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, Cohen DJ, Matsumoto AH, Steffes M, Jaff MR, Prince MR, Lewis EF, Tuttle KR, Shapiro JI, Rundback JH, Massaro JM, D'Agostino RB Sr, Dworkin LD. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med* 2014;**370**:13–22.
230. Murphy TP, Cooper CJ, Matsumoto AH, Cutlip DE, Pencina KM, Jamerson K, Tuttle KR, Shapiro JI, D'Agostino R, Massaro J, Henrich W, Dworkin LD. Renal artery stent outcomes: effect of baseline blood pressure, stenosis severity, and translesion pressure gradient. *J Am Coll Cardiol* 2015;**66**:2487–2494.
231. Wheatley K, Ives N, Gray R, Kalra PA, Moss JG, Baigent C, Carr S, Chalmers N, Eadington D, Hamilton G, Lipkin G, Nicholson A, Scoble J. Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med* 2009;**361**:1953–1962.
232. Bax L, Woittiez AJ, Kouwenberg HJ, Mali WP, Buskens E, Beek FJ, Braam B, Huysmans FT, Schultze Kool LJ, Rutten MJ, Doorenbos CJ, Aarts JC, Rabelink TJ, Plouin PF, Raynaud A, van Montfrans GA, Reekers JA, van den Meiracker AH, Pattynama PM, van de Ven PJ, Vroegindeweij D, Kroon AA, de Haan MW, Postma CT, Beutler JJ. Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. *Ann Intern Med* 2009;**150**:840–848.
233. Olin JW, Gornik HL, Bacharach JM, Biller J, Fine LJ, Gray BH, Gray WA, Gupta R, Hamburg NM, Katzen BT, Lookstein RA, Lumsden AB, Newburger JW, Rundek T, Sperati CJ, Stanley JC. Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. *Circulation* 2014;**129**:1048–1078.
234. Davies MG, Saad WE, Peden EK, Mohiuddin IT, Naoum JJ, Lumsden AB. The long-term outcomes of percutaneous therapy for renal artery fibromuscular dysplasia. *J Vasc Surg* 2008;**48**:865–871.
235. Mousa AY, Campbell JE, Stone PA, Broce M, Bates MC, AbuRahma AF. Short- and long-term outcomes of percutaneous transluminal angioplasty/stenting of renal fibromuscular dysplasia over a ten-year period. *J Vasc Surg* 2012;**55**:421–427.
236. Trinquart L, Mounier-Vehier C, Sapoval M, Gagnon N, Plouin PF. Efficacy of revascularization for renal artery stenosis caused by fibromuscular dysplasia: a systematic review and meta-analysis. *Hypertension* 2010;**56**:525–532.
237. Kane GC, Xu N, Mistrik E, Roubicek T, Stanson AW, Garovic VD. Renal artery revascularization improves heart failure control in patients with atherosclerotic renal artery stenosis. *Nephrol Dial Transplant* 2010;**25**:813–820.
238. Ritchie J, Green D, Chrysochou C, Chalmers N, Foley RN, Kalra PA. High-risk clinical presentations in atherosclerotic renovascular disease: prognosis and response to renal artery revascularization. *Am J Kidney Dis* 2014;**63**:186–197.
239. van den Berg DT, Deinum J, Postma CT, van der Wilt GJ, Riksen NP. The efficacy of renal angioplasty in patients with renal artery stenosis and flash oedema or congestive heart failure: a systematic review. *Eur J Heart Fail* 2012;**14**:773–781.
240. Cianci R, Martina P, Borghesi F, di Donato D, Polidori L, Lai S, Ascoli G, de Francesco I, Zaccaria A, Gigante A, Barbano B. Revascularization versus medical

therapy for renal artery stenosis: antihypertensive drugs and renal outcome. *Angiology* 2011;**62**:92–99.
241. Abela R, Ivanova S, Lidder S, Morris R, Hamilton G. An analysis comparing open surgical and endovascular treatment of atherosclerotic renal artery stenosis. *Eur J Vasc Endovasc Surg* 2009;**38**:666–675.
242. Balzer KM, Neuschafer S, Sagban TA, Grotemeyer D, Pfeiffer T, Rump LC, Sandmann W. Renal artery revascularization after unsuccessful percutaneous therapy: a single centre experience. *Langenbecks Arch Surg* 2012;**397**:111–115.
243. Balzer KM, Pfeiffer T, Rossbach S, Voiculescu A, Modder U, Godehardt E, Sandmann W. Prospective randomized trial of operative vs interventional treatment for renal artery ostial occlusive disease (RAOOD). *J Vasc Surg* 2009;**49**:667–674.
244. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, Chan C, Celic L, Pearce WH, Schneider JR, Sharma L, Clark E, Gibson D, Martin GJ. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. *JAMA* 2001;**286**:1599–1606.
245. Leng GC, Fowkes FG. The Edinburgh Claudication Questionnaire: an improved version of the WHO/Rose Questionnaire for use in epidemiological surveys. *J Clin Epidemiol* 1992;**45**:1101–1109.
246. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007;**45**(suppl S):S5–S67.
247. Abou-Zamzam AM Jr, Gomez NR, Molkara A, Banta JE, Teruya TH, Killeen JD, Bianchi C. A prospective analysis of critical limb ischemia: factors leading to major primary amputation versus revascularization. *Ann Vasc Surg* 2007;**21**:458–463.
248. Abu Dabrh AM, Steffen MW, Undavalli C, Asi N, Wang Z, Elamin MB, Conte MS, Murad MH. The natural history of untreated severe or critical limb ischemia. *J Vasc Surg* 2015;**62**:1642–1651.
249. Sigvant B, Lundin F, Wahlberg E. The risk of disease progression in peripheral arterial disease is higher than expected: a meta-analysis of mortality and disease progression in peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2016;**51**:395–403.
250. Xu D, Zou L, Xing Y, Hou L, Wei Y, Zhang J, Qiao Y, Hu D, Xu Y, Li J, Ma Y. Diagnostic value of ankle-brachial index in peripheral arterial disease: a meta-analysis. *Can J Cardiol* 2013;**29**:492–498.
251. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, Fowkes FG, Hiatt WR, Jonsson B, Lacroix P, Marin B, McDermott MM, Norgren L, Pande RL, Preux PM, Stoffers HE, Treat-Jacobson D. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation* 2012;**126**:2890–2909.
252. Tehan PE, Santos D, Chuter VH. A systematic review of the sensitivity and specificity of the toe-brachial index for detecting peripheral artery disease. *Vasc Med* 2016;**21**:382–389.
253. Collins R, Cranny G, Burch J, Aguiar-Ibanez R, Craig D, Wright K, Berry E, Gough M, Kleijnen J, Westwood M. A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease. *Health Technol Assess* 2007;**11**:1–184.
254. Met R, Bipat S, Legemate DA, Reekers JA, Koelemay MJ. Diagnostic performance of computed tomography angiography in peripheral arterial disease: a systematic review and meta-analysis. *JAMA* 2009;**301**:415–424.
