Guidelines for CLI & Diabetic foot

Chapter I
Definitions, Epidemiology, Clinical presentation, Prognosis

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## METHODOLOGY

levels of evidence from the Oxford Centre For Evidence-Based Medicine

<table>
<thead>
<tr>
<th>Level</th>
<th>Therapy/Prevention, Aetiology/Harm</th>
<th>Prognosis</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>SR (with homogeneity) of RCTs</td>
<td>SR (with homogeneity) of inception cohort studies; CDR validated in different populations</td>
<td>SR (with homogeneity) of Level 1 diagnostic studies; CDR with 1b studies from different clinical centres</td>
</tr>
<tr>
<td>1b</td>
<td>Individual RCT (with narrow Confidence Interval)</td>
<td>Individual inception cohort study with &gt; 80% follow-up; CDR validated in a single population</td>
<td>Validating cohort study with good reference standards; or CDR tested within one clinical centre</td>
</tr>
<tr>
<td>1c</td>
<td>All or none</td>
<td>All or none case-series</td>
<td>Absolute SpPins and SnNouts</td>
</tr>
<tr>
<td>2a</td>
<td>SR (with homogeneity) of cohort studies</td>
<td>SR (with homogeneity) of either retrospective cohort studies or untreated control groups in RCTs</td>
<td>SR (with homogeneity) of Level 2 diagnostic studies</td>
</tr>
<tr>
<td>2b</td>
<td>Individual cohort study (including low quality RCT; e.g., &lt;80% follow-up)</td>
<td>Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR or validated on split-sample only</td>
<td>Exploratory cohort study with good reference standards; CDR after derivation, or validated only on split-sample or databases</td>
</tr>
<tr>
<td>2c</td>
<td>&quot;Outcomes&quot; Research; Ecological studies</td>
<td>&quot;Outcomes&quot; Research</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>SR (with homogeneity) of case-control studies</td>
<td></td>
<td>SR (with homogeneity) of 3b and better studies</td>
</tr>
<tr>
<td>3b</td>
<td>Individual Case-Control Study</td>
<td></td>
<td>Non-consecutive study; or without consistently applied reference standards</td>
</tr>
<tr>
<td>4</td>
<td>Case-series (and poor quality cohort and case-control studies)</td>
<td>Case-series (and poor quality prognostic cohort studies)</td>
<td>Case-control study, poor or non-independent reference standard</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion without explicit critical appraisal, or based on physiology, bench research or &quot;first principles&quot;</td>
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METHODOLOGY
levels of evidence from
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Definitions of the grades of recommendation are:

Grade A ➔ Consistent level 1 studies

Grade B ➔ Consistent level 2 or 3 studies or extrapolations from level 1 studies

Grade C ➔ Level 4 studies or extrapolations from level 2 or 3 studies

Grade D ➔ Level 5 evidence or troublingly inconsistent or inconclusive studies of any level
General consideration

Since there are almost no RCT exclusively among CLI patients, most of the lessened recommendation are based on evidence from subgroup analyses of “PAOD” trials (extrapolation from RCT), or from prospective cohorts.
Where data originates from a RCT, the level of evidence is given by that study design (i.e. level 1a or 1b).

Where results of subgroup analysis are applied to a particular recommendation, it has been downgraded (i.e. grade A ➔ grade B).
The concept of downgrading recommendations based on extrapolation from higher level studies may be considered a limitation of these guidelines, but we accept it, since evidence for the subset of CLI tends to be extremely poor.
General consideration

The validation of a new technique (Endovasc) not only on a comparison with the traditional technique (open surgery) but on the results that can be obtained by this treatment with regard to the objectives for the treatment of CLI.
General consideration

These objectives (limb salvage etc) can clearly be reached with the new technique and therefore there is evidence for its use, but with a downgraded recommendation.
General consideration

To require that the evidence depends on the presence of direct comparisons with the traditional technique could also be reversed:

*there is no absolute evidence for the traditional technique as there are no RCTs comparing this to the new technique*
Chapter I

• Definitions
  - Historical background of the concept of CLI

• Epidemiology
  - Incidence
  - Prevalence
  - Risk factors

• Clinical presentation

• Prognosis
Chapter I

- **Definitions**
  - Historical background of the concept of CLI

- **Epidemiology**
  - Incidence
  - Prevalence
  - Risk factors

- **Clinical presentation**

- **Prognosis**
Historical background of the concept of CLI

• in the 1950s* was based merely on clinical findings (rest pain, ulcer)

* Fontaine et al. 1st meeting of the European Society for Cardio-Vascular Surgery dedicated to aorto-iliac lesions, 1952
Historical background of the concept of CLI

- Later, the importance of haemodynamic abnormalities with well defined thresholds of perfusion pressures was emphasize.
Historical background of the concept of CLI

- objective criterion to each clinical category*

* In 1986 the 1st SVS/ISCVS Standards for reports dealing with lower extremity ischemia was published (will become known as the Rutherford classification)
Historical background of the concept of CCLI


*Recommandation 1*

a) persistently recurring ischemic rest pain requiring regular adequate analgesia (two weeks)

b) or ulceration or gangrene of the foot or toes
Historical background of the concept of CCLI

- **TASC I**
  Ischemic rest pain, ulcers, or gangrene attributable to objectively proven arterial occlusive disease.

\[ TcPO2 < 30-50 \text{ mmHg} \]

\[ \leq 30-50 \text{ mmHg} \]

\[ \leq 50-70 \text{ mmHg} \]

thresholds just below the lower limit values for patients with intermittent claudication, and even the lower limit of normality for forefoot TcPO$_2$
Historical background of the concept of CCLI

- TASC II.

Ischemic rest pain, ulcers, or gangrene

No objective criteria in the summary boxes.
Historical background of the concept of CLI

- Unfortunately, the evolution over the years has been to ignore the second part of the definition of CLI (i.e. the haemodynamic criteria) and to include all patients with rest pain or trophic changes in clinical studies regardless of the severity of the PAOD.
Haemodynamic criteria

- ankle pressure (expressed as absolute value or as ABI) is not a perfect parameter in patients with suspected CLI.

- The measurements providing functional information on tissue perfusion and skin viability, such as forefoot TcPO$_2$, are too rarely used and should be strongly encouraged (➔ Section: prognosis).
Chapter I

- Definitions
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- Prognosis
Lack of accurate data on the incidence and prevalence of CLI.

