Limb Salvage in CLI

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Critical Limb Ischemia (CLI)?

- Chronic (more than 2 weeks) ischemic rest pain,
- May have ulcers or gangrene attributable to objectively proven arterial occlusive disease.
- Distinguished from acute limb ischemia

1~3% of all PAD
# Classification of PAD

<table>
<thead>
<tr>
<th>Fontaine</th>
<th>Rutherford</th>
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</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic (ABI&lt;0.9)</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
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<tr>
<td>IIb</td>
<td>Moderate to severe claudication</td>
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<tr>
<td>III</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or Gangrene</td>
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</table>

**Critical Limb Ischemia (CLI)**
Major causes of PAD

1. Atherosclerosis is the leading cause of PAD in patients >40 years old.

2. Other causes include
   1) Thrombosis
   2) Embolism
   3) Vasculitis
   4) Fibromuscular dysplasia
   5) Entrapment
   6) Cystic adventitial disease
   7) Trauma
Overlap of Atherosclerotic Disease

Coronary Artery Disease 40%
Cerebrovascular Disease 15%
Peripheral Arterial Disease 16%

38% overlap of 2 vascular beds

Patients with one manifestation often have coexistent disease in other vascular beds

Co-prevalence of coronary artery disease and carotid disease

• $1/3 \sim 2/3$ with PAD; evidence of CAD
• $12 \sim 25\%$ with PAD; significant carotid artery stenosis

Conversely

• $1/3$ for men and $1/4$ for women with known coronary or cerebrovascular disease; evidence of PAD
Clinical Outcomes of Patients With Critical Limb Ischemia who Undergo Routine Coronary Angiography and Subsequent Percutaneous Coronary Intervention

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ABSTRACT: Background. Critical limb ischemia (CLI) is associated with a high risk of cardiovascular ischemic events. We assessed the strategy of routine coronary angiography and subsequent coronary revascularization, if clinically indicated, in patients with CLI who underwent percutaneous transluminal angioplasty (PTA). Methods. Of a total 286 consecutive CLI patients treated by PTA, 252 patients who underwent coronary angiography before or after PTA were enrolled. Coronary artery disease (CAD) was defined as angiographic stenosis ≥ 50% and significant CAD as ≥ 70% stenosis. Results. Of the 252 patients with CLI who underwent coronary angiography, a total of 167 patients [66.3%] had CAD and 85 patients [33.7%] did not have CAD. Patients in the CAD group were older, had a higher prevalence of diabetes and cerebrovascular disease, and had a lower mean ejection fraction. In the CAD group, of the 145 patients with significant CAD, percutaneous coronary intervention (PCI) was performed in 114 patients [78.6%]. At 1 year, the CAD and non-CAD groups had no statistically significant differences in mortality [7.1% vs 4.7%; P=.45], myocardial infarction [1.1% vs 0%; P=.31], and PCI [4.7% vs 1.1%; P=.31]. These outcomes were similar after the adjustment of baseline confounders. At 1 year, the CAD and non-CAD groups had similar rates of repeat PTA [16.7% vs 17.6%; P=.86], target lesion revascularization [13.7% vs 14.1%; P=.94], and amputation [19.1% vs 16.4%; P=.60]. Conclusion. A strategy of routine coronary angiography and coronary revascularization may be a reasonable treatment option for these patients who have high risk for severe CAD. A randomized trial is needed to determine if this is the preferred strategy for CLI patients.

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KEY WORDS: critical limb ischemia, coronary artery disease

Lee MS, Rha SW et al. JIC 2015
Comparison of Diabetic and Non-Diabetic Patients Undergoing Endovascular Revascularization for Peripheral Arterial Disease

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ABSTRACT: Objective. Peripheral arterial disease (PAD) is associated with poor outcomes. We assessed the clinical outcomes of diabetic versus non-diabetic patients with PAD who underwent peripheral transluminal angioplasty (PTA). Methods. The outcomes of 239 consecutive patients with symptomatic PAD who underwent PTA were analyzed. Restenosis and clinical outcomes were assessed at a follow-up of 2 years. Results. Diabetic patients had a higher percentage of wound as the initial diagnosis for PTA [72.7% vs 14.2%; P<.001], chronic kidney disease [26.7% vs 6.3%; P<.01], need for dialysis [19.3% vs 3.1%; P<.01], and coronary artery disease [67.6% vs 50.7%; P=.02]. Infrapopliteal PTA was more commonly performed in the diabetic group [70.4% vs 25.3%; P<.001]. Diabetic patients had lower rates of angiographic follow-up at 8 months [38.6% vs 60.3%; P<.01]. Diabetic patients had higher binary restenosis [54.4% vs 31.5%; P=.02] and had a trend toward a higher incidence of total occlusion [34.0% vs 19.5%; P=.08]. At 2-year follow-up, the amputation rate was higher in the diabetic group [24.4% vs 1.5%; P<.001] despite PTA. Conclusion. Diabetic patients more frequently presented with critical limb ischemia compared with non-diabetic patients and had higher rates of restenosis and amputation at 2 years following standard PTA. Improved therapies are needed for this high-risk group of patients.