255. Menke J, Larsen J. Meta-analysis: accuracy of contrast-enhanced magnetic resonance angiography for assessing steno-occlusions in peripheral arterial disease. *Ann Intern Med* 2010;**153**:325–334.
256. Koelemay MJ, Lijmer JG, Stoker J, Legemate DA, Bossuyt PM. Magnetic resonance angiography for the evaluation of lower extremity arterial disease: a meta-analysis. *JAMA* 2001;**285**:1338–1345.
257. Ouwendijk R, de Vries M, Stijnen T, Pattynama PM, van Sambeek MR, Buth J, Tielbeek AV, van der Vliet DA, SchutzeKool LJ, Kitslaar PJ, de Haan MW, van Engelshoven JM, Hunink MG. Multicenter randomized controlled trial of the costs and effects of noninvasive diagnostic imaging in patients with peripheral arterial disease: the DIPAD trial. *AJR Am J Roentgenol* 2008;**190**:1349–1357.
258. Barba A, Estallo L, Rodriguez L, Baquer M, Vega de Ceniga M. Detection of abdominal aortic aneurysm in patients with peripheral artery disease. *Eur J Vasc Endovasc Surg* 2005;**30**:504–508.
259. Giugliano G, Laurenzano E, Rengo C, De Rosa G, Brevetti L, Sannino A, Perrino C, Chiariotti L, Schiattarella GG, Serino F, Ferrone M, Scudiero F, Carbone A, Sorropago A, Amato B, Trimarco B, Esposito G. Abdominal aortic aneurysm in patients affected by intermittent claudication: prevalence and clinical predictors. *BMC Surg* 2012;**12**(suppl 1):S17.
260. Juergens JL, Barker NW, Hines EA Jr. Arteriosclerosis obliterans: review of 520 cases with special reference to pathogenic and prognostic factors. *Circulation* 1960;**21**:188–195.
261. Momsen AH, Jensen MB, Norager CB, Madsen MR, Vestersgaard-Andersen T, Lindholt JS. Drug therapy for improving walking distance in intermittent claudication: a systematic review and meta-analysis of robust randomised controlled studies. *Eur J Vasc Endovasc Surg* 2009;**38**:463–474.
262. Shahin Y, Barnes R, Barakat H, Chetter IC. Meta-analysis of angiotensin converting enzyme inhibitors effect on walking ability and ankle brachial pressure index in patients with intermittent claudication. *Atherosclerosis* 2013;**231**:283–290.
263. Vlachopoulos C, Terentes-Printzios D, Aboyans V, Brodmann M, De Carlo M, Tousoulis D. Angiotensin converting enzyme inhibitors and walking distance: have we walked the whole distance? *Atherosclerosis* 2016;**252**:199–200.
264. Bagger JP, Helligsoe P, Randsbaek F, Kimose HH, Jensen BS. Effect of verapamil in intermittent claudication A randomized, double-blind, placebo-controlled, cross-over study after individual dose-response assessment. *Circulation* 1997;**95**:411–414.
265. Espinola-Klein C, Weisser G, Jagodzinski A, Savvidis S, Warnholtz A, Ostad MA, Gori T, Munzel T. Beta-blockers in patients with intermittent claudication and arterial hypertension: results from the nebivolol or metoprolol in arterial occlusive disease trial. *Hypertension* 2011;**58**:148–154.
266. Soga Y, Iida O, Takahara M, Hirano K, Suzuki K, Kawasaki D. Beta-blocker treatment does not worsen critical limb ischemia in patients receiving endovascular therapy. *J Atheroscler Thromb* 2015;**22**:481–489.
267. Mirault T GA, Cambou JP, Lacroix P, Aboyans V, Boulon C, Constans J, Bura-Riviere A, Messas E. Impact of beta-blockers on general and local outcome in patients hospitalized for lower extremity peripheral artery disease. The COPART Registry. *Medicine (Baltimore)* 2017;**96**:e5916.
268. Lane R, Ellis B, Watson L, Leng GC. Exercise for intermittent claudication. *Cochrane Database Syst Rev* 2014;**7**:CD000990.
269. Fokkenrood HJ, Bendermacher BL, Lauret GJ, Willigendael EM, Prins MH, Teijink JA. Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. *Cochrane Database Syst Rev* 2013;**8**:CD005263.
270. Gommans LN, Fokkenrood HJ, van Dalen HC, Scheltinga MR, Teijink JA, Peters RJ. Safety of supervised exercise therapy in patients with intermittent claudication. *J Vasc Surg* 2015;**61**:512–518.
271. Bermingham SL, Sparrow K, Mullis R, Fox M, Shearman C, Bradbury A, Michaels J. The cost-effectiveness of supervised exercise for the treatment of intermittent claudication. *Eur J Vasc Endovasc Surg* 2013;**46**:707–714.
272. Al-Jundi W, Madbak K, Beard JD, Nawaz S, Tew GA. Systematic review of home-based exercise programmes for individuals with intermittent claudication. *Eur J Vasc Endovasc Surg* 2013;**46**:690–706.
273. Back M, Jivegard L, Johansson A, Nordanstig J, Svanberg T, Adania UW, Sjogren P. Home-based supervised exercise versus hospital-based supervised exercise or unsupervised walk advice as treatment for intermittent claudication: a systematic review. *J Rehabil Med* 2015;**47**:801–808.
274. Lauret GJ, Fakhry F, Fokkenrood HJ, Hunink MG, Teijink JA, Spronk S. Modes of exercise training for intermittent claudication. *Cochrane Database Syst Rev* 2014;**7**:CD009638.
275. Jakubseviciene E, Vasiliauskas D, Velicka L, Kubilius R, Milinaviciene E, Vencloviene J. Effectiveness of a new exercise program after lower limb arterial blood flow surgery in patients with peripheral arterial disease: a randomized clinical trial. *Int J Environ Res Public Health* 2014;**11**:7961–7976.
276. Kruidenier LM, Nicolai SP, Rouwet EV, Peters RJ, Prins MH, Teijink JA. Additional supervised exercise therapy after a percutaneous vascular intervention for peripheral arterial disease: a randomized clinical trial. *J Vasc Interv Radiol* 2011;**22**:961–968.
277. Gargiulo G, Giugliano G, Brevetti L, Sannino A, Schiattarella GG, Serino F, Carbone A, Scudiero F, Ferrone M, Corrado R, Izzo R, Chiariotti L, Perrino C, Amato B, Trimarco B, Esposito G. Use of statins in lower extremity artery disease: a review. *BMC Surg* 2012;**12**(suppl 1):S15.
278. McDermott MM, Guralnik JM, Greenland P, Pearce WH, Criqui MH, Liu K, Taylor L, Chan C, Sharma L, Schneider JR, Ridker PM, Green D, Quann M. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. *Circulation* 2003;**107**:757–761.
