ΠΕΡΙΦΕΡΙΚΕΣ ΑΓΓΕΙΟΠΑΘΕΙΕΣ

ΣΠΥΡΟΜΗΤΡΟΣ ΓΕΩΡΓΙΟΣ
Καρδιολόγος, Ε/Α, Γ.Ν.Κατερίνης.
F.E.S.C
Presentations of Peripheral Arterial Diseases (PADs)

Atherosclerosis

- Aorta disease
- Coronary Artery Disease (CAD)

Territories

- Cerebrovascular diseases:
  - Carotid artery disease
  - Vertebral artery disease
- Upper-Extremity Artery Disease (UEAD)
- Mesenteric artery disease
- Renal Artery Disease (RAD)
- Lower-Extremity Artery Disease (LEAD)

Presentations

- Stroke, Transient Ischaemic Attack (TIA), acute monocular blindness
- Subclavian steal syndrome, pain on exertion, digital symptoms, acute ischaemia
- Chronic Mesenteric Ischaemia (CMI)
  - Acute Mesenteric Ischaemia (AMI)
- Hypertension, renal failure
- Typical claudication, atypical symptoms, Chronic Limb-Threatening Ischaemia (CLTI), Acute Limb Ischaemia (ALI)

www.escardio.org/guidelines
2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with ESVS
(European Heart Journal 2017; doi:10.1093/eurheartj/ehx095)
Περιφερική αρτηριοπάθεια
Παράγοντες κινδύνου...οι γνωστοί!

Ο κίνδυνος για ΠΑ αυξάνει με την ηλικία

Ανεξάρτητοι παράγοντες κινδύνου για ΠΑ:
AY, Κάπνισμα, Υπερλιπιδαιμία

Relative Risk vs the General Population

- Diabetes: 4.05
- Smoking: 2.55
- Hypertension: 1.51
- Total cholesterol (10 mg/dL): 1.10

* PAD diagnosis based on ABI <0.90.
Παράγοντες Κινδύνου για PAN

- Διαβήτης
- Κάπνισμα
- Υπέρταση
- Υπερχολιστερολαιμία
- Υπερομοκυστεϊναιμία
- CRP

Σχετικός κίνδυνος

Περιφερική Αρτηριακή Νόσος

Γιατί ενδιαφέρει τον καρδιολόγο;

Οι ασθενείς με ΠΑ κινδυνεύουν από καρδιαγγειακά νοσήματα

Patients with symptomatic PAD face up to 6x greater risk of death from CVD, including MI and stroke

10-ετής επιβίωση ατόμων με ΠΑΝ ανάλογα με τη βαρύτητα της νόσου
The San Diego Artery Study

Επιβίωση (% ασθενών)

Αίτια θανάτου:
55% στεφανιαία νόσος
10% αγγειοεγκεφαλική νόσος
25% μη-αγγειακά αίτημα
< 10% άλλα αγγειακά αίτημα

Φυσιολογικοί
Ασυμπτωματική ΠΑΝ
Συμπτωματική ΠΑΝ
Πολύ σοβαρή ΠΑΝ

Καμπύλες επιβίωσης Kaplan-Meier,
βασισμένες στη θνησιμότητα από όλες τις αιτίες.

Εξέλιξη συμπτωματικής ΠΑΝ

Διαλείπουσα Χωλότητα

5 ετής έκβαση ΠΑΝ

- Σταθερή Χωλότητα 70-80%
- Επιδείνωση Χωλότητας 10-20%
- Κρίσιμη Ισχαιμία 1-2%

Ετήσια έκβαση

- Επιβίωση αρτιμέλης 25%
- Ακρωτηριασμός 25%
- Θνητότητα 25%

5ετής ΚΑΚ έκβαση

- Μη θανατηφόρο ΚΑΚ επεισόδιο 20%
- Θνητότητα 30%
- 75% ΚΑΚ απολογίας

ΚΑΚ: Καρδιαγγειακή
* Οξύ έμφραγμα μυοκαρδίου / ΑΕΕ

Hirsch AT et al., Circulation 2006
Atherothrombosis is commonly found in more than one arterial bed. (CAPRIE study, n = 19,185)