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KEY WORDS: amputation, critical limb ischemia, peripheral transluminal angioplasty, PTA

Lee MS, Rha SW et al. JIC 2015
Cardiovascular Intervention Research Institute

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   4) Broadcasting Information

President
Seung-Woon Rha, MD., PhD.,
FACC, FAHA, FSCAI, FESC, FAPSIC.
Research Coordinators/Associates
Risk Factors of PAD

- Smoking
- Hypertension
- DM
- Hyperlipidemia
- Age
Relative effect of risk factors on the development of CLI

Risk of Developing CLI

Diabetic
X4

Smoker
X3

Lipid Abnormalities
Triglyceride
X2

Age
>65
X2

ABPI
<0.7
X2
<0.5
X2.5
Algorithm for evaluating in whom peripheral arterial disease (PAD) is suspected. From N Eng J Med. With permission of the Massachusetts Medical Society. Copyright 2001. All rights reserved.
KUGH Diagnostic Processing

1. Routine coronary work-up
   ; 2D Echo, Coronary Angiography/CT

2. Pre-intervention Studies
   1) ABI
   2) CT Angiography (No CRI)
   3) Duplex Sono or CO₂ Angiography (CRI)
   4) MR Angiography (For Osteomyelitis)
   5) TcPO₂, Thermography (Wounded Patients)
   6) Wound culture; Bacteriology

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Effect of percutaneous transluminal angioplasty on tissue oxygenation in ischemic diabetic feet

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ABSTRACT

Percutaneous transluminal angioplasty (PTA) has been performed as an alternative to bypass surgery for improving tissue oxygenation in ischemic diabetic feet because the former is less invasive than the latter. The purpose of this study was to evaluate the effect of PTA on tissue oxygenation in ischemic diabetic feet. This study included 29 ischemic diabetic feet, as determined by a transcutaneous oxygen pressure (TcPO₂) < 30 mmHg. The PTA was carried out in 29 limbs. The PTA procedure was considered successful, acceptable, and failed when residual stenosis was < 30%, between 30 and 50%, and > 50%, respectively. For evaluation of tissue oxygenation, the foot TcPO₂ was measured before PTA and weekly for 6 weeks after PTA. Immediately after PTA, 26 feet were evaluated as being successful and the remaining three as acceptable. Before PTA, the average foot TcPO₂ was 12.7 ± 8.9 mmHg. The TcPO₂ values were increased to 43.6 ± 24.1, 51.0 ± 22.6, 58.3 ± 23.0, 61.3 ± 24.2, 59.0 ± 22.2, and 53.8 ± 21.0 mmHg 1, 2, 3, 4, 5, and 6 weeks after PTA, respectively (p < 0.01). The PTA procedure significantly increases tissue oxygenation in ischemic diabetic feet. The maximal level of tissue oxygenation was measured on the fourth week following PTA.
Max Tissue Oxygenation Level was at 4th week after the PTA in 2010

Figure 3. Sequential values of TcPO₂. The statistical significance between each week was evaluated (*p < 0.05, **p < 0.01). All treated feet (29 feet) were assessed at each time point. The pins at each time point represent 1 SD. Every TcPO₂ value measured after PTA represented a statistically significant improvement when compared with the baseline value.
Comparison of perfusion values after percutaneous transluminal angioplasty according to the severity of ischaemia in the diabetic foot.

Percutaneous transluminal angioplasty (PTA) is now more frequently used to improve tissue perfusion in ischemic diabetic feet. However, there are concerns about its feasibility and effectiveness in severely ischaemic feet. This study aimed to compare the perfusion values after PTA according to the ischaemic degree of diabetic feet.

This study included 133 ischaemic diabetic feet. The foot transcutaneous oxygen pressure (TcPO$_2$) and toe pressure were measured before the procedure and every second postoperative week for 6 weeks. The patients were divided into three groups according to ischaemic severity on the basis of TcPO$_2$ and toe pressures. In the "severely ischaemic" group, the TcPO$_2$ increased from 7.5 ± 4.9 to 40.3 ± 11.3 mm Hg (5.4-fold) 6 weeks after the PTA (P < 0.001). The toe pressure increased from 8.5 ± 8.8 to 42.2 ± 19.3 mm Hg (5.0-fold, P < 0.001). In the "mild" group, the TcPO$_2$ increased from 35.4 ± 2.5 to 41.8 ± 12.4 mm Hg (1.2-fold, P = 0.003), and the toe pressure increased from 45.7 ± 12.3 to 54.3 ± 31.3 mm Hg (1.2-fold, P > 0.05). Results of the "intermediate" group were in between.

The most severely ischaemic group had the most dramatic increase of tissue perfusion after PTA. As such, PTA can be an effective method for increasing tissue perfusion even in the severely ischaemic diabetic feet.