279. Robertson L, Andras A. Prostanoids for intermittent claudication. *Cochrane Database Syst Rev* 2013;**4**:CD000986.
280. Stevens JW, Simpson E, Harnan S, Squires H, Meng Y, Thomas S, Michaels J, Stansby G. Systematic review of the efficacy of cilostazol, naftidrofuryl oxalate and pentoxifylline for the treatment of intermittent claudication. *Br J Surg* 2012;**99**:1630–1638.
281. Indes JE, Pfaff MJ, Farrokhyar F, Brown H, Hashim P, Cheung K, Sosa JA. Clinical outcomes of 5358 patients undergoing direct open bypass or endovascular treatment for aortoiliac occlusive disease: a systematic review and meta-analysis. *J Endovasc Ther* 2013;**20**:443–455.
282. Grimme FA, Goverde PC, Verbruggen PJ, Zeebregts CJ, Reijnen MM. Editor's choice—first results of the covered endovascular reconstruction of the aortic bifurcation (CERAB) technique for aortoiliac occlusive disease. *Eur J Vasc Endovasc Surg* 2015;**50**:638–647.
283. Anderson JL, Antman EM, Harold JG, Jessup M, O'Gara PT, Pinto FJ, Vardas PE, Zamorano JL. Clinical practice guidelines on perioperative cardiovascular

evaluation: collaborative efforts among the ACC, AHA, and ESC. *Circulation* 2014;**130**:2213–2214.
284. Klinkert P, Post PN, Breslau PJ, van Bockel JH. Saphenous vein versus PTFE for above-knee femoropopliteal bypass. A review of the literature. *Eur J Vasc Endovasc Surg* 2004;**27**:357–362.
285. Malgor RD, Alahdab F, Elraiyah TA, Rizvi AZ, Lane MA, Prokop LJ, Phung OJ, Farah W, Montori VM, Conte MS, Murad MH. A systematic review of treatment of intermittent claudication in the lower extremities. *J Vasc Surg* 2015;**61**(3 suppl):54s–73s.
286. Murphy TP, Cutlip DE, Regensteiner JG, Mohler ER, Cohen DJ, Reynolds MR, Massaro JM, Lewis BA, Cerezo J, Oldenburg NC, Thum CC, Goldberg S, Jaff MR, Steffes MW, Comerota AJ, Ehrman J, Treat-Jacobson D, Walsh ME, Collins T, Badenhop DT, Bronas U, Hirsch AT. Supervised exercise versus primary stenting for claudication resulting from aortoiliac peripheral artery disease: six-month outcomes from the Claudication: Exercise Versus Endoluminal Revascularization (CLEVER) study. *Circulation* 2012;**125**:130–139.
287. Bendermacher BL, Willigendael EM, Teijink JA, Prins MH. Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. *Cochrane Database Syst Rev* 2006;**2**:CD005263.
288. Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JA, Hoffmann WH, Smits TM, van Brussel JP, Stultiens GN, Derom A, den Hoed PT, Ho GH, van Dijk LC, Verhofstad N, Orsini M, van Petersen A, Woltman K, Hulst I, van Sambeek MR, Rizopoulos D, Rouwet EV, Hunink MG. Endovascular revascularization and supervised exercise for peripheral artery disease and intermittent claudication: a randomized clinical trial. *JAMA* 2015;**314**:1936–1944.
289. Vemulapalli S, Dolor RJ, Hasselblad V, Schmit K, Banks A, Heidenfelder B, Patel MR, Jones WS. Supervised vs unsupervised exercise for intermittent claudication: a systematic review and meta-analysis. *Am Heart J* 2015;**169**:924–937.
290. Greenhalgh RM, Belch JJ, Brown LC, Gaines PA, Gao L, Reise JA, Thompson SG. The adjuvant benefit of angioplasty in patients with mild to moderate intermittent claudication (MIMIC) managed by supervised exercise, smoking cessation advice and best medical therapy: results from two randomised trials for stenotic femoropopliteal and aortoiliac arterial disease. *Eur J Vasc Endovasc Surg* 2008;**36**:680–688.
291. Jongkind V, Akkersdijk GJ, Yeung KK, Wisselink W. A systematic review of endovascular treatment of extensive aortoiliac occlusive disease. *J Vasc Surg* 2010;**52**:1376–1383.
292. Ballotta E, Lorenzetti R, Piatto G, Tolin F, Da Giau G, Toniato A. Reconstructive surgery for complex aortoiliac occlusive disease in young adults. *J Vasc Surg* 2012;**56**:1606–1614.
293. Bredahl K, Jensen LP, Schroeder TV, Sillesen H, Nielsen H, Eiberg JP. Mortality and complications after aortic bifurcated bypass procedures for chronic aortoiliac occlusive disease. *J Vasc Surg* 2015;**62**:75–82.
294. Bosiers M, Deloose K, Callaert J, Maene L, Beelen R, Keirse K, Verbist J, Peeters P, Schroe H, Lauwers G, Lansink W, Vanslembroeck K, D'Archambeau O, Hendriks J, Lauwers P, Vermassen F, Randon C, Van Herzeele I, De Ryck F, De Letter J, Lanckneus M, Van Betsbrugge M, Thomas B, Deleersnijder R, Vandekerkhof J, Baeyens I, Berghmans T, Buttiens J, Van Den Brande P, Debing E, Rabbia C, Ruffino A, Tealdi D, Nano G, Stegher S, Gasparini D, Piccoli G, Coppi G, Silingardi R, Cataldi V, Paroni G, Palazzo V, Stella A, Gargiulo M, Muccini N, Nessi F, Ferrero E, Pratesi C, Fargion A, Chiesa R, Marone E, Bertoglio L, Cremonesi A, Dozza L, Galzerano G, De Donato G, Setacci C. BRAVISSIMO: 12-month results from a large scale prospective trial. *J Cardiovasc Surg (Torino)* 2013;**54**:235–253.
295. Ye W, Liu CW, Ricco JB, Mani K, Zeng R, Jiang J. Early and late outcomes of percutaneous treatment of TransAtlantic Inter-Society Consensus class C and D aorto-iliac lesions. *J Vasc Surg* 2011;**53**:1728–1737.
296. Goode SD CT, Gaines PA. Randomized clinical trial of stents versus angioplasty for the treatment of iliac artery occlusions (STAG trial). *Br J Surg* 2013;**100**:1148–1153.
297. Antoniou GA, Sfyroeras GS, Karathanos C, Achouhan H, Koutsias S, Vretzakis G, Giannoukas AD. Hybrid endovascular and open treatment of severe multilevel lower extremity arterial disease. *Eur J Vasc Endovasc Surg* 2009;**38**:616–622.
298. Dosluoglu HH, Lall P, Cherr GS, Harris LM, Dryjski ML. Role of simple and complex hybrid revascularization procedures for symptomatic lower extremity occlusive disease. *J Vasc Surg* 2010;**51**:1425–1435.
299. Kavanagh CM, Heidenreich MJ, Albright JJ, Aziz A. Hybrid external iliac selective endarterectomy surgical technique and outcomes. *J Vasc Surg* 2016;**64**:1327–1334.