CVD: Cerebrovascular Disease, CAD: Coronary Arterial Disease, PAD: Peripheral Arterial Disease

Lancet 1996;348:1329–39
Περιφερεική Αρτηριακή Νόσος
Διαγνωστική προσέγγιση

- Ατομικό και κληρονομικό αναμνηστικό
- Κλινική εξέταση
- Εργαστηριακός έλεγχος
- Εξειδικευμένες τεχνικές για ΠΑ
  - Σφυρο-βραχιόνιος δείκτης (Ankle-brachial index-ABI)
  - Duplex ultrasound
  - CT αγγειογραφία
  - MR αγγειογραφία
Διάγνωση ΠΑΝ (2)

Φυσική εξέταση:

➢ Επισκόπηση κάτω άκρων: ωχρότητα, κυανέρυθρη χροιά, δυστροφία νυχιών, απόπτωση τριχών, ατροφία δέρματος/μυών, μυκητιάσεις, εξελκώσεις

➢ Ψηλάφηση αρτηριών: απουσία σφύξεων, αδύνατες σφύξεις, ψυχρά άκρα

➢ Ακρόαση αρτηριών: συστολικά φυσήματα
An ABI < 0.90 has 75% sensitivity and 86% specificity to diagnose LEAD.

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.

A post-exercise ankle SBP decrease > 30mmHg or a post-exercise ABI decrease > 20% are diagnostic for LEAD.
Patients with peripheral arterial diseases: best medical therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking cessation is recommended in all patients with PADs.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Healthy diet and physical activity are recommended for all patients with PADs.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Statins are recommended in all patients with PADs.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>In patients with PADs, it is recommended to reduce LDL-C to $&lt;1.8$ mmol/L (70 mg/dL) or decrease it by $\geq 50%$ if baseline values are $1.8-3.5$ mmol/L (70-135 mg/dL).</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>
Effects of Exercise Training on Claudication

Meta-analysis of 21 Studies

- Onset of Claudication Pain
- Maximal Claudication Pain

Exercise Training vs Control

Change in Treadmill Walking Distance (%)

* P < 0.05

the Fourier trial demonstrated the additional benefits of evolocumab, in the subgroup of 1505 patients with LEAD alone.
Patients with peripheral arterial diseases: best medical therapy *(continued)*

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In diabetic patients with PADs, strict glycaemic control is recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Antiplatelet therapy is recommended in patients with symptomatic PADs.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with PADs and hypertension, it is recommended to control blood pressure at &lt;140/90 mmHg.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ACEIs or ARBs should be considered as first line therapy in patients with PADs and hypertension.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>
Efficacy of ACE-I, Statins and Antiplatelet therapy in PAD

- **APTC** Antiplatelet Trialists’ Collaboration BMJ 1994; 308:81-106
- **CAPRIE** Steering Committee Lancet 1996; 348: 1329-1339
- **HPS** Collaborative group Lancet; 2002; 360:7-22

*PAD Subgroup only*
In symptomatic LEAD, the strongest evidence in favour of aspirin to protect against MACE (combining non-fatal MI and stroke with CV death) comes from the Antithrombotic Trialists Collaboration.
CAPRIE Study
Efficacy of Clopidogrel in Primary Analysis of MI, Ischemic Stroke, or Vascular Death

ITT Analysis

CAPRIE Steering Committee  Lancet 1996; 348: 1329-1339
OAC should be continued only if a compelling indication exists (e.g. paroxysmal, persistent or permanent AF with a Congestive heart failure, Hypertension, Age \( \geq 75 \) (2 points), Diabetes mellitus, Stroke or TIA (2 points), Vascular disease, Age 65–74 years, Sex category (CHA2DS2-VASc) score \( \geq 2 \); Mechanical heart valve; recent or a history of recurrent deep venous thrombosis or pulmonary embolism)
# Recommendations on antithrombotic therapy in patients with peripheral arterial diseases