Statistics based on:

- the overall incidence of major amputations (assuming that about 25% of CLI patients will undergo amputation)

- or on the estimation of the natural history of PAOD

Both are debatable
Epidemiology

It is estimated that
- 5 to 10% of patients with PAOD (asymptomatic or with claudication), will progress to CLI at 5 years
- 1 to 3% of patients with PAOD are in CLI stage at initial presentation [older and sedentary patients who have limited mobility (and therefore do not claudicate), and by patients with sensitive neuropathy who have impaired pain sensation]
Epidemiology

-for one patient with known asymptomatic PAOD at least three have an unknown asymptomatic PAOD

Epidemiology - **Incidence**

- derived *from natural history of PAOD* and *from major amputation rates* has been estimated *500-1000/ million/ year* in a European or North American population

- based *on large prospective population studies* is *220 new cases/million/year* in the general population
Epidemiology - *Prevalence*

- The estimation of the prevalence of CCLI in the population aged 60 to 90 years ranges from 1% to 2%
CLI is recognized as a malignant disease (risk of major amputation, disability and mortality)

**Epidemiology – Natural history & prognosis**

- At presentation:
  - 20-25% → primary amputation
  - 50-60% → vascular reconstruction (bypass surgery or PTA-stenting)
  - 25% → treated medically
CLI is recognized as a malignant disease (risk of major amputation, disability and mortality)

At 1 year:
- 20-25% → died
- 25-30% → major amputation
- 20% → still CLI
- 20% → cured (no CLI signs)
The TAMARIS trial offers probably the most recent reliable data concerning the natural history and prognosis.

The TAMARIS trial
- 525 patients with CLI
- unsuitable for revascularization as assessed by a vascular surgeon,
- randomized to an angiogenic treatment (NV1FGF) or placebo.
- from Dec 2007 to July 2009
- 171 hospitals in 30 countries (from 2007 to 2009)
Epidemiology –

*Natural history & prognosis*

The TAMARIS trial ➔ natural history (placebo group)

@ 1 year
- Major amputation 21%
- Death 15%

The cause of death
- cardio-vascular 49%,
- non-cardiovascular 41%
- unknown in 10%

Lancet. 2011 Jun 4;377(9781):1929-37
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As inclusion criteria, distal pressure measurements are important (limited precision)

The evaluation of *perfusion reserve* and *foot viability* ➔ Forefoot TcPO$_2$
Forefoot TcPO$_2$, if measured according to the methodological rules (particularly avoiding areas of thick or edematous skin) is probably the best non-invasive method in clinical practice to quantify the degree of ischemia and assess prognosis.
RISK STRATIFICATION
based of forefoot TcPO₂: degree 1-4
Recommendation grade B

Degree 1:
10 < TcPO₂ ≤ 35 mmHg in supine position

Degree 2:
forefoot TcPO₂ < 10 mmHg in supine position but clear improvement (≥ 40 mmHg) in sitting position or under oxygen inhalation.
RISK STRATIFICATION (based of forefoot TcPO$_2$)
Recommendation grade B

Degree 3: 
forefoot TcPO$_2$ < 10 mmHg in supine position but inadequate or no improvement (< 30-40 mmHg) in sitting position or under oxygen inhalation.

Degree 4: 
forefoot TcPO$_2$ < 10 mmHg in supine and in sitting position and/or under oxygen inhalation
GUIDELINES FOR CRITICAL LIMB ISCHEMIA
CHAPTER II: DIAGNOSTIC METHODS

Piergiorgio Cao, Hans-Henning Eckstein, Paola De Rango
In patients with critical limb ischemia (CLI) an accurate diagnosis can be established with modern non-invasive vascular diagnostic techniques to provide adequate information for creation of a therapeutic plan.

Non-invasive data will be supplemented by the use of more invasive imaging techniques, such as computed tomography angiography (CTA) or magnetic resonance angiography (MRA), and selective use of lower extremity Angiography.
The objective in noninvasive testing of patients with vascular disease is:
• to confirm the presence of the disease,
• to provide reproducible physiologic data concerning disease severity,
• to document the location and hemodynamic importance of vascular lesions

These tests can be repeated over time to follow disease progression and results of treatment
Non-invasive assessment of patients with CLI can be broadly grouped into three general categories of techniques:

1. physiologic or hemodynamic measurements
2. measurements of tissue perfusion
3. anatomic imaging
Non-invasive Vascular Laboratory

- DOPPLER ULTRASONOGRAPHY
  - Ankle brachial and toe-brachial indices
  - Segmental limb pressure
  - Continuous-wave doppler measurements

- PLETHYSMOGRAPHY
  - Pulse volume recording
  - Measurements of tissue perfusion
Ankle brachial index (ABI)

A routine measurement for screening
• in 50-69 years old patients with smoking history,
• in >70y patients
• in all diabetic patients

A quick and cost-effective way to establish or refute CLI diagnosis

• provides information on long-term prognosis.
• ABI <0.90 is associated with a 3-6 fold increased risk of cardiovascular mortality
• may not be accurate in the presence of non compressible infracrural arteries
Recommendations

The resting ABI should be measured on both legs in patients with CLI to confirm diagnosis and establish baseline and should be used in individuals with non-healing ulcer, lower limb rest pain (Level 2c)

ABI should be used to assess cardiovascular risk in those patients who are >70 years or >50 years with other cardiovascular risk factors as diabetes and history of smoking (Level 2a)
Toe-brachial index is a quick way to noninvasively establish or refute the CLI diagnosis in patients with lower limb rest pain or nonhealing ulcers.
Recommendation

Toe-brachial index should be used in patients in whom CLI is clinically suspected and the ABI test is not reliable due to noncompressible vessels as in patients with diabetes, advanced age or long-standing renal failure (Level 2b, Grade B)
Segmental limb pressure

1) Segmental pressure examination is useful to provide **anatomical localization** of lower limb vascular disease

2) It can provide information on the efficacy of therapeutic intervention and the need of further additional revascularization

3) Measurements of segmental pressure can provide **only indirect information** on vascular disease and results can be biased by a number of artifacts and drawbacks
Recommendation

Lower limb segmental pressure measurements are useful to define the CLI initial diagnosis and localization of arterial lesion along lower limb (Level 2b, Grade B)
Continuous-wave doppler ultrasound

The test enables qualitative evaluation of blood flow, vessel localization and flow detection.

It can evaluate qualitative waveform assessment and quantitative data before and after revascularization.

It is outdated as a single examination due to multiple artifacts but is maximized by combining this analysis with imaging (ultrasound grayscale or color visualization of the arterial wall, “Duplex”)
Recommendations

Continuous-wave doppler ultrasound is useful to provide initial qualitative and quantitative assessment (Class 2a, Level B)

Continuous doppler ultrasound does should be maximized by combining waveform analysis with imaging ("Duplex") (Class 2c, Level B)
Pulse volume recording (PVR)

PVR can provide a tool to evaluate small-vessel disease and CLI in individuals with noncompressible vessels in whom ABI and segmental pressures are spuriously elevated.

PVR does not allow quantitative measure of perfusion and may not be accurate in more distal segments of the leg.