300. Matsagkas M, Kouvelos G, Arnaoutoglou E, Papa N, Labropoulos N, Tassiopoulos A. Hybrid procedures for patients with critical limb ischemia and severe common femoral artery atherosclerosis. *Ann Vasc Surg* 2011;**25**:1063–1069.
301. Crawford JD, Perrone KH, Wong VW, Mitchell EL, Azarbal AF, Liem TK, Landry GJ, Moneta GL. A modern series of acute aortic occlusion. *J Vasc Surg* 2014;**59**:1044–1050.
302. Lammer J, Zeller T, Hausegger KA, Schaefer PJ, Gschwendtner M, Mueller-Huelsbeck S, Rand T, Funovics M, Wolf F, Rastan A, Gschwandtner M, Puchner S, Beschorner U, Ristl R, Schoder M. Sustained benefit at 2 years for covered stents versus bare-metal stents in long SFA lesions: the VIASTAR trial. *Cardiovasc Intervent Radiol* 2015;**38**:25–32.
303. Lammer J, Zeller T, Hausegger KA, Schaefer PJ, Gschwendtner M, Mueller-Huelsbeck S, Rand T, Funovics M, Wolf F, Rastan A, Gschwandtner M, Puchner S, Ristl R, Schoder M. Heparin-bonded covered stents versus bare-metal stents for complex femoropopliteal artery lesions: the randomized VIASTAR trial (Viabahn endoprosthesis with PROPATEN bioactive surface [VIA] versus bare nitinol stent in the treatment of long lesions in superficial femoral artery occlusive disease). *J Am Coll Cardiol* 2013;**62**:1320–1327.
304. Laird JR, Katzen BT, Scheinert D, Lammer J, Carpenter J, Buchbinder M, Dave R, Ansel G, Lansky A, Cristea E, Collins TJ, Goldstein J, Cao AY, Jaff MR. Nitinol stent implantation vs. balloon angioplasty for lesions in the superficial femoral and proximal popliteal arteries of patients with claudication: three-year follow-up from the RESILIENT randomized trial. *J Endovasc Ther* 2012;**19**:1–9.
305. Schillinger M, Sabeti S, Dick P, Amighi J, Mlekusch W, Schlager O, Loewe C, Cejna M, Lammer J, Minar E. Sustained benefit at 2 years of primary femoropopliteal stenting compared with balloon angioplasty with optional stenting. *Circulation* 2007;**115**:2745–2749.
306. Liistro F, Grotti S, Porto I, Angioli P, Ricci L, Ducci K, Falsini G, Ventoruzzo G, Turini F, Bellandi G, Bolognese L. Drug-eluting balloon in peripheral intervention for the superficial femoral artery: the DEBATE-SFA randomized trial (drug eluting balloon in peripheral intervention for the superficial femoral artery). *JACC Cardiovasc Interv* 2013;**6**:1295–1302.
307. Rosenfield K, Jaff MR, White CJ, Rocha-Singh K, Mena-Hurtado C, Metzger DC, Brodmann M, Pilger E, Zeller T, Krishnan P, Gammon R, Muller-Hulsbeck S, Nehler MR, Benenati JF, Scheinert D. Trial of a paclitaxel-coated balloon for femoropopliteal artery disease. *N Engl J Med* 2015;**373**:145–153.
308. Tepe G, Laird J, Schneider P, Brodmann M, Krishnan P, Micari A, Metzger C, Scheinert D, Zeller T, Cohen DJ, Snead DB, Alexander B, Landini M, Jaff MR. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. *Circulation* 2015;**131**:495–502.
309. Tepe G, Zeller T, Albrecht T, Heller S, Schwarzwalder U, Beregi JP, Claussen CD, Oldenburg A, Scheller B, Speck U. Local delivery of paclitaxel to inhibit restenosis during angioplasty of the leg. *N Engl J Med* 2008;**358**:689–699.
310. Werk M, Albrecht T, Meyer DR, Ahmed MN, Behne A, Dietz U, Eschenbach G, Hartmann H, Lange C, Schnorr B, Stiepani H, Zoccai GB, Hanninen EL. Paclitaxel-coated balloons reduce restenosis after femoro-popliteal angioplasty: evidence from the randomized PACIFIER trial. *Circ Cardiovasc Interv* 2012;**5**:831–840.
311. Geraghty PJ, Mewissen MW, Jaff MR, Ansel GM. Three-year results of the VIBRANT trial of VIABAHN endoprosthesis versus bare nitinol stent implantation for complex superficial femoral artery occlusive disease. *J Vasc Surg* 2013;**58**:386–395.
312. Scheinert D, Werner M, Scheinert S, Paetzold A, Banning-Eichenseer U, Piorkowski M, Ulrich M, Bausback Y, Braunlich S, Schmidt A. Treatment of complex atherosclerotic popliteal artery disease with a new self-expanding interwoven nitinol stent: 12-month results of the Leipzig SUPERA popliteal artery stent registry. *JACC Cardiovasc Interv* 2013;**6**:65–71.
313. Tosaka A, Soga Y, Iida O, Ishihara T, Hirano K, Suzuki K, Yokoi H, Nanto S, Nobuyoshi M. Classification and clinical impact of restenosis after femoropopliteal stenting. *J Am Coll Cardiol* 2012;**59**:16–23.
314. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, Ruckley CV, Raab GM. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: a survival prediction model to facilitate clinical decision making. *J Vasc Surg* 2010;**51**(5 suppl):52s–68s.
315. Arvela E, Venermo M, Soderstrom M, Alback A, Lepantalo M. Outcome of infrainguinal single-segment great saphenous vein bypass for critical limb ischemia is superior to alternative autologous vein bypass, especially in patients with high operative risk. *Ann Vasc Surg* 2012;**26**:396–403.
316. Brass EP, Anthony R, Dormandy J, Hiatt WR, Jiao J, Nakanishi A, McNamara T, Nehler M. Parenteral therapy with lipo-ecraprost, a lipid-based formulation of a PGE1 analog, does not alter six-month outcomes in patients with critical leg ischemia. *J Vasc Surg* 2006;**43**:752–759.
317. Mills JL Sr, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy AN, Andros G. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). *J Vasc Surg* 2014;**59**:220–234.e2.
318. Singh S, Armstrong EJ, Sherif W, Alvandi B, Westin GG, Singh GD, Amsterdam EA, Laird JR. Association of elevated fasting glucose with lower patency and increased major adverse limb events among patients with diabetes undergoing infrapopliteal balloon angioplasty. *Vasc Med* 2014;**19**:307–314.

319. Takahara M, Kaneto H, Iida O, Gorogawa S, Katakami N, Matsuoka TA, Ikeda M, Shimomura I. The influence of glycemic control on the prognosis of Japanese patients undergoing percutaneous transluminal angioplasty for critical limb ischemia. *Diabetes Care* 2010;**33**:2538–2542.