## Lower extremities artery disease

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term SAPT is recommended in symptomatic patients.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Long-term SAPT is recommended in all patients who have undergone revascularization.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>SAPT is recommended after infra-inguinal bypass surgery.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>In patients requiring antiplatelet therapy, clopidogrel may be preferred over aspirin.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Vitamin K antagonists may be considered after autologous vein infra-inguinal bypass.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>DAPT with aspirin and clopidogrel for at least 1 month should be considered after infra-inguinal stent implantation.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>DAPT with aspirin and clopidogrel may be considered in below-the-knee bypass with a prosthetic graft.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Because of a lack of proven benefit, antiplatelet therapy is not routinely indicated in patients with isolated asymptomatic LEAD.</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

## Antithrombotic therapy for PADs patients requiring oral anticoagulant

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with PADs and AF, OAC:</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>• is recommended when the CHA₂DS₂-VASc score is ≥ 2</td>
<td>I Ia</td>
<td>B</td>
</tr>
<tr>
<td>• should be considered in all other patients.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>In patients with PADs who have an indication for OAC (e.g. AF or mechanical prosthetic valve), oral anticoagulants alone should be considered.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>After endovascular revascularization, aspirin or clopidogrel should be considered in addition to OAC for at least 1 month if the bleeding risk is low compared with the risk of stent/graft occlusion.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>After endovascular revascularization, OAC alone should be considered if the bleeding risk is high compared with the risk of stent/graft occlusion.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>OAC and SAPT may be considered beyond 1 month in high ischaemic risk patients or when there is another firm indication for long-term SAPT.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>
MACE or MALE or Major Amputation

COMPASS: Rivaroxaban Reduces CV and Limb Events in PAD
The total number of individuals with LEAD is booming, with a 23% increase in the last decade as a result of the total population increase, global ageing, increased incidence of diabetes worldwide and smoking in low- and middle-income countries.

In high income countries, LEAD, especially when symptomatic, is overall more frequent in men, although the difference is mitigated in the elderly.

In low- and middle-income countries, the prevalence is higher overall in women than in men.
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’
Ερωτηματολόγιο Εδιμβούργου για τη Χωλότητα
CAD/PVD

• Θετική διάγνωση για Χωλότητα μέσω του ερωτηματολόγιου επιτυγχάνεται μόνο αν έχει δοθεί «σωστή» απάντηση σε όλες τις ερωτήσεις

<table>
<thead>
<tr>
<th>Ερωτήσεις</th>
<th>Σωστές Απαντήσεις</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Νιώθετε πόνο ή ενόχληση στο πόδι(α) σας όταν περπατάτε?</td>
<td>Ναι</td>
</tr>
<tr>
<td>2 Ο πόνος ξεκινάει όταν είστε καθιστός(η) ή όταν στέκεστε όρθιος(α)?</td>
<td>Όχι</td>
</tr>
<tr>
<td>3 Νιώθετε τον πόνο όταν περπατάτε βιαστικά ή σε ανηφορική επιφάνεια?</td>
<td>Ναι</td>
</tr>
<tr>
<td>4 Νιώθετε τον πόνο όταν περπατάτε με το συνήθη ρυθμό βάδισης?</td>
<td>Ναι</td>
</tr>
<tr>
<td>5 Συνήθως τι συμβαίνει όταν παραμένετε ακίνητος(η)?</td>
<td>Όχι</td>
</tr>
<tr>
<td>a. Ο πόνος συνήθως συνεχίζει για περισσότερα από 10 λεπτά</td>
<td>Όχι</td>
</tr>
<tr>
<td>b. Ο πόνος συνήθως σταματάει σε 10 λεπτά ή λιγότερο</td>
<td>Ναι</td>
</tr>
<tr>
<td>6 Πού νιώθετε συνήθως αυτόν τον πόνο ή την ενόχληση?</td>
<td>Σημειώστε με ένα &quot;Χ&quot; το σημείο στο διπλάνο διάγραμμα</td>
</tr>
</tbody>
</table>
### Recommendations for ankle-brachial index measurement

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement of the ABI is indicated as a first-line non-invasive test for screening and diagnosis of LEAD.(^{250,251})</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In the case of incompressible ankle arteries or ABI &gt;1.40, alternative methods such as the toe-brachial index, Doppler waveform analysis or pulse volume recording are indicated.(^{252})</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

### Recommendations on imaging in patients with lower extremity artery disease

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS is indicated as a first-line imaging method to confirm LEAD lesions.(^{253})</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>DUS and/or CTA and/or MRA are indicated for anatomical characterization of LEAD lesions and guidance for optimal revascularization strategy.(^{254–257})</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Data from an anatomical imaging test should always be analysed in conjunction with symptoms and haemodynamic tests prior to a treatment decision.(^{246})</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>DUS screening for AAA should be considered.(^{258,259})</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

ABI = ankle-brachial index; LEAD = lower extremity artery disease.