PVR may be abnormal in patients with low cardiac stroke volume.
Recommendations

Pulse volume recording can be used as an initial step in the evaluation of patients with suspected CLI and follow-up but accuracy is limited (Class 2a)

Pulse volume recording is reasonable to establish the initial CLI diagnosis in diabetic patients and patients with non-compressible arteries (Class 2a)

Pulse volume recording is reasonable in predicting outcome, risk of amputation and monitor limb perfusion in CLI and diabetes (Class 2a)
Measurements of tissue perfusion include microcirculation techniques, the most common employed being transcutaneous partial pressure of oxygen (TcPO2) measurements.
Recommendations

Patients with ischemic rest pain or foot ulcers should be investigated with objective tests to confirm diagnosis of CLI (Level B), these may include TcPO2, laser doppler and hyperspectral measurements to assess metabolic state of tissue perfusion (Level C)

Tissue perfusion tests (TcPO2, laser doppler, spectral imaging) can be used to assess healing potential of ulcers/amputation in patients with CLI (Level C)
CHAPTER II: DIAGNOSTIC METHODS

- Imaging techniques

- Duplex Ultrasound
- Computed Tomography Angiography
- Magnetic Resonance Angiography
- Digital Subtraction Angiography
Duplex Ultrasound

Duplex ultrasound (DUS) enables identification of the anatomic location and the degree of stenosis by combining both B-mode ultrasound and colour Doppler ultrasound.

Hemodynamic assessment is performed by measuring peak systolic velocity (PSV) and PSV ratios beyond an obstruction compared with the adjacent upstream segment.

A PSV ratio of greater than 2:1 is considered to indicate a >50% stenosis, a PSV ratio greater than 4:1 a >75% stenosis and a PSV ratio of greater than 7:1 a >90% stenosis.
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Grade of recommendation</th>
<th>Level of Evidence</th>
</tr>
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<tbody>
<tr>
<td>Duplex of the extremities is useful to diagnosis anatomic location and degree of obstruction</td>
<td>A</td>
<td>1a</td>
</tr>
<tr>
<td>Duplex may be considered for routine surveillance after revascularisation</td>
<td>B</td>
<td>2b</td>
</tr>
<tr>
<td>Duplex can be useful to select patients as candidates for endovascular intervention</td>
<td>B</td>
<td>2b</td>
</tr>
<tr>
<td>Duplex ultrasound may be considered for routine surveillance after femoro-popliteal bypass with a synthetic conduit</td>
<td>B</td>
<td>3b</td>
</tr>
</tbody>
</table>
Computed Tomography Angiography

Shorter acquisition times, thinner slice thicknesses, higher spatial resolution, and improvement of multidetector computed tomographic (CT) scanners enable scanning of the entire vascular tree.

CTA offers by comparison to MRA better patient acceptance, a higher speed of examination, a better spatial resolution and the ability to evaluate previously stented arteries.

Disadvantages of CTA include image interference from calcified arteries and the need for potentially nephrotoxic contrast and radiation exposure.
# Computed Tomography Angiography

## Recommendations

<table>
<thead>
<tr>
<th>CTA of the extremities may be considered to diagnose anatomic location and presence of significant stenosis in patients with lower extremity PAD</th>
<th>B</th>
<th>3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTA of the extremities may be considered as a substitute for MRA for those patients with contraindications to MRA</td>
<td>B</td>
<td>3a</td>
</tr>
</tbody>
</table>
Magnetic Resonance Angiography

There have been major technical advances in recent years including 3-D contrast enhanced magnetic resonance angiography (ce-MRA) and the development of moving tabletops which enable whole limb examinations with a single contrast injection.

Unlike DUS and CTA it is unaffected by arterial calcification.

Relative disadvantages include a tendency to overestimate stenosis.
## Magnetic Resonance Angiography

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Grade of Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRA of the extremities is useful to diagnose anatomic location and degree of stenosis of PAD</td>
<td>A</td>
<td>1a</td>
</tr>
<tr>
<td>MRA of the extremities should be performed with gadolinium enhancement</td>
<td>A</td>
<td>2a</td>
</tr>
<tr>
<td>MRA of the extremities is useful in selecting patients with lower extremity PAD as candidates for endovascular intervention</td>
<td>A</td>
<td>2a</td>
</tr>
<tr>
<td>MRA of the extremities may be considered for postrevascularization (endovascular and surgical bypass) surveillance in patients with lower extremity PAD</td>
<td>B</td>
<td>3b</td>
</tr>
</tbody>
</table>
### Recommendations

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<th>Level of Evidence</th>
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<tbody>
<tr>
<td>DSA is not recommended as the primary imaging modality</td>
<td>A</td>
<td>1a</td>
</tr>
<tr>
<td>DSA provides detailed information about arterial anatomy and is recommended when revascularization is contemplated</td>
<td>A</td>
<td>2a</td>
</tr>
<tr>
<td>A history of contrast reaction should be documented before the performance of contrast angiography and appropriate pretreatment before contrast is given</td>
<td>A</td>
<td>2a</td>
</tr>
<tr>
<td>Decisions regarding the potential utility of invasive therapeutic interventions should be made with a complete anatomic assessment of the affected arterial territory or a combination of angiography and noninvasive vascular techniques</td>
<td>A</td>
<td>2a</td>
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# Digital Subtraction Angiography

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<tr>
<td>Before performance of contrast angiography, a full history and complete vascular examination should be performed to optimize decisions regarding the treatment plan</td>
<td>A</td>
<td>3b</td>
</tr>
<tr>
<td>The diagnostic lower extremity arteriogram should image the iliac, femoral, and tibial bifurcations in profile without vessel overlap</td>
<td>A</td>
<td>2b</td>
</tr>
<tr>
<td>When conducting a diagnostic lower extremity arteriogram in which the significance of an obstructive lesion is ambiguous, trans-stenotic pressure gradients and supplementary angulated views should be obtained</td>
<td>A</td>
<td>2b</td>
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<td>Patients with baseline renal insufficiency should receive hydration before</td>
<td>A</td>
<td>2b</td>
</tr>
<tr>
<td>Follow-up clinical evaluation, including a physical examination and measurement of renal function, is recommended within 2 weeks after contrast angiography to detect the presence of delayed adverse effects, such as atheroembolism, deterioration in renal function, or access site injury (e.g., pseudoaneurysm or arteriovenous fistula)</td>
<td>A</td>
<td>3a</td>
</tr>
<tr>
<td>Noninvasive imaging modalities, including MRA, CTA, and color flow duplex imaging may be used in advance of invasive imaging to develop an individualized diagnostic strategic plan</td>
<td>A</td>
<td>2a</td>
</tr>
</tbody>
</table>
CLI Guidelines
Medical Treatment

Jürg Schmidli
Nicolas Diehm
Bern, Switzerland
Management of Cardiovascular Risk Factors and Medical Therapy

- **Critical issue:**
- Most of the outlined recommendations apply to PAD patients in general. Thus, it has to be kept in mind that recommendations are frequently extrapolated to the subgroup of PAD with critical limb ischemia.
Cigarette Smoking

- **Recommendations:**
- CLI patients should be strongly and repeatedly advised to stop smoking (Level 2a, Grade B).
- Smoking cessation rates can be improved by offering medical advice, group counseling session, nicotine replacement, nicotine receptor partial agonists (varenicline) or antidepressant drug therapy (bupropion) (Level 1a, Grade A).
Hyperlipidemia

