Statins Have a Dose-dependent Effect on Amputation Risk and Survival in Peripheral Arterial Disease (PAD) Patients

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Introduction: Statin dose guidelines for PAD patients are based on coronary artery disease and stroke data. The aim of our study was to determine the effect of statin dose (based on 2013 ACC/AHA guidelines) on PAD outcomes of amputation and mortality. Methods: Patients with PAD in the Veterans Affairs database were identified from 2003-2014. The exposure was highest statin dose usage (none, low-moderate and high intensity) around diagnosis of PAD (within 1 year). The outcomes were risk of incident amputation (below knee or above knee) and mortality at 1, 3 and 5 years. The effect of statin dose on the two outcomes was also analyzed using Cox proportional hazards modeling to adjust for covariates. **Results:** In 208,275 patients with PAD [Males: 98.1%; Mean age: 67.4 yrs (SD 9.9)], 17,643 amputations and 99,951 deaths occurred in a median follow up of 5.2 years. Almost a quarter (27.7%) of patients were not on a statin while 30.4% were on simvastatin 80 mg (no longer recommended due to drug toxicity). The risk of incident amputation declined significantly at the high intensity statin dose as seen in Table 1. In Cox models adjusting for age, gender, race, comorbidities, cholesterol levels and creatinine, the high intensity statins were associated with lower amputation risk and mortality as compared to no statin [HR 0.67; 95% CI (0.63, 0.72) and HR 0.71; 95% CI (0.68, 0.73), respectively]. Low-moderate-dose statins also had significant but smaller reductions in risk of amputation and mortality [HR amputation 0.78 (0.75, 0.82), HR death 0.78 (0.77, 0.80)]. **Conclusion:** This is one of the largest population based studies to examine the effect of statins on long-term PAD outcomes and the first to explore the dose-dependent effect of statins on amputation and mortality. High intensity statins are associated with a significant reduction in limb loss and mortality in PAD patients followed by a smaller risk reduction by low-moderate intensity statins as compared to no statin therapy.

Table 1. Association of Statin Intensity Dose with Peripheral Arterial Disease (PAD) Outcomes: Amputation risk and Mortality at 1, 3 and 5 years						
Statin Intensity Dose	Amputation Risk			Mortality		
	1-year	3-year	5-year	1-year	3-year	5-year
No	4.97%	7.03%	8.33%	8.92%	22.83%	33.85%
Low-Moderate	4.06%	5.84%	6.93%	5.91%	18.13%	29.02%
High	4.41%	5.82%	6.43%	5.58%	14.51%	20.20%
p-value (chi square)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

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