Class of recommendation:

- I: Strong evidence, practice changing intervention.
- II: Evidence consistent with the class above, no significant risks/benefits.
- III: No evidence or evidence inconclusive.

Level of evidence:

- A: Randomized controlled trials (RCTs), systematic reviews, meta-analyses.
- B: Non-randomized studies (including case control studies), cohort studies, case series.
- C: Expert opinion, descriptive studies, case reports.

DUS = duplex ultrasound; LEAD = lower extremity artery disease; MRA = magnetic resonance angiography; AAA = abdominal aorta aneurysm; CTA = computed tomography angiography.
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. Supervised ExT is more effective than unsupervised ExT.
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.

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.
In patients with LEAD, some antihypertensive drugs, (e.g. Verapamil) statins, antiplatelet agents and prostanoids (prostaglandins I2 and E1) have favourable effects on walking distance (INVEST) study, Circulation 2003;107:757–761

(HOPE) and (ONTARGET) have shown that ACEIs and ARBs significantly reduce CV events in patients with PADs, Vlachopoulos Tousoulis D. Angiotensin converting enzyme inhibitors and walking distance: have we walked the whole distance? Atherosclerosis 2016;252:199–200.

Cilostazol is an inhibitor of phosphodiesterase type III.

Several clinical trials have shown an improvement of maximal walking distance (MWD) with cilostazol compared with placebo. Cochrane analysis, the CASTLE study

Beta-blockers are not contraindicated in patients with LEAD, as they do not alter walking capacity in patients with mild to moderate LEAD. Hypertension 2011;58:148–154.
Cornerstones of Medical Therapies in PAD

- Antiplatelet
- Smoking cessation
- Ace Inhibitors
- Statins
- Cilostazol
- Exercise
Chronic limb-threatening ischaemia

**Risk of amputation: the WIFI classification**

<table>
<thead>
<tr>
<th>Component</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>W (Wound)</td>
<td>0</td>
<td>No ulcer (ischaemic rest pain).</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Small, shallow ulcer on distal leg or foot without gangrene.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Deeper ulcer (exposed bone), joint or tendon ± gangrenous changes limited to toes.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene.</td>
</tr>
<tr>
<td>I (Ischaemia)</td>
<td></td>
<td>ABI</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>≥0.80</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.60-0.79</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.40-0.59</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&lt;0.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ankle pressure (mmHg)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>&gt;100</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>70-100</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>50-70</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&lt;50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toe pressure or TcPO₂</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>≥60</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>40-59</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>30-39</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&lt;30</td>
</tr>
<tr>
<td>fl (foot Infection)</td>
<td>0</td>
<td>No symptoms/signs of infection.</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Local infection involving only skin and subcutaneous tissue.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Local infection involving deeper than skin/subcutaneous tissue.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Systemic inflammatory response, sepsis.</td>
</tr>
</tbody>
</table>

**Interpretation of the WIFI classification**

<table>
<thead>
<tr>
<th>Estimate risk of amputation at 1 year for each combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-0</td>
</tr>
<tr>
<td>W-1</td>
</tr>
<tr>
<td>W-2</td>
</tr>
<tr>
<td>W-3</td>
</tr>
<tr>
<td>fl-0</td>
</tr>
</tbody>
</table>

fl = foot infection; H = high-risk; L = low-risk; M = moderate risk; VL = very low risk; W = wound.
Management of patients with chronic limb-threatening ischaemia

Chronic limb-threatening ischaemia (CLTI)

- Pain control, risk factor management, wound care, antibiotics if needed, drainage of septic foot if needed

Patient candidate for revascularization

Urgent imaging

Revascularization feasible

- Stenotic lesions, short occlusions
  - No GSV or increased risk for open surgery
    - Endovascular first

- Long occlusions
  - GSV available and patients fit for surgery
    - Bypass first

Revascularization non feasible

(continued)

Management of patients with chronic limb-threatening ischaemia

Endovascular first

Successful revascularization

Wound care

Maintenance of revascularization

New procedures if mandatory

Management of risk factors

Bypass first

Failure

Redo EVT or open bypass if possible

Revascularization non feasible

Patient candidate for revascularization

Failure

Revascularization non feasible

Patient candidate for revascularization

Impossible

Amputation mandatory?