- **Recommendations:**
  - In CLI patients, statins should be the primary agents to lower LDL cholesterol levels to reduce the risk of cardiovascular events (Level 1a, Grade A).
  - For CLI patients, LDL cholesterol should be <100mg/dl (Level 5, Grade C).
  - Dietary modification is aimed at controlling body weight and lipid disorders (Level 5, Grade D).
  - Statins are indicated for secondary prevention of cardiovascular events in patients with CLI (Level 1a, Grade A).
Arterial Hypertension

• **Recommendations:**
  • CLI patients with arterial hypertension should be treated with antihypertensive medical therapy aimed at lowering cardiovascular mortality (Level 1c, Grade B).
  • Treatment goals for CLI patients with arterial hypertension: arterial blood pressure should be <140/90mmHg and <130/80mmHg in case of concomitant diabetes mellitus or renal insufficiency (Level 1c, Grade B).
  • ACE inhibitors are recommended in CLI patients (Level 5, Grade C).
  • Beta-adrenergic blocking drugs are not contraindicated in CLI patients (Level 1a, Grade A) and should be administered to patients undergoing surgical lower limb revascularization (Level 1c, Grade B).
Diabetes Mellitus

- **Recommendation:**
- Blood glucose levels should be monitored in CLI patients with a hemoglobin A1c (HbA1c) goal of <7.0% (Level 5, Grade D).
Antiplatelet Therapy

**Recommendations:**
- Antiplatelet (aspirin or clopidogrel) therapy is indicated in patients with symptomatic peripheral arterial disease (Level 1a, Grade A).
- Both aspirin and clopidogrel reduce rates of cardiovascular events in patients with symptomatic peripheral arterial disease (Level 1b, Grade A).
- In line with recommendations for patients with coronary heart disease, intermittent administration of dual antiplatelet therapy (aspirin plus clopidogrel) may be considered for patients undergoing stent implantation or drug eluting balloon angioplasty of femoro-popliteal or infrapopliteal arteries (Level 5, Grade D).
Vasoactive Drugs

- **Recommendation:**
- Parenteral prostanoids can be used in patients with critical limb ischemia not suitable for arterial revascularization or after unsuccessful revascularization
- (Level 1a, Grade B).
Gene and Stem Cell Therapy

- **Recommendation:**
  - Due to conflicting or missing data, neither gene nor stem cell therapy can be recommended as a treatment for CLI outside clinical trials
  - (Level 5, Grade D).
Exercise and Lower Limb Rehabilitation

- **Recommendation:**
- Due to the risk of worsening pre-existing or causing new ischemic wounds in the affected lower limb, walking exercise is contraindicated in CLI patients (Level 5, Grade D).
Treatment of Co-Existing Disease

- **Coronary artery disease (CAD)**
- **Recommendation:**
- CLI patients with clinical evidence of CAD (angina, ischemic congestive heart failure) should be evaluated and treated according to current guidelines for coronary revascularization
  - (Level 1c, Grade A).
- Routine treatment with beta blockers before vascular surgery is recommended
  - (Level 1c, Grade B).
- Routine coronary revascularization before vascular surgery is not recommended (Level 1b, Grade A).
Treatment of Co-Existing Disease

- **Carotid artery disease**
- **Recommendation:**
- The treatment for both symptomatic and asymptomatic carotid artery disease in PAD patients should be based on current guidelines
- (Level 1a, Grade A).
Treatment of Co-Existing Disease

- Renal artery disease
- **Recommendation:**
- In significant renal artery disease, as evidenced by poorly controlled hypertension or renal insufficiency, patients should be referred to a vascular physician and be treated according to current guidelines (Level 2c, Grade B).
Health economics of risk-factor interventions

- Cost-effectiveness
  - smoking cessation interventions
  - pharmacologic interventions

- No literature available!

- No recommendations!
Summary

• Besides arterial revascularization, risk factor modification and administration of antiplatelet therapy is a major goal in the treatment of CLI patients.

• Key elements

• smoking cessation, treatment of hyperlipidemia and arterial hypertension; diabetes mellitus should be adequately adjusted.

• In CLI patients not suitable for arterial revascularization parenteral prostanoids may be considered.

• Gene and cell stem therapy are OUT

• Walking exercise is contraindicated

• Co-existing comorbidities should be managed according to current guidelines.

• Considering the above-mentioned treatment goals, interdisciplinary treatment approaches for CLI patients are warranted.
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- Key elements
  - smoking cessation, treatment of hyperlipidemia and arterial hypertension; diabetes mellitus should be adequately adjusted.
- In CLI patients not suitable for arterial revascularization parenteral prostanoids may be considered.
- Gene and cell stem therapy are OUT
- Walking exercise is contraindicated
- Co-existing comorbidities should be managed according to current guidelines.
- **Considering the above-mentioned treatment goals, interdisciplinary treatment approaches for CLI patients are warranted.**
ESVS Guidelines for CLI Surgical Treatment

C. Setacci¹, G. de Donato¹, M. Teraa, F. Moll³
& JB Ricco⁴

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² Department of Vascular Surgery, University Medical Center Utrecht, The Netherlands
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Surgical treatment of CLI - Introduction

Decision making in revascularization strategies in CLI differs substantially from that in patients with claudication as *wound healing, leg salvage and maintained ambulation* are different treatment aims than improved walking ability and there are often considerable time constraints.
Surgical treatment of CLI - Introduction

Since there are almost no RCT exclusively among CLI patients, most of the lessened recommendation are based on prospective evidence from subgroup analyses of “PAOD” trials (*extrapolation from RCT*), or from prospective cohorts.
Treatment options:

**CHOICE BASED ON:**

- AFFECTED ARTERIAL SEGMENT
- LENGTH OF DISEASED SEGMENT
- PATIENT CHARACTERISTICS

- Endovascular:
  - PTA
  - PTA with stent or stent graft

- Hybrid

- Non-reconstructive
Guidelines and Classifications

• Classifications and guidelines aim at:
  – Standardized care
  – Evidence-based medicine
  – Highlighting gaps in current knowledge

• TASC-classification widely used, but:
  – Complex loco-regional classification
  – Quickly out-dated due to fast technical developments
  – Poor inter-observer consensus

• New and simplified classification based on arterial segment and lesion length is preferred
ESVS Guidelines - Treatment by segment

• Aortoiliac

• Infrainguinal:
  – Common Femoral Artery (CFA)
  – Deep Femoral Artery (DFA)
  – Superficial Femoral Artery (SFA)

• Popliteal

• Infrapopliteal
Aortoiliac Obstructive Disease (AIOD)

- Endovascular lower long-term primary patency (PP), but similar secondary patency (SP)
- 5-year PP of open procedures in CLI:
  - AFB, IFB, and AIE approximately 75-80%

Treatment choice:

- First-line: PTA with provisional stenting (Level 3a, Grade C)
- Diffuse lesions: Aorto-(bi)femoral bypass (Level 2a, Grade B)
- Limited lesions: Endarterectomy → lower morbidity and mortality (Level 4, Grade C)
- Extra-anatomical bypass reserved for high risk patient or hostile abdomen (Level 4, Grade C)
Common Femoral Artery (CFA)

- CFA steno-occlusive disease:
  - Endarterectomy (potential for hybrid procedure)
  - PTA (with stent)

**Treatment choice:**

- First choice: endarterectomy (5-year PP 91% SP 100%) *(Level 4, Grade C)*
- Provides access to perform hybrid revascularization of parallel EIA, DFA or SFA pathology with good results *(Level 3b, Grade C)*
Deep Femoral Artery (DFA)

- Recanalization of the DFA:
  - Rarely performed as isolated procedure for limb salvage
  - Limbsalvage rates:
    - 67%, 49% and 36% at 1, 3, and 5 years
  - Profundoplasty can be of value to preserve the knee joint when amputation is necessary

**Treatment choice:**
- First choice: surgical profundoplasty
  *(Level 3b, Grade C)*
Superficial Femoral Artery (SFA)

- SFA steno-occlusive disease:
  - Short lesions (<5 cm)
  - Intermediate lesions (5-15 cm)
  - Long lesions (>15 cm)

- Long-term patency of PTA in CLI is much lower than in claudicants: 20-37% 3-year PP

- Different attempts to reduce low patency due to:
  - Recoil
  - Dissection
  - Intimal hyperplasia
Options for stententing

- Balloon-expandable stent
- Self-expandable stent
- Stent graft
- Drug eluting stent

Target recoil and dissection
Aim at reduction of intimal hyperplasia
**Recommendation:** A new and simplified classification system for peripheral arterial disease lesions is needed to improve inter-individual interpretation as this is problematic for the TASC classification. Therefore we would recommend a system based on lesion length to classify lesions for research applications and clinical management (EUSC classification).

Future research should prove the applicability and reproducibility of the classification and the additional value of a potential subdivision of stenotic versus occlusive lesions.

**Level 5, Grade D**
CLI (partially) based on SFA lesion

- Lesion length < 5cm
  - PTA with provisional stenting

- Lesion length 5-15 cm
  - PTA with self-expandable stent

- Lesion length > 15cm
  - Physical condition suitable for open procedure
    - Yes
      - Open bypass procedure (especially in younger patients and occlusive lesions):
        1. Venous
        2. Synthetic
    - No
      - Alternative for open:
        1. Stent graft
        2. Remote endarterectomy
        3. (Future cell-based therapies)
Choice of treatment

- Short lesions (>5cm):
  - PTA with provisional stenting (Level 1a, Grade B)

- Intermediate lesions (5-15 cm):
  - PTA with self-expandable stent (Level 1b, Grade B)

- Long lesions (>15 cm):
  - Venous bypass
  - Synthetic bypass
  - Thru-pass for pts at high risk for open (Level 3b, Grade C)
  - (Hybrid and Remote Endarterectomy) (Level 2b, Grade B)

Especially beneficial in patients with life-expectancy >2 years (Level 1b, Grade B)
Choice of treatment – SFA long lesions (>15 cm)

**Recommendation:** Hybrid procedures are the preferred treatment modality irrespective of lesion length in high-risk patients not suitable for open bypass surgery or when no suitable vein is available if minimally open revascularisation is mandated, such as CFE. Level 2b, Grade B
Infrapopliteal disease

• Infrapopliteal PTA and crural/pedal bypass:
  – Similar long-term clinical and procedural success rates (Level 4, Grade C)

• PTA is preferred when it does not preclude future surgical intervention

• Primary stenting beneficial?
  – In case of short lesions drug eluting stents are beneficial (Level 2b, Grade B)

• Vein (single-segment or composed) is the preferred bypass material in BTK bypass (Level 3b, Grade B)
What to do when there is no option left?

- **Prostanoids:**
  - Early studies reported effectiveness, however not supported by more recent data

- **Sympathectomy:**
  - No limb salvage, but reduces symptoms *(Level 2a, Grade B)*

- **Spinal Cord Stimulation:**
  - Expensive and no proven benefit for CLI *(Level 1a, Grade A)*

- **Regenerative Therapies:**
  - Gene and growth factor therapies not very successful thus far
  - Cell-based therapies are very promising *(Level 5, Grade D)*
Conclusions

• CLI has a major impact on:
  – Patient
  – Physician
  – Health care system

• A more concise and simplified classification is advocated

• Treatment consists of endovascular and surgical options with an increasing trend towards an endovascular first approach
Conclusions

• Principle-first-line treatment:
  – AIOD: PTA with provisional stenting
  – CFA: Endarterectomy
  – DFA: Endarterectomy
  – SFA:
    • Short lesion: PTA with provisional stenting
    • Intermediate: PTA with self-expandable stent
    • Long lesion: Venous (or synthetic) bypass
  – Infrapopliteal: PTA (with DES in short lesions)
Questions???

Limbsalvage is the goal, but it can’t be as nice as it was before...
Chapter V, Follow-up

ESVS CLI guidelines 2011
F. Dick, AH. Davies, JB Ricco, et al.
Follow-up

- sustained treatment success
- continued best patient care
Follow-up IMPORTANT

- sustained treatment success
- continued best patient care

- CLI: frail and elderly
- ambulation=independency
nonetheless...

- neglected previously
RECOMMENDATIONS

Class I

1. Unless contraindicated, all patients undergoing revascularization for CLI should be placed on antiplatelet therapy (see Sections 2.4.2 and 2.6.1.6 in the full-text guidelines), and this treatment should be continued indefinitely. (Level of Evidence: A)

2. Patients who have undergone femoral bypass grafts should be periodic evaluations that record progression of ischemic symptoms, rhoral pulses, and ABIs. (Level of Evidence: B)

3. If infection, ischemic ulcers, or persist and the ABI is less than 0.8 after correction of inflow, an outflow procedure should be performed that bypasses all major distal stenoses and occlusions. (Level of Evidence: A)

4. Patients who have undergone placement of a lower extremity bypass with autogenous vein should undergo for at least 2 years periodic examinations that record any return or progression of ischemic symptoms; a physical examination, with concentration on pulse examination of the proximal, graft, and outflow vessels; and duplex imaging of the entire length of the graft, with measurement of peak systolic velocities and calculation of velocity ratios across all lesions. (Level of Evidence: A)

