Lipid Lowering Therapy in Patients with Peripheral Artery Disease

J. Pitha
Contents:

• The role of dyslipidemia in PAD
• The type of dyslipidemia in PAD
• Treatment of dyslipidemia in PAD
• Evidence of the effectiveness of treatment of dyslipidemia in PAD
• Summary
Main risk factors for CVD

**NON-MANAGEABLE**

1) AGE
2) MALE GENDER
3) GENETICS

**MANAGEABLE**

1) SMOKING
2) DYSLIPIDEMIA
3) HYPERTENSION
4) DIABETES M.
Smoking

Hypertension

Dyslipidemia

Diabetes mellitus/Insulin resistance
Smoking

Hypertension

Dyslipidemia

Diabetes mellitus/
Insulin resistance
MORTALITY OVER A PERIOD OF 10 YEARS IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE


Figure 1. Kaplan–Meier Survival Curves Based on Mortality from All Causes among Normal Subjects and Subjects with Symptomatic or Asymptomatic Large-Vessel Peripheral Arterial Disease (LV-PAD).

Remnant removal disease

Human Apolipoprotein E

ApoE3
- Arg-158
- Asp-154
- Arg-150

ApoE2
- Cys-158
- Asp-154
- Arg-150
ApoE2/2 effect

ApoE 2/2
ApoE2/2 effect

Menopause, obesity, hypothyroidism, diabetes mellitus …
Remnant removal disease

- Cholesterol 8-26 mmol/L
- Triglycerides 5-15 mmol/L

- Frequency 1:50-60 000 (?)

- Often affects arteries of the lower limbs
BMI: 35 kg\(\cdot\)m\(^{-2}\)
Waist – 115 cm
SBP – 140 mm Hg
Chol – 6,2 mmol/L
TAG – 2,1 mmol/L
HDL - 1,08 mmol/L
LDL – 3,8 mmol/L
Prevalence of atherosclerotic plaques in female population

- n=341 (70%)
- n=110 (22%)
- n=18 (4%)
- n=17 (4%)
Femoral x carotid arteries

RLP-C (mmol/L)

p<0.01

FEM                   CAR
Femoral x carotid arteries

RLP-C (mmol/L)

SMOKERS

n=13

n=6

p<0.03
Peripheral artery disease

Remnant lipoproteins
- Triglycerides
- HDL cholesterol

Smoking
Poorly controlled diabetes mellitus
Dysbetalipoproteinaemia
Management of dyslipidemia

• **Lifestyle modification**

• **Pharmacotherapy**

• **LDL/Lp(a) apheresis**

• **Transplantation (liver)**

• **Genetic therapy**
## LIFESTYLE INTERVENTION

<table>
<thead>
<tr>
<th></th>
<th>PHYSICAL ACTIVITY, IDEAL WEIGHT, IDEAL WAIST</th>
<th>LESS of SATURATED FATS IN THE DIET</th>
<th>LESS of SIMPLE SUGARS AND MORE VEGETABLES IN THE DIET</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL (LDL) CHOLESTEROL</td>
<td>+</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>TRIGLYCERIDES</td>
<td>++++</td>
<td>+</td>
<td>++++</td>
</tr>
<tr>
<td>HDL CHOLESTEROL</td>
<td>++++</td>
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</table>
## EFFECT OF HYPOLIPEMERIC DRUGS

<table>
<thead>
<tr>
<th></th>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
<th>Compliance</th>
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<tbody>
<tr>
<td><strong>BILE ACID SEQUESTRANTS</strong></td>
<td>decrease 15–30%</td>
<td>increase 3–5%</td>
<td>neutral</td>
<td>bad</td>
</tr>
<tr>
<td><strong>NICOTINIC ACID</strong></td>
<td>decrease 25%</td>
<td>increase 15–30%</td>
<td>decrease 20–50%</td>
<td>acceptable</td>
</tr>
<tr>
<td><strong>FIBRATES</strong></td>
<td>decrease 5–15%</td>
<td>increase 20%</td>
<td>decrease 20–50%</td>
<td>fine</td>
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<tr>
<td><strong>STATINS</strong></td>
<td>decrease 25–50%</td>
<td>increase 4–12%</td>
<td>decrease 14–29%</td>
<td>fine</td>
</tr>
<tr>
<td><strong>EZETIMIBE</strong></td>
<td>decrease 18%</td>
<td>increase 1%</td>
<td>decrease 8%</td>
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Effects of Colestipol-Niacin Therapy on Human Femoral Atherosclerosis

David H. Blankenhorn, MD; Stanley P. Azen, PhD; Donald W. Crawford, MD; Sharon A. Nessim, DrPH; Miguel E. Sanmarco, MD; Robert H. Selzer, MS; Anne M. Shircore, BS; and Emily C. Wickham, MS

**Figure 2.** Bar graphs of percent distribution of progressors, nonchangers, and regressors by treatment. Solid bars represent drug and diet group (experimental), and striped bars represent placebo and diet group (control). Numbers above bars indicate number of patients. See text for definitions of regressors, progressors, and nonchangers. Top right panel is similar to left panel for patients with baseline total cholesterol of 240 mg/dl or less. Bottom right panel is similar to left panel for patients with baseline total cholesterol of more than 240 mg/dl.
STATINS IN PERIPHERAL ARTERY DISEASE

REDUCTION OF CARDIOVASCULAR EVENTS:

MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo controlled trial. 
**Lancet 2002, 360(9326):7-22.**
6,748 participants PAD; 5-year-follow-up, significant 19% relative and a 6.3% absolute reduction in major cardiovascular events

IMPROVEMENT IN CLAUDICATIONS (50-163 m)

Pedersen TR, Kjekshus J, Pyorala K, et al. 
Effect of simvastatin on ischemic signs and symptoms in the Scandinavian simvastatin survival study (4S). 
**Am J Cardiol 1998, 81(3):333-335.**
## EFFECT OF HYPOLIPEMIC DRUGS

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TREATMENT OF DYSLIPIDEMIA IN PAD

- IMPROVES SURVIVAL (CVD)
- IMPROVES QUALITY OF LIFE
- REDUCES CLAUDICATION
Treatment goals in patients with PAD:

- LDL cholesterol less than 1.5-1.8 mmol/L
- HDL more than 1.1 mmol/L (men) 1.3 mmol/L (women)
- Triglycerides less than 2.0 mmol/L
- Non-smoking status
- Physical activity more than 15 minutes daily
- BMI less than 25 kg/m², waist circumference less than 94 cm (men), 80 cm (women)
- Blood pressure 130-140/80-85 mm Hg
Thank you for your attention

My Doctor said "Only 1 glass of alcohol a day". I can live with that.