Yes

Amputation Rehabilitation

No

Pain control, Wound care

Management of risk factors

(continued)
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).
The epidemiology of subclavian stenosis is mostly based on an interarm systolic blood pressure (SBP) difference >10 or 15mmHg, poorly sensitive (50%), highly specific (90%), when compared with angiography.

Prevalence of subclavian stenosis is estimated to be 2% in the general population but increases to 9% in the case of concomitant LEAD.

Doppler assessment of subclavian arteries enables the detection of high velocity flows indicating >50% stenosis.
## Management of subclavian artery stenosis

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In symptomatic patients with subclavian artery stenosis/occlusion revascularization should be considered.</strong></td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td><strong>In symptomatic patients with a stenotic/occluded sub-clavian artery, both revascularization options (stenting or surgery) should be considered and discussed case by case according to the lesion characteristics and patient’s risk.</strong></td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

## Management of subclavian artery stenosis (continued)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In asymptomatic subclavian artery stenosis, revascularization:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• should be considered in the case of proximal stenosis in patients undergoing CABG using the ipsilateral internal mammary artery.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>• should be considered in the case of proximal stenosis in patients who already have the ipsilateral internal mammary artery grafted to coronary arteries with evidence of myocardial ischaemia.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>• should be considered in the case of subclavian artery stenosis and ipsilateral arteriovenous fistula for dialysis.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>• may be considered in the case of bilateral stenosis, in order to be able to monitor blood pressure accurately</td>
<td>IIb</td>
<td>C</td>
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</table>
Mesenteric artery disease, acute or chronic, is underdiagnosed and highly lethal. The prerequisite of diagnosis is clinical suspicion, followed by imaging.

Acute thromboembolic occlusion affects mostly the superior mesenteric artery. Due to the extensive collaterals in the mesenteric circulation, the coeliac trunk or the inferior mesenteric artery, occlusion leads infrequently to intestinal infarction. In most population studies, acute mesenteric ischaemia is more often related to embolism than to thrombotic occlusion.

Chronic mesenteric artery disease includes stenosis or chronic occlusion of the coeliac trunk or the mesenteric arteries.

Its prevalence increases with age, especially in the presence of other atherosclerotic diseases and abdominal aortic aneurysms (AAAs).

In patients with an AAA and LEAD, significant stenosis (mostly asymptomatic) of at least one of the three arteries was detected in 40% and 27%,
### Recommendations on the management of acute mesenteric ischaemia

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>** Diagnosis**</td>
<td></td>
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<tr>
<td>In patients with suspected acute mesenteric ischaemia, urgent CTA is recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with suspicion of acute mesenteric ischaemia, the measurement of D-dimer should be considered to rule out the diagnosis.</td>
<td>IIa</td>
<td>B</td>
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<tr>
<td>** Treatment**</td>
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<tr>
<td>In patients with acute thrombotic occlusion of the superior mesenteric artery, endovascular therapy should be considered as first-line therapy for revascularization.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>In patients with acute embolic occlusion of the superior mesenteric artery, both endovascular and open surgery therapy should be considered.</td>
<td>IIa</td>
<td>B</td>
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</tbody>
</table>

### Recommendations for management of chronic mesenteric artery disease

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>** Diagnosis**</td>
<td></td>
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<tr>
<td>In patients with suspected CMI, DUS is recommended as the first-line examination.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with suspected CMI, occlusive disease of a single mesenteric artery makes the diagnosis unlikely and a careful search for alternative causes should be considered.</td>
<td>IIa</td>
<td>C</td>
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<tr>
<td>** Treatment**</td>
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<tr>
<td>In patients with symptomatic multivessel CMI, revascularization is recommended.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with symptomatic multivessel CMI, it is not recommended to delay revascularization in order to improve the nutritional status.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>
RAD is generally considered when renal artery stenosis (RAS) is > 60%, although additional functional assessment by haemodynamic criteria is advisable.