5. Patients who have undergone placement of a synthetic lower extremity bypass graft should undergo periodic examinations that record any return of ischemic symptoms; a pulse examination of the proximal, graft, and outflow vessels; and assessment of ABIs at rest and after exercise for at least 2 years after implantation. (Level of Evidence: A)

benefit of revascularization and to limit the risk of ischemic events (MI and myocardial infarction) and death, usually aspirin or clopidogrel. In patients with lower extremity PAD, the use of dual antiplatelet therapy is recommended. The use of an ACE inhibitor might decrease mortality (165). To maintain optimal outcomes, patients should undergo periodic graft surveillance for at least 2 years after placement. For vein grafts, ultrafast imaging of the donor and recipient arteries, proximal and distal anastomoses, and the entire graft length is of benefit for the detection of grafts with reduced flow secondary to intraluminal lesions. Duplex imaging is of limited benefit for the detection of lesions within synthetic grafts. Therefore, the periodic recording of ABIs is sufficient.
ACC/AHA 2005 guidelines

- class I, level A (B) recommendations
- ...no references presented...
TASC II 2007

F5 SURVEILLANCE PROGRAMS FOLLOWING REVASCULARIZATION

Following construction of an infrainguinal autogenous bypass graft, it has been recommended in the past that a program of regular graft review with duplex scanning be undertaken. The purpose of this is to identify lesions that predispose to graft thrombosis prior to graft occlusion. A recent randomized, controlled trial has shown that after venous femoral distal bypass grafting, surveillance scanning has proven to be not cost-effective according to this study. In practice, many surgeons continue a program of vein graft surveillance awaiting further confirmation of the findings of this trial.

Recommendation 41
Antiplatelet drugs as adjuvant pharmacotherapy after revascularization

- Antiplatelet therapy should be started preoperatively and continued as adjuvant pharmacotherapy after an endovascular or surgical procedure [A]. Unless subsequently contraindicated, this should be continued indefinitely [A].

Recommendation 42
Clinical surveillance program for bypass grafts

The ongoing bypass graft surveillance program should enter the patient for the treatment of claudication or severe ischemia and should be entered into a surveillance program. This program should consist of:
- Interval history (new symptoms)
- Vascular examination of the leg with palpation of proximal, graft, and outflow vessel pulses
- Periodic measurement of resting and, if possible, post-exercise ankle-brachial indices
- Clinical surveillance programs should be performed in the immediate postoperative period and at regular intervals (usually every 6 months) for at least 2 years [C].
TASC II 2007

- grade A (C) recommendations
- ...not stratified for CLI...
• ? lack of (stratified) studies
• ? pessimistic of prognosis
- Lack of (stratified) studies
- Pessimistic perception of prognosis
- 12mt: 85% alive (PREVE)
- 24mt: 70% alive (BASIL)
Follow-up: current guidelines

- systematic review
- lack of stratified studies
- inconsistent CLI definition
Follow-up: current guidelines...

- systematic review
- lack of stratified studies
- inconsistent CLI definition
- (A) best medical therapy
- (B) surveillance
- (C) initiation of re-intervention
...based on extrapolations

- grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Consistent level 1 studies</td>
</tr>
<tr>
<td>B</td>
<td>Consistent level 2 or 3 studies or extrapolations from level 1 studies</td>
</tr>
<tr>
<td>C</td>
<td>Level 4 studies or extrapolations from level 2 or 3 studies</td>
</tr>
<tr>
<td>D</td>
<td>Level 5 evidence or troublingly inconsistent or inconclusive studies of any level</td>
</tr>
</tbody>
</table>

- degradation of recommendation strength

- critical issue 1: need for well-designed studies
(A) best medical therapy

- grade B:
  - VKA for vein bypass
  - low dose ASA for prosthetic/PTA

- grade C:
  - INR 2-4 efficient; 3-4 preferable

- grade D:
  - (supervised) exercise if possible
critical issues A:
- statin effect on patency?
- systemic benefits of ASA versus local benefits of VKA (vein bp)
- duration of VKA?
- clopidogrel/new antithrombotic agents?
(B) surveillance

.grade B:
- early duplex for vein bypass
- no routine long-term duplex prgr.
- clinical surveillance every 3-6 mts

.grade C:
- early duplex after PTA
- duplex surveillance for graft at risk
critical issues B:

- role of distal landing zone (i.e., above/below knee)?
- duplex surveillance after use of endovascular adjuncts?
- cost-effectiveness analyses?
(C) repeat interventions

❖ grade B:
  • PTA and surgery equivalent for short and late appearing stenosis

❖ grade C:
  • early and recurrent stenoses benefit from surgery
  • clinical/duplex surveillance after re-intervention
critical issues C:

- best approach to graft failure?
- best approach to complex endotherapy?
- role of drug-eluting adjuncts?
summary:

- follow-up important for CLI
- largely ignored previously
- weak body of evidence
- critical issues
conclusions:

- extrapolated recommendations (no grade A)
- valid evidence to be developed
- important contexts: diabetes, renal failure, functionally impaired
Guidelines for Critical Limb Ischemia & Diabetic Foot

Mauri Lepäntalo, MD, PhD, Helsinki
Jan Apelqvist, MD, PhD, Malmö

The previous work of International Working Group on the Diabetic Foot – Peripheral Arterial Disease is acknowledged
Diabetic foot ulcers

- Over 55 million diabetics in Europe
- Indicative annual costs for EU have been estimated to be 4-6 billion Euro’s
- Complications of foot ulcers are a leading cause of hospitalization and amputation
- 20-40% of health care resources for diabetes is related to diabetic foot
- Annual incidence of foot ulceration is over 2-5% among diabetics
- Major amputation will be needed within a year in 5-8% of patients with diabetic ulcers
  - 85% preceded by a foot ulcer
Neuropathy and ischemia are the initiating factors, with a different weight in different patients, and infection is mostly a consequence.
Ischemia and neuroischemia of the diabetic foot

Underestimation of the role of ischemia

• up to 60% of neuroischemic or ischemic origin

• **Recommendation:** Ischemia should not be excluded as a cause of diabetic foot ulcer unless proven absent. **Level 5; Grade D**
Inadequate understanding of neuroischemia

- Ischemia is caused by peripheral arterial disease, typically affecting infrapopliteal arteries.
- The combined effect of diabetic neuropathy and ischemia, often called neuroischemia, decreases the foot perfusion even further.
- Microvascular dysfunction
  - presence of arterio-venous shunting
  - pre-capillary sphincter malfunction
  - capillary leakage
  - venous pooling
  - hormonal activity in the vessel
  - inflammation in its wall
Inadequate understanding of neuroischemia

**Recommendation:**

- In neuroischemic legs the healing is primarily affected by the severity of ischemia.
- Therefore, from a practical point of view neuroischemic and ischemic lesions should be considered together as both may need revascularisation. *Level 2b;Grade C*
Why CLI criteria for non-diabetics are not applicable in diabetics

- Use of rigid noninvasive methods not good enough
  - bias due to medial sclerosis, tissue lesions
- A clear need to introduce and recognize decreased perfusion as indicator for need for revascularization in the diabetic foot to achieve and maintain healing and to avoid or delay a future amputation
Why CLI criteria for non-diabetics are not applicable in diabetics

- **Recommendation:** International Working Group for Diabetic Foot recommends further vascular studies in case ulcer has not healed in proper treatment in six weeks although initial diagnostics have suggested only questionable or mild disease. Level 5; Grade D

- **Critical issue:** Criteria for impaired perfusion should be established
Delay of revascularisation

- Less than 25% of diabetic individuals with PAD report intermittent claudication
- Rest pain is far less common than in non-diabetics
- Diagnosis of ischemia is often delayed
- 30-50% of foot ulcers already have gangrene at presentation
  - far too often vascular surgeons are not consulted at all
Delay of revascularization

- **Recommendation:** To prevent the delay of vascular consultation and revascularization, early noninvasive vascular evaluation is important in identifying patients with poor ulcer healing and high risk for amputation. 
  
