Claudication Due To Aorto-Iliac Disease: Supervised Exercise Is As Effective As Stenting
The CLEVER RCT Results

Are you ready to deliver “claudication best practices” to your patients?

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Conflict of Interest Disclosure
(Relationships with Industry)

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Consultant: Bayer; Merck; Novartis

The Functional Risk: Claudication

The $4.3 Billion Dollar Question:
Why not use an invasive stent approach for most individuals with PAD and claudication?

After all, stent technology is improving, atherectomy can open the lumen without deploying metal that would impair later bypass, and drug coated balloons have improved one year patency rates.

Let’s Think About the Leg

• The leg is a complex end organ
• There is no relationship between ankle perfusion (ABI) or anatomic PAD severity and claudication symptoms: None
• The scientific evidence base for symptom improvement (benefit > risk) is ranked:
  Exercise > cilostazol > endovascular > open surgery

The Evaluation of Exercise Performance in Patients with Peripheral Vascular Disease

20 subjects with PAD and claudication; mean age 62, graded symptom limited treadmill exercise tests


Mechanisms by Which Exercise Improves Claudication

The CLEVER Trial: “Claudication Endoluminal Revascularization vs Exercise”

Informed Consent ABI, Th-BI Duplex ETT #1 ETT #2 Pedometer Review Cilostazol Rx

Screening Visit 1 Randomization PTA Endpoint Assessment Visits End of Study Visit

Subjects w/ PAD & claudication: Men & women > 50 yrs Resting ABI < 0.90 Aorto-iliac dz by non-invasive criteria

Angioplasty/stent (n = 84) Supervised Exercise (n = 84) Cilostazol Rx, limb evaluation visits

Month 6 & 18 ETT QOL visits OMC (n = 42) ST + OMC (n = 46)

OMC + SE (n = 42)

Supervised Exercise (n = 84)

Angioplasty/stent (n = 84)

Change in ABI at 6 mo. Change in ABI at 18 mo.

Subcutaneous QOL, MAPE health economics, Risk factors

OMC, SE, ST

Crossover Rates:
None at six months

Cilostazol Compliance:
>90% in all treatment groups

Exercise Compliance:
71%

Technical Success of Stenting:
All ST patients successfully stented
Pre-procedure mean lesion length 3.9±3.4 cm
Mean stenosis 83±19%; post-procedure stenosis 5±8%
ABI 0.66±0.2 at baseline, improved by 0.29±0.33

Primary Endpoint: Peak Walking Time (PWT) on a graded treadmill test (Gardner protocol)

Secondary Endpoints:
Claudication Onset Time (COT)
Community-based walking by pedometer
Quality of Life (QOL) by WIQ, PAQ, SF-12
Atherosclerosis biomarkers

Primary Endpoint Assessed at Six (6) Months
Eighteen (18) months long-term follow-up pending

Primary Endpoint Assessed at Six (6) Months

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OMC</th>
<th>SE + OMC</th>
<th>ST + OMC</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Primary Endpoint</td>
<td></td>
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<tr>
<td>Peak Walking Time (PWT) (minutes)</td>
<td>5.3±2.5</td>
<td>5.3±2.3</td>
<td>5.3±2.0</td>
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<tr>
<td>Claudication Onset Time (COT) (minutes)</td>
<td>1.7±0.7</td>
<td>1.6±0.9</td>
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<td>Community-based Walking Hourly Free-Living Steps</td>
<td>363±41</td>
<td>364±16</td>
<td>295±186</td>
<td>0.693</td>
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Primary Endpoint: Peak Walking Time

Change from Baseline to Six (6) Months

<table>
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<tr>
<th>Group</th>
<th>Mean Change (minutes)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>OMC vs. Exercise</td>
<td>3.8</td>
<td>&lt;0.001</td>
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<tr>
<td>ST vs. Exercise</td>
<td>3.7</td>
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<tr>
<td>OMC vs. ST</td>
<td>0.1</td>
<td>0.59</td>
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</table>

Baseline Performance Characteristics

These patients have severe claudication:
A bit more than 1.5 minutes of pain-free walking and less than 5.5 minutes of maximal treadmill walking

Treatment Strategies

Optimal Medical Care (OMC):
- Cilostazol 100 mg bid as tolerated, written and oral advice about exercise and diet, with monthly coordinator contact

Supervised Exercise (SE):
- OMC plus 78 sessions of supervised exercise, 3x/wk, for 1 hr sessions

Stenting (ST):
- OMC plus stent revascularization of aortoiliac PAD

11/17/2015
Walking Impairment Questionnaire

“Superior” WIQ QOL scores, in the absence of real measured benefit and in the absence of a sham stenting procedure group, are by definition, a placebo effect.

<table>
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<tr>
<th>SE vs. OMC</th>
<th>P Value</th>
<th>SE vs. ST</th>
<th>P Value</th>
<th>ST vs. SE</th>
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<td>0.25</td>
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PAD exercise rehabilitation is durable, safe, & cost-effective

Cost-Effectiveness of Supervised Exercise, Stenting, and Optimal Medical Care for Claudication: Results From the Claudication Exercise Versus Endovascular Revascularization (CLEVER) Trial

Supervised Exercise, Stent Revascularization, or Medical Therapy for Claudication Due to Aortoiliac Peripheral Artery Disease
J Am Coll Cardiol 2015; 65:999–1009

CLEVER Outcomes: Durability and Cost Effectiveness


PAD Exercise Rehabilitation in “M Health”: Setting a New Standard

Goal: Every primary care and vascular clinician will recognize and treat claudication. This is not a disease that could ever be cured by stents alone ...

Enter the EPIC order
Patient is called by rehab services
The closest PAD rehab site to each patient is selected
Efficacy and barriers to efficacy are charted & solved. No excuses

PAD rehabilitation is real in Minnesota
Wellness and Exercise for Life (WEL) program

Patients prefer non-invasive care
It is effective.
It costs < $48 / month

University of Minnesota Medical School-Riverside
Health

Fairview Ridges Hospital (Teresa Fietek and others)

Fairview Southdale Hospital

Mercy Hospital (Dennis Argento and others)

And at Fairview Lakes (Wyoming), Fairview Northland (Princeton); and United and Methodist Hospitals ...
... and is thus available everywhere!
A Brighter Day for Individuals with PAD

Thank You!