The prevalence of RAD increases with advancing age and is mostly related to atherosclerosis. It is associated with male gender, hypertension, smoking, diabetes mellitus, CKD, aorto-iliac occlusive disease and CAD.

5–10% of the general population, with a higher prevalence in high-risk populations. Approximately 20% have bilateral disease or a single functioning kidney may be affected.

Less frequent causes of RAD are fibromuscular dysplasia (FMD) and arteritis. The former is the most frequent cause of RAD in young hypertensive patients (especially in women).
Clinical situations raising suspicion for renal artery disease

- Onset of HTN < 30 years
- Onset of severe HTN (e.g., > 200/110 mmHg) when associated with other systemic diseases
- HTN and abdominal bruits
- Rapid and persistent rise in blood pressure unresponsive to previously controlled therapy
- Resistant HTN (other causes of HTN are unlikely and target organ damage is present)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class (^a)</th>
<th>Level (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS (as first-line), CTA(^c) and MRA(^d) are recommended imaging modalities to establish a diagnosis of RAD. (^{204,212})</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>DSA may be considered to confirm a diagnosis of RAD when clinical suspicion is high and the results of non-invasive examinations are inconclusive. (^{212,215})</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Renal scintigraphy, plasma renin measurements before and after ACEI provocation and vein renin measurements are not recommended for screening of atherosclerotic RAD. (^{204})</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

\(^{a}\)Class: I (strong recommendation), II (moderate recommendation), III (weak recommendation) \n\(^{b}\)Level: A (very high quality of evidence, very low expected impact on treatment decision), B (high quality of evidence, low expected impact on treatment decision), C (low quality of evidence, moderate expected impact on treatment decision)
The Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial reported no benefit from endovascular therapy over BMT.

### Recommendations for treatment strategies for renal artery disease

<table>
<thead>
<tr>
<th>Recommendations</th>
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<tbody>
<tr>
<td>Medical therapy</td>
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<tr>
<td>ACEIs/ARBs are recommended for treatment of hypertension associated with unilateral RAS.(^{219-222,240})</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Calcium channel blockers, beta-blockers and diuretics are recommended for treatment of hypertension associated with renal artery disease.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>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})</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

### Revascularization

Routine revascularization is not recommended in RAS secondary to atherosclerosis.\(^{229,231,232}\)

In cases of hypertension and/or signs of renal impairment related to renal arterial fibromuscular dysplasia, balloon angioplasty with bailout stenting should be considered.\(^{234-236}\)

Balloon angioplasty, with or without stenting, may be considered in selected patients with RAS and unexplained recurrent congestive heart failure or sudden pulmonary oedema.\(^{229,237,238}\)

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.\(^{241-243}\)
Reported rate ranges of other localizations of atherosclerosis in patients with a specific arterial disease

- **CAD**: 39% (9%) to 61% (15%)
- **Carotid stenosis >70%**: 16% (5%) to 22% (18%)
- **LEAD (ABI <0.90)**: 7% (4%) to 19% (14%)
- **RAS >75%**: 5% (4%) to 23% (10%)

• 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.

• The Aggressive detection and Management of the Extension of atherothrombosis in high Risk coronary patients Incomparison 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);

Does not exclude a role for screening for asymptomatic LEAD in CAD patients for prognostic stratification
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.

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.

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).

In patients undergoing surgery for LEAD, the probability of significant concomitant CAD at coronary angiography is 50–60%.

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%.

In the REACH registry, 57% of the participants with LEAD also suffered from CAD. The severity of LEAD is related to the prevalence of associated CAD to 90% of patients presenting with CLTI also have CAD.
Screening for CAD in LEAD patients may be useful for risk stratification, as morbidity and mortality are mainly cardiac.
Interrelations between heart failure and lower extremity artery disease

- Inflammation
- Diabetes
- Hypertension
- Atherosclerosis
  - CAD
  - Aorta stiffness
- Heart failure
  - Physical impairment and deconditioning
- LEAD
  - Ageing
- Smoking
- Dyslipidaemia

ESC
European Society of Cardiology

One-third of patients with symptomatic PADs have reduced left ventricular (LV) ejection fraction.