  **Level 2b; Grade B**
Neuroischemia, infection and tissue damage

• An infection in the diabetic foot is a limb-threatening condition
  – immediate cause for amputation in 25-50% of diabetic patients
  – feet with a combination of ischemia, infection and tissue damage fare even worse
Clinical examination

- **Recommendation:** Every foot ulcer should be examined for the presence of ischemia.
  - **Level 5; Grade 4**

- **Recommendation:** Every foot ulcer should be examined for the presence of neuropathy.
  - **Level 5; Grade 4**

- **Recommendation:** Every diabetic foot ulcer should be examined for the presence of infection.
  - **Level 5; Grade D**
Non-invasive vascular studies

- **Recommendation:** Trust ABI when low but not when high. An ABI <0.6 indicates significant ischemia in respect to wound healing potential whereas on ABI >0.6 has little predictive value and therefore at least the toe pressure should be measured.  
  Level 5; Grade D

- **Recommendation:** An ulceration of the foot in diabetes will generally heal if the toe pressure is >55 mmHg, whereas healing is usually severely impaired when toe pressure is <30 mmHg.  
  Level 2b; Grade B

- **Recommendation:** Ulceration of the foot in diabetes will generally heal if the tcpO2 >50 mmHg. Healing is usually severely impaired when tcpO2 <30 mmHg.  
  Level 2b; Grade B
Probability of healing (%) as related to noninvasive data

Vascular imaging and revascularization should be considered irrespective of pressure values if diabetic foot ulcer does not heel in conservative treatment.
Vascular imaging

• When PAD a potential cause for the clinical picture
• How to treat the arterial lesions
• Options:
  – Duplex ultrasound
  – magnetic resonance angiography (MRA)
  – computed tomography angiography (CTA)
  – digital subtraction angiography (DSA)

• Recommendation: Any of the techniques is useful for mere imaging as the accuracy of different techniques in diagnosing stenosis of >50% in the infrapopliteal segment is acceptable and similar when using DSA as the reference. Level 2a; Grade B

• Recommendation: Detailed visualisation of infrapopliteal arteries, including the arteries of the foot, is necessary for complete evaluation of diabetic patients. Level 5; Grade D
Specific problems in imaging

- **Duplex and CT**
  - extensive calcification of infrapopliteal arterial tree may prevent proper Duplex diagnostics and computed tomography angiography
  - multi-sliced devices decreases interpretation difficulties caused by arterial wall calcifications

- **MRA**
  - limited spatial resolution
  - its images may be distorted by previous stents, implants and flow disturbances
  - use of paramagnetic contrast material gadolinium has been reported to cause nephrogenic systemic fibrosis typically in patients with renal failure

- **Critical issue**: The risks of gadolinium-enhanced MRA for imaging diabetic patients with kidney failure should be considered and further evaluated
# Multifactorial treatment of diabetic foot ulcer

## Goal

### Improvement of perfusion
- Endovascular revascularization (PTA)
- Reconstructive vascular surgery (bypass)
- Vascular drugs
- Reduction of edema
- Hyperbaric oxygen

### Treatment of infection
- Antibiotics (oral or parenteral)
- Incision, drainage
- Resection

### Reduction of edema
- External compression therapy
- Intermittent compression (pumps)
- Diuretics

### Pain control
- Analgesic drugs (local or systemic)
- Immobilisation, off loading, relief of anxiety and fear, TNS

### Improvement of metabolic control
- Insulin treatment
- Necessary nutritional support
<table>
<thead>
<tr>
<th>Off loading</th>
<th>Protective and therapeutic footwear</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insoles, orthosis</td>
</tr>
<tr>
<td></td>
<td>Total contact cast, walkers</td>
</tr>
<tr>
<td></td>
<td>Crutches, wheelchair, bed rest</td>
</tr>
<tr>
<td>Wound bed preparation</td>
<td>Debridement, removal of debris</td>
</tr>
<tr>
<td></td>
<td>Topical treatment, dressings</td>
</tr>
<tr>
<td></td>
<td>Control of exudation, moist wound healing, GCSF infection control, NPWT</td>
</tr>
<tr>
<td></td>
<td>Tissue engineering, growth factors, matrix modulation</td>
</tr>
<tr>
<td>Removal of dead tissue</td>
<td>Incision, drainage, amputation</td>
</tr>
<tr>
<td>Correction of foot deformities</td>
<td>Corrective foot surgery, skin transplant, amputation</td>
</tr>
<tr>
<td>Improvement of general condition</td>
<td>Fluid and nutrition replacement therapy</td>
</tr>
<tr>
<td></td>
<td>Aggressive treatment of concomitant disease, antiplatelet drugs, antihypertensive agents, lipid decreasing agents</td>
</tr>
<tr>
<td></td>
<td>Cessation of smoking</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy</td>
</tr>
<tr>
<td>Implementation of systematic care</td>
<td>Patient and staff education</td>
</tr>
<tr>
<td></td>
<td>Support and follow up</td>
</tr>
<tr>
<td></td>
<td>Multidisciplinary co-ordination, communication, staggered treatment chains</td>
</tr>
<tr>
<td></td>
<td>Improvement of concordance process oriented approach</td>
</tr>
</tbody>
</table>
Multifactorial approach mandatory

- **Recommendation**: Intensive management of diabetes, including glycaemic and platelet aggregation control, treatment of hypertension and dyslipidemia, as well as non-pharmacological interventions, decrease vascular complications in the long run. **Level 1a; Grade A**

- **Recommendation**: Any diabetic foot ulcer should always be considered ischemic until proven otherwise by extensive clinical examination and non-invasive, vascular testing to identify those patients in need of revascularisation to improve perfusion to achieve healing. **Level 5; Grade D**
Revascularization

• The crucial issue is to decide whether revascularization is needed for a certain lesion, for a certain patient
• Although noninvasive evaluation is helpful, the decision to intervene is made due to presenting symptoms and clinical findings
• Anatomic imaging should be considered only strategic