320. Dominguez A 3rd, Bahadorani J, Reeves R, Mahmud E, Patel M. Endovascular therapy for critical limb ischemia. *Expert Rev Cardiovasc Ther* 2015;**13**:429–444.
321. Lumsden AB, Davies MG, Peden EK. Medical and endovascular management of critical limb ischemia. *J Endovasc Ther* 2009;**16**(2 suppl 2):31–62.
322. Manzi M, Palena L, Cester G. Endovascular techniques for limb salvage in diabetics with crural and pedal disease. *J Cardiovasc Surg (Torino)* 2011;**52**:485–492.
323. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, Fowkes FG, Gillepsie I, Ruckley CV, Raab G, Storkey H. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005;**366**:1925–1934.
324. Zeller T, Baumgartner I, Scheinert D, Brodmann M, Bosiers M, Micari A, Peeters P, Vermassen F, Landini M, Snead DB, Kent KC, Rocha-Singh KJ. Drug-eluting balloon versus standard balloon angioplasty for infrapopliteal arterial revascularization in critical limb ischemia: 12-month results from the IN.PACT DEEP randomized trial. *J Am Coll Cardiol* 2014;**64**:1568–1576.
325. Menard MT, Farber A. The BEST-CLI trial: a multidisciplinary effort to assess whether surgical or endovascular therapy is better for patients with critical limb ischemia. *Semin Vasc Surg* 2014;**27**:82–84.
326. Popplewell MA, Davies H, Jarrett H, Bate G, Grant M, Patel S, Mehta S, Andronis L, Roberts T, Deeks J, Bradbury A. Bypass versus angio plasty in severe ischaemia of the leg - 2 (BASIL-2) trial: study protocol for a randomised controlled trial. *Trials* 2016;**17**:11.
327. Teraa M, Conte MS, Moll FL, Verhaar MC. Critical limb ischemia: current trends and future directions. *J Am Heart Assoc* 2016;**5**:e002938.
328. Belch J, Hiatt WR, Baumgartner I, Driver IV, Nikol S, Norgren L, Van Belle E. Effect of fibroblast growth factor NV1FGF on amputation and death: a randomised placebo-controlled trial of gene therapy in critical limb ischaemia. *Lancet* 2011;**377**:1929–1937.
329. Moazzami K, Moazzami B, Roohi A, Nedjat S, Dolmatova E. Local intramuscular transplantation of autologous mononuclear cells for critical lower limb ischaemia. *Cochrane Database Syst Rev* 2014;**12**:CD008347.
330. Peeters Weem SM, Teraa M, de Borst GJ, Verhaar MC, Moll FL. Bone marrow derived cell therapy in critical limb ischemia: a meta-analysis of randomized placebo controlled trials. *Eur J Vasc Endovasc Surg* 2015;**50**:775–783.
331. Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008;**133**(6 suppl):815s–843s.
332. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, Jones DN. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg* 1997;**26**:517–538.
333. Berridge DC, Kessel D, Robertson I. Surgery versus thrombolysis for acute limb ischaemia: initial management. *Cochrane Database Syst Rev* 2002;**3**:CDd002784.
334. Savji N, Rockman CB, Skolnick AH, Guo Y, Adelman MA, Riles T, Berger JS. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. *J Am Coll Cardiol* 2013;**61**:1736–1743.
335. Aboyans V, Desormais I, Magne J, Morange G, Mohty D, Lacroix P. Renal Artery stenosis in patients with peripheral artery disease: prevalence, risk factors and long-term prognosis. *Eur J Vasc Endovasc Surg* 2016;**53**:380–385.
336. Aboyans V. Polyvascular disease: definition, epidemiology, relevance. In: P Lanzer, ed. *PanVascular Medicine*, 2nd ed. Berlin: Springer, 2015:4779–4810.
337. Ahmed B Al-Khaffaf H. Prevalence of significant asymptomatic carotid artery disease in patients with peripheral vascular disease: a meta-analysis. *Eur J Vasc Endovasc Surg* 2009;**37**:262–271.
338. Durand DJ, Perler BA, Roseborough GS, Grega MA, Borowicz LM Jr, Baumgartner WA, Yuh DD. Mandatory versus selective preoperative carotid screening: a retrospective analysis. *Ann Thorac Surg* 2004;**78**:159–66; discussion 159–66.
339. Fowkes FG, Low LP, Tuta S, Kozak J. Ankle-brachial index and extent of atherothrombosis in 8891 patients with or at risk of vascular disease: results of the international AGATHA study. *Eur Heart J* 2006;**27**:1861–1867.
340. Mukherjee D, Eagle KA, Kline-Rogers E, Feldman LJ, Juliard JM, Agnelli G, Budaj A, Avezum A, Allegrone J, FitzGerald G, Steg PG. Impact of prior peripheral arterial disease and stroke on outcomes of acute coronary syndromes and effect of evidence-based therapies (from the Global Registry of Acute Coronary Events). *Am J Cardiol* 2007;**100**:1–6.
341. Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. *Eur J Vasc Endovasc Surg* 2002;**23**:283–294.
342. Steinvil A, Sadeh B, Arbel Y, Justo D, Belei A, Borenstein N, Banai S, Halkin A. Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. *J Am Coll Cardiol* 2011;**57**:779–783.
343. Subherwal S, Bhatt DL, Li S, Wang TY, Thomas L, Alexander KP, Patel MR, Ohman EM, Gibler WB, Peterson ED, Roe MT. Polyvascular disease and long-term cardiovascular outcomes in older patients with non-ST-segment-elevation myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2012;**5**:541–549.
344. Collet JP, Cayla G, Ennezat PV, Leclercq F, Cuisset T, Elhadad S, Henry P, Belle L, Cohen A, Silvain J, Barthelemy O, Beygui F, Diallo A, Vicaut E, Montalescot G, for the AMERICA Investigators. Systematic detection of polyvascular disease combined with aggressive secondary prevention in patients presenting with severe coronary artery disease: the randomized AMERICA Study (submitted).
345. Lin JC, Kabbani LS, Peterson EL, Masabni K, Morgan JA, Brooks S, Wertella KP, Paone G. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. *J Vasc Surg* 2016;**63**:710–714.
346. Masabni K RS, Blackstone EH, Gornik HL, Sabik JF 3rd. Does preoperative carotid stenosis screening reduce perioperative stroke in patients undergoing coronary artery bypass grafting? *J Thorac Cardiovasc Surg* 2015;**149**:1253–1260.
347. Naylor AR, Bown MJ. Stroke after cardiac surgery and its association with asymptomatic carotid disease: an updated systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2011;**41**:607–624.
348. Schoof J, Lubahn W, Baeumer M, Kross R, Wallesch CW, Kozian A, Huth C, Goertler M. Impaired cerebral autoregulation distal to carotid stenosis/occlusion is associated with increased risk of stroke at cardiac surgery with cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 2007;**134**:690–696.