LV dysfunction is at least twice as prevalent in patients with LEAD as in the general population, matched for age and sex.

This association with LV dysfunction may be even stronger for carotid artery disease than for LEAD.

Combination is associated with increased CV morbidity and mortality

Observational studies and meta-analyses consistently show that the presence of LEAD in heart failure patients is an independent predictor of hospitalizations and mortality.

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).

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
## Management of HF associated with PADs

<table>
<thead>
<tr>
<th>Recommendations</th>
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<tbody>
<tr>
<td>Full vascular assessment is indicated in all patients considered for heart transplantation or cardiac assist device implantation.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients with symptomatic PADs, screening for heart failure with TTE and/or natriuretic peptides assessment should be considered.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Screening for LEAD may be considered in patients with heart failure.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Testing for renal artery disease may be considered in patients with flash pulmonary oedema.</td>
<td>IIb</td>
<td>C</td>
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</tbody>
</table>
Cardiovascular Health Study, LEAD was associated with a higher risk of AF (HR 1.52, P < 0.01).

Among 41,882 patients hospitalized for LEAD, the prevalence of AF was 13%.

ATRIA study

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 the REACH registry, AF was present in 10% of patients with LEAD.

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).
Management of AF associated with PADs

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<tbody>
<tr>
<td>In patients with LEAD and atrial fibrillation, oral anticoagulation:</td>
<td></td>
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<tr>
<td>• is recommended when CHA\textsubscript{2}DS\textsubscript{2}-VASc score ≥2,</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>• should be considered in all other patients.</td>
<td>IIa</td>
<td>B</td>
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</table>
Peripheral arterial diseases and valvular heart disease

PADs are common among patients with VHD, especially among the elderly with **symptomatic aortic stenosis**

Among patients with **symptomatic aortic stenosis not** eligible for surgical aortic valve replacement, the **prevalence of LEAD** is as high as 40%.

**Systematic CT scan** imaging of the aorta, including all major peripheral arteries, has become the **standard of care** in patients eligible for TAVI.

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.
Management of valvular heart disease associated with PADs

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Screening for LEAD and UEAD is indicated in patients undergoing TAVI or other structural interventions requiring an arterial approach.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

### 2017 NEW RECOMMENDATIONS

**All Peripheral Arterial Diseases (PADs)**
- Screening for heart failure (BNP, TTE)
- Stable PADs + other conditions requiring anticoagulants (e.g. AF): anticoagulation alone

**Mesenteric Artery Disease**
- D-dimers to rule out acute mesenteric ischaemia
- No delay for re-nutrition in case of symptomatic CMI

**Renal Artery Disease**
- Fibromuscular dysplasia: balloon angioplasty with bailout stenting

**Lower Extremity Artery Disease (LEAD)**
- Statins to improve walking distance
- LEAD + AF: Anticoagulation if CHADS-VASc > 2
- Angiography in CLTI with below-the-knee lesions
- Duplex screening for AAA
- In case of CABG: screen LEAD with ABI, limit vein harvesting if LEAD
- Screening for LEAD in CAD patients
- Screening for LEAD in HF patients
- Clopidogrel preferred over aspirin
- Antiplatelet therapy in isolated asymptomatic LEAD

### CHANGE IN RECOMMENDATIONS

#### Upper Extremity Artery Disease
- Revascularization for symptomatic subclavian artery stenosis
- Subclavian stenosis revascularization
  - Endovascular first
  - Stenting or surgery
- Revascularization for asymptomatic subclavian stenosis in patients with/planned for CABG

#### Renal Artery Disease
- Stenting for symptomatic atherosclerotic stenosis >60%

#### Lower Extremity Artery Disease
- Aorto-iliac lesions
  - Primary endovascular therapy for "TASC-D"
  - Surgery for aorto-iliac or aorto-bi-femoral occlusions
  - Endovascular as an alternative in experienced centres
- Infra-popliteal lesions
  - Endovascular first
  - Bypass using GSV
  - Endovascular therapy
ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