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EDITORIAL COMMENT

PAD Is No Longer Related to Rodney

The Benefit of Statins*

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When Jacob Cohen was born in Babylon, New York, in 1921, few would have expected that his pleas for "respect" would have resulted in a long and successful career in comedy as Rodney Dangerfield. However, those who have been managing atherosclerotic syndromes for decades appreciate that until recently, peripheral artery disease (PAD) patients may have been referred to as victims of "Dangerfield's syndrome." Little research was focused on the role of medical interventions for PAD until recently, and PAD rarely received attention in the scientific literature compared to patients with other atherosclerotic syndromes. Identification and aggressive medical therapy for

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patients with PAD have lagged behind their counterparts with coronary artery disease (CAD). Data on the role of "standard" medical therapy for PAD patients, including the use of antiplatelet therapy and statins, have been woefully inadequate compared with data on patients with CAD (1).

Despite the recommendations of experts, the routine use of statins in patients with PAD is far less common than among patients with CAD (2). The benefits of statin therapy in PAD have been suspected for decades. In 1 series of 1,374 patients with PAD followed for a mean of 6.4 years, all-cause and cardiac-related mortality rates were lower in the patients on higher statin doses with resultant lower low-density lipoprotein (LDL) levels (3). The Heart Protection Study advanced our understanding of the intensity of statin therapy by evaluating >20,000 patients with or without known PAD (4). In this series, the relative reduction in the first peripheral vascular event was 16%, regardless of the entry level LDL cholesterol.

In the paper by Westin et al. (5) in this issue of the *Journal*, the current real-world management of the most severe manifestations of PAD is highlighted. All of the patients had, by definition, critical limb ischemia (CLI). Disappointingly, only 65% were receiving statins. Not only did the patients on statins have lower LDL cholesterol levels and have fewer major adverse cardiovascular events and death, but interestingly, these patients also had improved amputation-free survival and more durable results if treated with endovascular therapy for infrapopliteal occlusive disease.

There have been studies suggesting an improvement in physical function in patients with intermittent claudication treated with statins (6–9). A Cochrane review reported by pooling all the published series that 6-min walk and pain-free walking distances actually improved among those PAD patients treated with statins (10). However, the mechanism(s) whereby statins may actually improve arterial outcomes in PAD remain uncertain. In a small series of 68 patients with PAD treated with statins with or without ezetimibe, despite an impressive reduction in LDL cholesterol and improvement in the ankle-brachial index, there was no improvement in calf muscle perfusion or physical functioning (11).

It is exciting to learn through this retrospective, single-center propensity analysis that aggressive statin therapy may not only reduce myocardial infarction, stroke, and death, but may actually improve limb survival in the most advanced PAD patients. As the authors mention, the major limitation of widespread adoption of statins in CLI is the lack of data on the duration of statin therapy and compliance of patients on the medications. This certainly provides motivation for a prospective analysis of patients with all manifestations of PAD, including those with ischemic rest pain and nonhealing ischemic ulcerations, treated with statin therapy to aggressively low LDL cholesterol levels and include imaging of treated arterial segments. If the data of such a protocol mirrored those of Westin et al., the power of statin therapy would be raised to a level equal to that of patients treated for CAD, leaving only Mr. Cohen as the disrespected one.

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