349. Stamou SC Hill PC, Dangas G, Pfister AJ, Boyce SW, Dullum MK, Bafi AS, Corso PJ. Stroke after coronary artery bypass: incidence, predictors, and clinical outcome. *Stroke* 2001;**32**:1508–1513.
350. Naylor AR. Delay may reduce procedural risk, but at what price to the patient? *Eur J Vasc Endovasc Surg* 2008;**35**:383–391.
351. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaijyanath P, Reddy S, Tao L, Olavegogeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Ng J, Chrolavicius S, Yusuf S; CORONARY Investigators. Off-pump or on-pump coronary-artery bypass grafting at 30 days. *N Engl J Med* 2012;**366**:1489–1497.
352. Illuminati G, Ricco JB, Calio F, Pacile MA, Miraldi F, Frati G, Macrina F, Toscano M. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting. *J Vasc Surg* 2011;**54**:993–999.
353. Randall MS McKevitt F, Cleveland TJ, Gaines PA, Venables GS. Is there any benefit from staged carotid and coronary revascularization using carotid stents? A single-center experience highlights the need for a randomized controlled trial. *Stroke* 2006;**37**:435–439.
354. Van der Heyden J SM, Bal ET, Ernst JM, Ackerstaff RG, Schaap J, Kelder JC, Schepens M, Plokker HW. Staged carotid angioplasty and stenting followed by cardiac surgery in patients with severe asymptomatic carotid artery stenosis: early and long-term results. *Circulation* 2007;**116**:2036–2342.
355. Versaci F, Del Giudice C, Scafuri A, Zeitani J, Gandini R, Nardi P, Salvati A, Pampana E, Sebastiano F, Romagnoli A, Simonetti G, Chiariello L. Sequential hybrid carotid and coronary artery revascularization: immediate and mid-term results. *Ann Thorac Surg* 2007;**84**:1508–1513.
356. Chiariello L NP, Pellegrino A, Saitto G, Chiariello GA, Russo M, Zeitani J, Versaci F. Simultaneous carotid artery stenting and heart surgery: expanded experience of hybrid surgical procedures. *Ann Thorac Surg* 2015;**99**:1291–1297.
357. Shishehbor MH, Venkatachalam S, Sun Z, Rajeswaran J, Kapadia SR, Bajzer C, Gornik HL, Gray BH, Bartholomew JR, Clair DG, Sabik JF 3rd, Blackstone EH. A direct comparison of early and late outcomes with three approaches to carotid revascularization and open heart surgery. *J Am Coll Cardiol* 2013;**62**:1948–1956.
358. Aboyans V, Lacroix P. Indications for carotid screening in patients with coronary artery disease. *Presse Med* 2009;**38**:977–986.
359. Naylor AR, Cuffe RL, Rothwell PM, Bell PR. A systematic review of outcomes following staged and synchronous carotid endarterectomy and coronary artery bypass. *Eur J Vasc Endovasc Surg* 2003;**25**:380–389.
360. Paraskevas KI, Nduwayo S, Saratzis AN, Naylor AR. Carotid stenting prior to coronary bypass surgery: an updated systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2017;**53**:309–319.
361. Imori Y, Akasaka T, Ochiai T, Oyama K, Tobita K, Shishido K, Nomura Y, Yamanaka F, Sugitatsu K, Okamura N, Mizuno S, Arima K, Suenaga H, Murakami M, Tanaka Y, Matsumi J, Takahashi S, Tanaka S, Takeshita S, Saito S. Co-existence of carotid artery disease, renal artery stenosis, and lower extremity peripheral arterial disease in patients with coronary artery disease. *Am J Cardiol* 2014;**113**:30–35.
362. Kim EK SP, Yang JH, Song YB, Hahn JY, Choi JH, Gwon HC, Lee SH, Hong KP, Park JE, Kim DK, Choi SH. Peripheral artery disease in Korean patients undergoing percutaneous coronary intervention: prevalence and association with coronary artery disease severity. *J Korean Med Sci* 2013;**28**:87–92.

363. Hussein AA UK, Wolski K, Kapadia S, Schoenhagen P, Tuzcu EM, Nissen SE, Nicholls SJ. Peripheral arterial disease and progression of coronary atherosclerosis. *J Am Coll Cardiol* 2011;**57**:1220–1225.
364. Eagle KA, Rihal CS, Foster ED, Mickel MC, Gersh BJ. Long-term survival in patients with coronary artery disease: importance of peripheral vascular disease. The Coronary Artery Surgery Study (CASS) Investigators. *J Am Coll Cardiol* 1994;**23**:1091–1095.
365. Grenon SM, Vittinghoff E, Owens CD, Conte MS, Whooley M, Cohen BE. Peripheral artery disease and risk of cardiovascular events in patients with coronary artery disease: insights from the Heart and Soul Study. *Vasc Med* 2013;**18**:176–184.
366. Saw J, Bhatt DL, Moliterno DJ, Brener SJ, Steinhubl SR, Lincoff AM, Tcheng JE, Harrington RA, Simoons M, Hu T, Sheikh MA, Kereiakes DJ, Topol EJ. The influence of peripheral arterial disease on outcomes: a pooled analysis of mortality in eight large randomized percutaneous coronary intervention trials. *J Am Coll Cardiol* 2006;**48**:1567–1572.
367. Aboyans V, Lacroix P, Postil A, Guilloux J, Rolle F, Cornu E, Laskar M. Subclinical peripheral arterial disease and incompressible ankle arteries are both long-term prognostic factors in patients undergoing coronary artery bypass grafting. *J Am Coll Cardiol* 2005;**46**:815–820.
368. Rihal CS, Sutton-Tyrrell K, Guo P, Keller NM, Jandova R, Sellers MA, Schaff HV, Holmes DR Jr. Increased incidence of periprocedural complications among patients with peripheral vascular disease undergoing myocardial revascularization in the bypass angioplasty revascularization investigation. *Circulation* 1999;**100**:171–177.
369. Hlatky MA, Boothroyd DB, Baker L, Kazi DS, Solomon MD, Chang TI, Shilane D, Go AS. Comparative effectiveness of multivessel coronary bypass surgery and multivessel percutaneous coronary intervention: a cohort study. *Ann Intern Med* 2013;**158**:727–734.
370. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR Jr, Mack M, Feldman T, Morice MC, Ståhle E, Onuma Y, Morel MA, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet* 2013;**381**:639–650.
371. Dencker D, Pederson F, Engstrom T, Kober L, Hojberg S, Nielsen MB, Schroeder TV, Lon L. Major femoral vascular access complications after coronary diagnostic and interventional procedures: a Danish register study. *Int J Cardiol* 2016;**202**:604–608.
372. Neufang A, Dorweiler B, Espinola-Klein C, Savvidis S, Doemland M, Schotten S, Vahl CF. Outcomes of complex femorodistal sequential autologous vein and biologic prosthesis composite bypass grafts. *J Vasc Surg* 2014;**60**:1543–1553.
