**Management of Patients With Peripheral Artery Disease**

(Compilation of 2005 and 2011 ACCF/AHA Guideline Recommendations)

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

2011 New Recommendation CLASS IIb:
The combination of aspirin and clopidogrel may be considered to reduce the risk of cardiovascular events in patients with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or CLI, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia. (Level of Evidence: B)

2011 Updated Recommendation CLASS I:
Clopidogrel (75 mg per day) is recommended as a safe and effective alternative antiplatelet therapy to aspirin to reduce the risk of MI, ischemic stroke, or vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or CLI, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia and who are not at increased risk of bleeding and who are high perceived cardiovascular risk. (Level of Evidence: B)

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**Network meta-analysis**

- **Indirect evidence obtained across RCTs**
- **Direct evidence obtained within RCTs**
- **Combine direct and indirect evidence**

Li et al. BMC Medicine 2011, 9:79

**Composite endpoint analysis**

Composite endpoint of Vascular deaths, non-fatal MI, non-fatal stroke
22-32% relative risk reduction

Major lower limb amputations above ankle
37% relative risk reduction


Direct frequentist analysis of >7,600 cases
CHARISMA, CASPAR & MIRROR studies
Mostly post revascularization
32% relative risk reduction


**Statin**

1. Cholesterol lowering & pleiotropic effects in plaque stabilization and vascular protection
2. Significant reduction of cardiovascular (CV) death, myocardial infarction (MI) and stroke in coronary patients
3. Significant reduction of all-cause mortality, cardiovascular and cerebrovascular events in PAD patients
4. Class I recommendation (Level of Evidence: A)

2005 and 2011 ACCF/AHA Guideline Recommendations
Katsanos K et al. Cardiovasc Intervent Radiol 2014
Antoniou GA et al. Vascular Pharmacology 2014

- PubMed (MEDLINE), EMBASE, AMED, and Scopus) in August 2015
- PRISMA selection process (COCHRANE)
- Statin users versus non-users
- Endpoint: Major amputations pooled on the log hazard scale (logHR)
- Random effects model (DerSimonian-Laird)

**Included studies**

- 18 clinical trials (6 randomized/propensity-matched trials, 6 multivariate and 6 univariate)
- 141,781 patients (34,952 following endovascular or surgical revascularization)
- RCTs: Atorvastatin, simvastatin, lovastatin, mixed
- CLI patients: range, 2-100%

**Methods**

- PubMed (MEDLINE), EMBASE, AMED, and Scopus) in August 2015
- PRISMA selection process (COCHRANE)
- Statin users versus non-users
- Endpoint: Major amputations pooled on the log hazard scale (logHR)
- Random effects model (DerSimonian-Laird)
Original random effects point estimate (95%CI): 0.74 (0.62-0.89)
Adjusted random effects point estimate (95%CI): 0.80 (0.60-0.95)

Aspirin + Clopidogrel prevent major amputations in PAD patients following revascularization (32% relative risk reduction)

Statins prevent major amputations in PAD patients for both primary and secondary prevention (20-26% relative risk reduction)

No significant confounders (effect modifiers) were identified