**Recommendation:** There are no convincing data that endovascular or open revascularization would give better outcome in diabetic patient with ischemic ulcer as the results strongly depend on the severity and distribution of peripheral arterial disease. **Level 2c; Grade B**
<table>
<thead>
<tr>
<th>Author</th>
<th>Patients; N / gender / age (mean/median)</th>
<th>Comorbidity</th>
<th>Intervention</th>
<th>Infrapopliteal distribution</th>
<th>30-day complications</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosenbaum, 1994</td>
<td>39 / M33, F6 / 62.3 yrs</td>
<td>NA</td>
<td>infrapopliteal bypass grafts</td>
<td>79 %</td>
<td>Major amputation 3%, mortality NA</td>
<td>21.2 months (mean), range 2-64</td>
<td>NA</td>
</tr>
<tr>
<td>Wolfe, 2000</td>
<td>125 / NA / 70 yrs</td>
<td>CAD 57%, ESRD 25%</td>
<td>infrapopliteal bypass vein grafts</td>
<td>100 %</td>
<td>Major amputation NA, mortality 2%</td>
<td>24 months (mean)</td>
<td>Limb salvage 80% at 1 yr, mortality 51% during fu</td>
</tr>
<tr>
<td></td>
<td>74 / NA / 68 yrs</td>
<td>CAD 48%, ESRD 42%</td>
<td>infrapopliteal PTA</td>
<td>100 %</td>
<td>Major amputation NA, mortality 6%</td>
<td>24 months (mean)</td>
<td>Limb salvage 82% at 1 yr, mortality 35% during fu</td>
</tr>
<tr>
<td>Schneider, 2001</td>
<td>110 / M67, F43 / 69 yrs (weighted mean)</td>
<td>CAD 43%, ESRD 69% (weighted mean)</td>
<td>Revascularisation using either fem-distal bypass, combined SFA PTA and distal bypass grafting or short distal bypass graft</td>
<td>100 %</td>
<td>NA</td>
<td>23 months (mean)</td>
<td>Limb salvage 89%, patency 78% at 2 yr, mortality NA (weighted mean)</td>
</tr>
<tr>
<td>Faglia, 2002</td>
<td>221 / NA / NA</td>
<td>CAD 55%, ESRD 4%</td>
<td>femorodistal and infrapopliteal PTA</td>
<td>94 %</td>
<td>Major amputation 5%, mortality 0%</td>
<td>12 months (median), range 5-30</td>
<td>Limb salvage NA, mortality 5.3% at 1 yr</td>
</tr>
<tr>
<td>Dorweiler, 2006</td>
<td>46 / M36, F10 / 69 yrs</td>
<td>CAD 46%, ESRD 13%</td>
<td>pedal bypass grafts</td>
<td>100 %</td>
<td>Major amputation 7%, mortality 2%</td>
<td>28 months (median), range 1-70</td>
<td>NA</td>
</tr>
<tr>
<td>Bargellini, 2008</td>
<td>60 / M41, F19 / 69.4 yrs</td>
<td>CAD 42%, CVD 25%</td>
<td>multilevel subintimal PTA in patients unfit for surgery</td>
<td>43 %</td>
<td>Major amputation 5%, mortality 5%</td>
<td>23 months (mean), range 0–48</td>
<td>Limb salvage 93.3%, mortality 10% at 1yr</td>
</tr>
<tr>
<td>Ferraresi, 2009</td>
<td>101 / M85, F16 / 66 yrs</td>
<td>CAD 28%, ESRD 3%</td>
<td>infrapopliteal PTA</td>
<td>100 %</td>
<td>NA</td>
<td>35 months (mean)</td>
<td>Limb salvage 93%, mortality 9% during FU</td>
</tr>
</tbody>
</table>
Management of infection

• Antibiotic therapy
  – necessary for virtually all infected wounds
  – not beneficial for noninfected ulcers
  – insufficient without appropriate wound care
  – Patients with uncontrolled or limb-threatening infections require immediate hospitalization, immobilization and intravenous antibiotics

• **Recommendation:** Surgical intervention for moderate or severe infections is likely to decrease the risk for major amputation. **Level 2c; Grade B**

• Timing of treatment of infection vs. revascularisation

• **Recommendation:** The severity of infection guides the decision whether to debride first or to revascularize first. **Level 2c; Grade C**
Debridement

- Surgical, enzymatic, biological or autolytic methods

  Recommendation: No single method is outstanding in terms of enhancing diabetic ulcer healing. Level 1c; Grade A

- Yet, in selected cases, systemic hyperbaric oxygen therapy may be effective in non-healing long standing ulcers, negative pressure wound therapy may promote healing of postoperative wounds and resection of plantar ulcers may be beneficial

  Recommendation: Hyperbaric oxygen therapy may be indicated for a selected group of diabetic ulcers but it is not clear which patients are likely to benefit and what is the optimal duration. Level 1b; Grade A

  Recommendation: Negative pressure wound therapy appears to be as effective and under certain circumstances more effective than other available local wound treatments in patients without significant infection. Level 1a; Grade A

- Recommendation: Foot surgery to offload pressure areas may be beneficial to prevent ulcer recurrence after revascularization for neuroischemic diabetic foot ulcer. Level 4; Grade 5
Minor amputation and removal of necrotic tissue

- **Recommendation:** Toe, ray and trans-metatarsal amputations are preferred whenever possible as they enable broader distribution of weight during ambulation. **Level 4; Grade 5**

- **Recommendation:** Bedridden patients, poor ambulation that is not worsened by amputation, life expectancy less than one year, and non-revascularizable leg are causes to perform major amputation, even above the knee when necessary. **Level 4; Grade D**
Outcomes

- **Wound healing**
  - Revascularizations improve ulcer healing
    - number of ulcers, severity of PAD, congestive heart failure and renal function impairment were associated with poor ulcer healing
- Completeness of revascularization seems important
- Complete tissue healing after revascularization very slow
- **Leg salvage**
  - Leg salvage rates around 80% at one year and around 70% at three years after revascularisations
- **Risk for major amputation**
  - occlusion of all three crural arteries
  - ESRD
  - wound infection
  - multiple ulcers
  - oedema
  - non-compliance to the treatment
Mortality

- Perioperative mortality below 5%
- Mortality 10-20% at one and 40-50% at five years after open surgery, whereas long term data are missing in endovascular series

**Recommendation:** Co-morbidities especially renal failure and impaired ambulatory status at presentation are major factors for poor outcome in diabetics with ischemic ulcers. These co-morbidities should be taken into consideration when and when not to revascularize. **Level 2a; Grade B**
**Multidisciplinary team approach**

- Diabetic foot ulcers need to be treated in a systematic way by a multidisciplinary team.
- Vascular surgeon should be a part of this team:
  - Urgent need to include vascular diagnostics and intervention as an integrated part of the strategy to achieve ulcer healing and to avoid major amputation.
  - Otherwise the window of opportunity could be easily missed.
- Up to 85% of the amputations may be prevented by a multidisciplinary approach.
Summary

- Urgent need for a paradigm shift in diabetic foot care, i.e. a new approach and classification of diabetics with impaired perfusion with regard to clinical practice and research
- This change will considerably increase the need of distal revascularizations for diabetic foot ulcers in near future