373. Spronk S, White JV, Ryjewski C, Rosenblum J, Bosch JL, Hunink MG. Invasive treatment of claudication is indicated for patients unable to adequately ambulate during cardiac rehabilitation. *J Vasc Surg* 2009;**49**:1217–1225.
374. Aboyans V, Lacroix P, Guilloux J, Rolle F, Le Guyader A, Cautres M, Cornu E, Laskar M. A predictive model for screening cerebrovascular disease in patient undergoing coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2005;**4**:90–95.
375. Valgimigli M, Gagnor A, Calabro P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briguori C, Ando G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S, Nazzaro M, Zingarelli A, de Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbuhler M, Vranckx P, Juni P. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. *Lancet* 2015;**385**:2465–2476.
376. Jones WS, Clare R, Ellis SJ, Mills JS, Fischman DL, Kraus WE, Whellan DJ, O'Connor CM, Patel MR. Effect of peripheral arterial disease on functional and clinical outcomes in patients with heart failure (from HF-ACTION). *Am J Cardiol* 2011;**108**:380–384.
377. Inglis SC, Bebchuk J, Al-Suhaim SA, Case J, Pfeffer MA, Solomon SD, Hou YR, Pitt B, Dargie HJ, Ford I, Kjekshus J, Zannad F, Dickstein K, McMurray JJ. Peripheral artery disease and outcomes after myocardial infarction: an individual-patient meta-analysis of 28,771 patients in CAPRICORN, EPEHESUS, OPTIMAAL and VALIANT. *Int J Cardiol* 2013;**168**:1094–1101.
378. Nakamura Y, Kunii H, Yoshihisa A, Takiguchi M, Shimizu T, Yamauchi H, Iwaya S, Owada T, Abe S, Sato T, Suzuki S, Oikawa M, Kobayashi A, Yamaki T, Sugimoto K, Nakazato K, Suzuki H, Saitoh S, Takeishi Y. Impact of peripheral artery disease on prognosis in hospitalized heart failure patients. *Circ J* 2015;**79**:785–793.
379. van Straten AH, Firanescu C, Soliman Hamad MA, Tan ME, ter Woorst JF, Martens EJ, van Zundert AA. Peripheral vascular disease as a predictor of survival after coronary artery bypass grafting: comparison with a matched general population. *Ann Thorac Surg* 2010;**89**:414–420.
380. Calvet D, Touze E, Varenne O, Sablayrolles JL, Weber S, Mas JL. Prevalence of asymptomatic coronary artery disease in ischemic stroke patients: the PRECORIS study. *Circulation* 2010;**121**:1623–1629.
381. Hofmann R, Kypta A, Steinwender C, Kerschner K, Grund M, Leisch F. Coronary angiography in patients undergoing carotid artery stenting shows a high incidence of significant coronary artery disease. *Heart* 2005;**91**:1438–1441.
382. Illuminati G, Ricco JB, Greco C, Mangieri E, Calio F, Ceccanei G, Pacile MA, Schiariti M, Tanzilli G, Barilla F, Paravati V, Mazzesi G, Miraldi F, Tritapepe L. Systematic preoperative coronary angiography and stenting improves postoperative results of carotid endarterectomy in patients with asymptomatic coronary artery disease: a randomised controlled trial. *Eur J Vasc Endovasc Surg* 2010;**39**:139–145.
383. Illuminati G, Schneider F, Greco C, Mangieri E, Schiariti M, Tanzilli G, Barilla F, Paravati V, Pizzardi G, Calio F, Miraldi F, Macrina F, Totaro M, Greco E, Mazzesi G, Tritapepe L, Toscano M, Vietri F, Meyer N, Ricco JB. Long-term results of a randomized controlled trial analyzing the role of systematic pre-operative coronary angiography before elective carotid endarterectomy in patients with asymptomatic coronary artery disease. *Eur J Vasc Endovasc Surg* 2015;**49**:366–774.
384. Vidakovic R, Schouten O, Kuiper R, Hoeks SE, Flu WJ, van Kuijk JP, Goei D, Verhagen HJ, Neskovic AN, Poldermans D. The prevalence of polyvascular disease in patients referred for peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2009;**38**:435–440.
385. Hur DJ, Kizilgul M, Aung WW, Roussillon KC, Keeley EC. Frequency of coronary artery disease in patients undergoing peripheral artery disease surgery. *Am J Cardiol* 2012;**110**:736–740.
386. Ishihara T, Iida O, Tosaka A, Soga Y, Sakamoto Y, Hirano K, Nanto S, Uematsu M. Severity of coronary artery disease affects prognosis of patients with peripheral artery disease. *Angiology* 2013;**64**:417–422.
387. Kristensen SD, Knuuti J, Saraste A, Anker S, Botker HE, De Hert S, Ford I, Gonzalez Juanatey JR, Gorenek B, Heyndrickx GR, Hoeft A, Huber K, Iung B, Kjeldsen KP, Longrois D, Luescher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Uva MS, Voudris V, Funck-Brentano C. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol* 2014;**31**:517–573.
388. Gallino A, Aboyans V, Diehm C, Cosentino F, Stricker H, Falk E, Schouten O, Lekakis J, Amann-Vesti B, Siclari F, Poredos P, Novo S, Brodmann M, Schulte KL, Vlachopoulos C, De Caterina R, Libby P, Baumgartner I. Non-coronary atherosclerosis. *Eur Heart J* 2014;**35**:1112–1119.
389. Cho I, Chang H, Sung JM, Pencina MJ, Lin FY, Dunning AM, Achenbach S, Al-Mallah M, Berman DS, Budoff MJ, Callister TQ, Chow BJ, Delago A, Hadamitzky M, Hausleiter J, Maffei E, Cademartiri F, Kaufmann P, Shaw LJ, Raff GL, Chinnaiyan KM, Villines TC, Cheng V, Nasir K, Gomez M, Min JK; CONFIRM Investigators. Coronary computed tomographic angiography and risk of all-cause mortality and nonfatal myocardial infarction in subjects without chest pain syndrome from the CONFIRM Registry (coronary CT angiography evaluation for clinical outcomes: an international multicenter registry). *Circulation* 2012;**126**:304–313.
390. Bhatt DL, Peterson ED, Harrington RA, Ou FS, Cannon CP, Gibson CM, Kleiman NS, Brindis RG, Peacock WF, Brener SJ, Menon V, Smith SC Jr, Pollack CV Jr, Gibler WB, Ohman EM, Roe MT; CRUSADE Investigators. Prior polyvascular disease: risk factor for adverse ischaemic outcomes in acute coronary syndromes. *Eur Heart J* 2009;**30**:1195–1202.
391. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabate M, Senior R, Taggart DP, van der Wall EE, Vrints CJ, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Ryden L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;**34**:2949–3003.
392. Sirimarco G, Amarenco P, Labreuche J, Touboul PJ, Alberts M, Goto S, Rother J, Mas JL, Bhatt DL, Steg PG; REACH Registry Investigators. Carotid atherosclerosis and risk of subsequent coronary event in outpatients with atherothrombosis. *Stroke* 2013;**44**:373–379.

