When and Why Should Vascular Surgeons Prescribe Maximal Dose Statins?

What Is the Dose?
What Are the Risks?

When your patient has atherosclerotic vascular disease

Statins and Vascular Disease

Observations
- Statins reduce cholesterol/LDL-C
- Cholesterol reduction associated with fewer CV events and improved survival

However...
- Statins show benefit out of proportion to reduction of cholesterol, and...
- Statins show early procedure related benefit...
...therefore mechanisms other than cholesterol reduction are operative (Pleiotropic Effects!!)

Pleiotrophic Effects

Anti-Inflammatory
- Cellular
- Fluid phase (biomarkers)

Anti-Thrombotic
- Reduced tissue-factor expression
- Clotting factors (V, VII, VIII)
- Increased thrombomodulin expression
- Increased protein-C

Heart Protection Study

Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions

Simvastatin 40mg/day vs placebo
Endpoints: MI, coronary death, stroke, revascularization

J Vasc Surg 2007;45:645-54
**Statins For PAD Patients**

**Heart Protection Study**

*N = 6,748*

- **Results** -

<table>
<thead>
<tr>
<th>Event at 5 years</th>
<th>Placebo</th>
<th>Statin</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Event</td>
<td>32.8%</td>
<td>25.6%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Major Revas.</td>
<td>17.5%</td>
<td>13.0%</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

**Statins and Vascular Disease**

**Non-Cardiac Vascular Surgery**

**Statins**

**DECREASE III Trial**

Fluvastatin and Perioperative Events in Patients Undergoing Vascular Surgery

- Study drug started 37 days (mean) preop
- Patients:
  - 250 – Fluvastatin
  - 247 – Placebo

**Results**

- Perioperative Myocardial Ischemia
  - Fluvastatin vs. Placebo: *p* = 0.01

- Perioperative Death from Cardiovascular Causes or Nonfatal Myocardial Infarction
  - Fluvastatin vs. Placebo: *p* = 0.03
Patients undergoing infrainguinal bypass to treat atherosclerotic vascular disease are underprescribed cardioprotective medications: Effect on graft patency, limb salvage, and mortality.

- Retrospective study
- 293 patients
- 338 infrainguinal bypasses
- 75% for CLI

John Hopkins Study
10 Year Review
Results

- 67% reduction in stroke
- 80% reduction in death
- 40% reduction in MI
- 33% reduction in LOS

How to Dose?

Maximal Dose Statin!
**Statins and Vascular Disease**

**Current Guidelines**

**2014 ACC/AHA**

**2013 ACC/AHA Blood Cholesterol Guide**

**Statin Therapy for ASCVD Prevention**

- Clinical ASCVD
- Primary LDL-C ≥ 190 mg/dL
- 40 – 75 years with diabetes and LDL-C ≥ 70 mg/dL
- 40 – 75 years, LDL-C ≥ 70 mg/dL and 10 years ASCVD risk ≥ 7.5%

**What are the risks?**

**Statins and Vascular Disease**

**Vascular Surgeons Prescribing Maximal Dose Statins**

- **What is the dose?**
  - Simvastatin: 40mg (Unless already on 80mg)
  - Atorvastatin: 80mg
  - Rosuvastatin: 40mg

**What is the dose?**

- **Increased GSM score – p=0.024** (Plaque Stability)
- **HDLC**

**Statins and Vascular Disease**

**Current Guidelines**

**2014 ACC/AHA**

**Circulation 2014; 129(S2):S1-S45**

**Statins and Vascular Disease**

**What are the risks?**

**Statins and Vascular Disease**

**Vascular Surgeons Prescribing Maximal Dose Statins**

- **What is the dose?**
  - Simvastatin: 40mg (Unless already on 80mg)
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**Increased GSM score – p=0.024** (Plaque Stability)

**HDLC**
Statins are effective cholesterol-lowering drugs that reduce the risk of cardiovascular disease events (heart attacks, strokes, and the need for arterial revascularisation). Adverse effects from some statins on muscles, such as myopathy and rhabdomyolysis, are rare at standard doses, and on the basis of low-hitting levels of transaminases, are minimal. Hypothyroidism—muscle pain or weakness with blood creatine kinase levels more than ten times the upper limit of the normal range—occurs in fewer than one in 10000 patients on standard statin doses. However, this risk tapers between statins, and increases with use of higher doses and interacting drugs. Rhabdomyolysis is a rare and more severe form of myopathy, with asymptomatic holding the transaminase output and risk of renal failure. Stepping statins are rare events that usually lead to a full recovery. Asymptomatic increase in transaminase levels of liver transaminases are recorded with all statins, but are usually associated with an increased risk of liver disease. For most people, statins are safe and well-tolerated, and their widespread use has the potential to have a major effect on the global burden of cardiovascular disease.

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

Nielson SF & Nordestgaard BG Lancet Diabetes Endocrinol 2014; 2:894-900

Funding: Herlev Hospital, Copenhagen University Hospital

Statin use before diabetes diagnosis and risk of microvascular disease: a nationwide nested matched study

Statin use amplifies the risk of diabetic retinopathy, diabetic neuropathy, diabetic nephropathy and gangrene of the foot in individuals in the general population with diabetes.
Randomly selected 15,679 individuals who used statins regularly before their diagnosis of diabetes

Matched with 47,037 individuals (1:3) who never used statins before diagnosis of diabetes

215,725 person years of follow-up

Results

Cumulative Incidence: DIABETIC NEPHROPATHY

p=0.37

Cumulative Incidence: GANGRENE OF THE FOOT

p=0.099

Cumulative Incidence: DIABETIC RETINOPATHY

p<0.0001

Cumulative Incidence: DIABETIC NEUROPATHY

p<0.0001

Conclusions

Maximal dose statins indicated for all patients with vascular disease (AHA/ACC guidelines)

Physicians caring for patients with vascular disease should comply with guidelines

Benefits of statins far outweigh their side effects and risk of accelerated diabetes.