Treatment Goals for the Patient with PAD

Clinical Treatment Goals

- Improve Functional Status
- Preserve the Limb
- Prevent Progression of Atherosclerosis
- Reduce Cardiovascular Morbidity and Mortality

- Improve Symptoms
- Improve Quality of Life
- Improve Exercise Capacity
- Decrease Need for Revascularization

- Reduce Nonfatal Events, such as MI and Stroke
Treatment of PAD

• Two major goals
  - Limb outcomes
    ; walking ability↑, CLI progression & amputation↓
  - Cardiovascular outcomes

• Treatment modalities
  - Asymptomatic
  - Non-lifestyle-disabling claudication
  - Lifestyle-disabling claudication
  - Rest pain
  - Ischemic ulcers
  - Gangrene

Revascularization
Treatment of the patient with critical limb ischemia

- CLI confirmed
  - Candidate for revascularization
    - Imaging (Duplex, angiography, MRA, CTA)
      - Revascularization as appropriate
  - Not candidate for revascularization
    - Not-tolerable pain, spreading infection
      - Amputation
    - Stable pain and lesion
      - Medical treatment (non-operative)
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Benefit on Treadmill/QoL</th>
<th>Limitations</th>
<th>PAD Cohort Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>100% / Improved</td>
<td>Availability</td>
<td>50%-85%</td>
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<td></td>
<td></td>
<td>Motivation</td>
<td></td>
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<tr>
<td>Cilostazol</td>
<td>50% / Improved</td>
<td>CHF</td>
<td>50%-85%</td>
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<td>Medication AEs</td>
<td></td>
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<tr>
<td>Angioplasty</td>
<td>Improvement</td>
<td>Proximal</td>
<td>10%-15%</td>
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<td></td>
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<td>arteries best</td>
<td></td>
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<tr>
<td>Surgery</td>
<td>150% / Improved</td>
<td>Graft failure</td>
<td>&lt; 5%</td>
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<tr>
<td></td>
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<td>Morbidity, mortality</td>
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</table>
KUGH Multi-disciplinary Approach for CLI

- Risk factor modification and antiplatelet therapy
  - Decrease risk of CV event and improve survival (EC, NE, CA)

- Claudication medical therapy
  - Supervised Exercise program (RH)
  - Pharmacological therapy

- Treatment of critical limb ischemia
  - Pain control (Ane, Pain Clinic)
  - Pharmacotherapy, Infection Control (CA, ID)
  - Management of ulcers (PS)
  - Revascularization (CA, IC, VS, CS)
  - Amputation (OS)
Risk Factors modification

- Smoking cessation; Counseling and adjunctive drug therapy with the nicotine patch, bupropion, or varenicline increase smoking cessation rates and reduce recidivism.
- LDL-C < 70mg/dL (high intensity statins)
- HbA1c < 6.5%
- BP < 140/90 mmHg (ACEI, beta blocker)
- BP < 130/80 mmHg if diabetic or renal dz
- Antiplatelet therapy (Aspirin, Clopidogrel, Cilostazol)
Role of Cilostazol in PAD

1. Inhibition of thrombus formation
   - ↓ Platelet aggregation

2. Blood flow improvement
   - ↑ Vasodilation (High femoral artery selectivity)
   - ↑ RBC deformability

3. Vascular normalization
   - Endothelium protection, Antiproliferation on VSMC, Promote Angiogenesis

4. Lipid metabolism improvement
   - ↓ TG  ↑ HDL
   - ↓ ApoB  ↓ RLP  ↑ DHA

Vasoprotective Beyond Platelet Inhibition!!

1. HDL: High Density Lipoprotein
2. ApoB: Apolipoprotein B
3. RLP: Remnant Lipoprotein
4. DHA: Docosa hexaenoic acid
5. RBC: Red Blood Cell
6. VSMC: Vascular Smooth Muscle Cell
7. TG: Triglyceride
Pharmacotherapy for CLI

- **Prostanoids**
  - prevent platelet and leukocyte activation and protect the vascular endothelium,

- **Vasodilator** – no value

- **Antiplatelet drugs**
  - No evidence that these drugs would improve outcomes but reduce the risk of systemic vascular events.

- **Anticoagulants** – no value

- **Vasoactive drugs** – no effect
Management of ulcers

- Restoration of perfusion
  - optimal treatment
- Local ulcer care and pressure relief
  - off loading, removing necrotic/fibrotic tissue from the ulcer, keeping a moist environment and prevent infection
- Treatment of infection
  - agressive systemic antibiotics is needed
- Salvage procedures
- Diabetes control and treatment of co-morbidity
- Local drug/cell therapy
Natural History of Atherosclerotic Lower Extremity PAD Syndromes

PAD Population (50 Years and Older)

Initial clinical presentation

- Asymptomatic PAD 40%
- Atypical leg pain 50%
- Claudication 10%
- Critical limb ischemia 1%~2%
Outcomes of CLI

Critical limb ischemia
1% - 2%

1-year outcomes

- Alive with two limbs: 50%
- Amputation: 25%
- CV Mortality: 25%
Peripheral Arterial Disease (PAD) Mortality*

*Kaplan-Meier survival curves based on mortality from all causes.
†Large-vessel PAD.
KUGH Multi-disciplinary Approach for CLI; Summary and Conclusion

- Risk factor modification and antiplatelet therapy
  - Decrease risk of CV event and improve survival (EC, NE, CA)
- Claudication medical therapy
  - Supervised Exercise program (RH)
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