393. Amighi J, Schlager O, Haumer M, Dick P, Mlekusch W, Loewe C, Bohmig G, Koppensteiner R, Minar E, Schillinger M. Renal artery stenosis predicts adverse cardiovascular and renal outcome in patients with peripheral artery disease. *Eur J Clin Invest* 2009;**39**:784–792.
394. Rauchhaus M, Doehner W, Francis DP, Davos C, Kemp M, Liebenthal C, Niebauer J, Hooper J, Volk HD, Coats AJ, Anker SD. Plasma cytokine parameters and mortality in patients with chronic heart failure. *Circulation* 2000;**102**:3060–3067.
395. Kahan T. The importance of myocardial fibrosis in hypertensive heart disease. *J Hypertens* 2012;**30**:685–687.
396. O'Rourke MF, Safar ME, Dzau V. The Cardiovascular Continuum extended: aging effects on the aorta and microvasculature. *Vasc Med* 2010;**15**:461–468.
397. Duscha BD, Annex BH, Green HJ, Pippen AM, Kraus WE. Deconditioning fails to explain peripheral skeletal muscle alterations in men with chronic heart failure. *J Am Coll Cardiol* 2002;**39**:1170–1174.
398. Mancini DM, Walter G, Reichek N, Lenkinski R, McCully KK, Mullen JL, Wilson JR. Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. *Circulation* 1992;**85**:1364–1373.
399. Hedberg P, Hammar C, Selmeryd J, Viklund J, Leppert J, Hellberg A, Henriksen E. Left ventricular systolic dysfunction in outpatients with peripheral atherosclerotic vascular disease: prevalence and association with location of arterial disease. *Eur J Heart Fail* 2014;**16**:625–632.
400. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, Gonzalez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;**18**:891–975.
401. Yamasaki S, Izawa A, Shiba Y, Tomita T, Miyashita Y, Koyama J, Ikeda U. Presence of diastolic dysfunction in patients with peripheral artery disease. *Angiology* 2013;**64**:540–543.
402. Meltzer AJ, Shrikhande G, Gallagher KA, Aiello FA, Kahn S, Connolly P, McKinsey JF. Heart failure is associated with reduced patency after endovascular intervention for symptomatic peripheral arterial disease. *J Vasc Surg* 2012;**55**:353–362.
403. Inglis SC, Hermis A, Shehab S, Newton PJ, Lal S, Davidson PM. Peripheral arterial disease and chronic heart failure: a dangerous mix. *Heart Fail Rev* 2013;**18**:457–664.
404. Inglis SC, McMurray JJ, Bohm M, Schaufelberger M, van Veldhuisen DJ, Lindberg M, Dunselman P, Hjalmarson A, Kjekshus J, Waagstein F, Wedel H, Wikstrand J. Intermittent claudication as a predictor of outcome in patients with ischaemic systolic heart failure: analysis of the Controlled Rosuvastatin Multinational Trial in Heart Failure trial (CORONA). *Eur J Heart Fail* 2010;**12**:698–705.
405. Ahmed MI, Aronow WS, Criqui MH, Aban I, Love TE, Eichhorn EJ, Ahmed A. Effects of peripheral arterial disease on outcomes in advanced chronic systolic heart failure: a propensity-matched study. *Circ Heart Fail* 2010;**3**:118–124.
406. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA* 2001;**285**:2370–2375.
407. Griffin WF, Salahuddin T, O'Neal WT, Soliman EZ. Peripheral arterial disease is associated with an increased risk of atrial fibrillation in the elderly. *Europace* 2016;**18**:794–798.
408. Aboyans V, Lacroix P, Echahidi N, Mohty D. Ankle-brachial index in patients with nonvalvular atrial fibrillation. *J Am Coll Cardiol* 2014;**63**:1456–1457.
409. Gallego P, Roldan V, Marin F, Jover E, Manzano-Fernandez S, Valdes M, Vicente V, Lip GY. Ankle brachial index as an independent predictor of mortality in anticoagulated atrial fibrillation. *Eur J Clin Invest* 2012;**42**:1302–1308.
410. O'Neal WT, Efird JT, Nazarian S, Alonso A, Heckbert SR, Soliman EZ. Peripheral arterial disease and risk of atrial fibrillation and stroke: the Multi-Ethnic Study of Atherosclerosis. *J Am Heart Assoc* 2014;**3**:e001270.
411. Wasmer K, Unrath M, Kobe J, Malyar NM, Freisinger E, Meyborg M, Breithardt G, Eckardt L, Reinecke H. Atrial fibrillation is a risk marker for worse in-hospital and long-term outcome in patients with peripheral artery disease. *Int J Cardiol* 2015;**199**:223–228.
412. euroSCORE interactive calculator. http://www.euroscore.org/calc.html.
413. Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lievre M, Prat A, Teiger E, Lefevre T, Himbert D, Tchetche D, Carrie D, Albat B, Cribier A, Rioufol G, Sudre A, Blanchard D, Collet F, Dos Santos P, Meneveau N, Tirouvanziam A, Caussin C, Guyon P, Boschat J, Le Breton H, Collart F, Houel R, Delpine S, Souteyrand G, Favereau X, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Van Belle E, Laskar M. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med* 2012;**366**:1705–1715.
414. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;**363**:1597–1607.
415. Skelding KA, Yakubov SJ, Kleiman NS, Reardon MJ, Adams DH, Huang J, Forrest JK, Popma JJ. Transcatheter aortic valve replacement versus surgery in women at high risk for surgical aortic valve replacement (from the CoreValve US High Risk Pivotal Trial). *Am J Cardiol* 2016;**118**:560–566.
416. Aronow WS. Peripheral arterial disease in the elderly. *Clin Interv Aging* 2007;**2**:645–454.
417. Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;**371**:967–968.
418. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;**364**:2187–2198.
419. Sinning JM, Horack M, Grube E, Gerckens U, Erbel R, Eggebrecht H, Zahn R, Linke A, Sievert H, Figulla HR, Kuck KH, Hauptmann KE, Hoffmann E, Hambrecht R, Richardt G, Sack S, Senges J, Nickenig G, Werner N. The impact of peripheral arterial disease on early outcome after transcatheter aortic valve implantation: results from the German Transcatheter Aortic Valve Interventions Registry. *Am Heart J* 2012;**164**:102–110.
420. Erdogan HB, Goksedef D, Erentug V, Polat A, Bozbuga N, Mansuroglu D, Guler M, Akinci E, Yakut C. In which patients should sheathless IABP be used? An analysis of vascular complications in 1211 cases. *J Card Surg* 2006;**21**:342–346.
421. Ohman JW, Vemuri C, Prasad S, Silvestry SC, Jim J, Geraghty PJ. The effect of extremity vascular complications on the outcomes of cardiac support device recipients. *J Vasc Surg* 2014;**59**:1622–1627.