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INVITED COMMENTARY

# Statins and Postoperative Renal Function

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Nowadays statins are a cornerstone in perioperative and long-term cardiovascular risk reduction in vascular surgery patients. As has been strongly advocated by the recent European Society of Cardiology guidelines for perioperative management statins should be prescribed to virtually all patients undergoing vascular surgery.[1] This recommendation has subsequently been reinforced by the results of the DECREASE III trial.[2] The results of this placebo-controlled randomized trial showed a two-fold reduction in perioperative cardiac complications in patients on statins. Though not powered for subgroup analyses there seemed to be no significant difference of effect in open or endovascular treated patients.

The study by Moulakakis focusses on a different, less well understood, potential beneficial effect of statins in vascular surgery patients.[3] In this retrospective study patients on statins experienced a significantly lower rate of renal function deterioration compared to patients not on statins when undergoing endovascular abdominal aneurysm repair requiring suprarenal fixation.

Data on the potential renal protective effect of statins in patients undergoing EVAR are scarce. However in open vascular surgery large cohort studies have found similar results. Welten et al. studied 1944 patients undergoing open vascular surgery.[4] In this population acute kidney injury, defined as >10% decrease in creatinine clearance, occurred in 664 (34%) patients within 2 days after surgery. Of the 664 patients with acute kidney injury, 313 patients (47%) had a complete recovery of kidney function at day 3 after surgery. Interestingly, in this study statin use was not associated with prevention of kidney injury. However, if kidney injury occurred, patients on statins were 2-fold more likely to have a complete recovery in kidney function within 3 days after surgery compared to those not on statins. In another study only patients with suprarenal aortic cross-clamping were included.[5] Seventy-seven patients with normal preoperative renal function requiring suprarenal aortic cross clamping were studied. Creatinine levels were obtained before surgery and on days 1, 2, 3, 7, and 30 after surgery. An analysis-of-variance model for repeated measurements was applied to compare creatinine levels between statin users and nonusers, with adjustment for clamping time and blood loss. Postoperative creatinine levels during the 30 days after surgery were significantly lower in statin users than in nonusers. Postoperative hemodialysis was required (temporarily) in 7 patients (9.1%), all statin nonusers. The mechanism of this beneficial effect of statins in open vascular surgery remains speculative due to the multifactorial causes of postoperative kidney function impairment. As already stated by Moulakakis there are several so-called "pleiotropic" effects of statins that might be relevant for postoperative kidney injury prevention such as improved endothelial function, modulated inflammatory response, decreased oxidative stress, and maintenance of plaque stability. These effects have been found in animal studies but are more difficult to assess in the clinical setting.

As stipulated by Moulakakis et al. renal dysfunction in EVAR may also be induced by the potential nephrotoxicity of the relatively high dose of administered contrast medium during endovascular procedures. In a large cohort study by Khanal et al. 29,409 patients undergoing

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a percutaneous coronary intervention both baseline preprocedure and peak postprocedure serum creatinine was measured.[6] When compared with patients who did not receive preprocedure statins, patients on preprocedure statins had a lower incidence of contrast induced nephropathy (4.4 vs. 5.9%, $P < 0.0001$) and nephropathy requiring dialysis (0.3 vs. 0.5, $P = 0.03$). However, in a recent randomized trial by Toso et al. of 304 patients with impaired preprocedural renal function short-term, i.e. 2 days pre to 2 days post-intervention, atorvastatin 80 mg on top of intravenous saline hydration and oral N-acetylcysteine 1200 mg 2 times/day did not result in a decrease in contrast-induced nephropathy.[7] These results were a confirmation of the PROMISS trial which also showed no beneficial effect of short term simvastatin 40 mg administration for the prevention of contrast induced nephropathy.[8] However, it should be noted that the patient population of the Moulakakis trial was substantially different in terms of timing of statin therapy, dosing of statins and preprocedural renal function.

The mechanism of a possible kidney protective effect of statins remains speculative. In daily clinical practice this should not hamper the liberal use of statins in patients presenting for abdominal aortic aneurysm repair. Even if the level of evidence for the use of statins for the prevention of kidney injury is weak, the overwhelming beneficial effect of perioperative and long-term statin use for cardiovascular risk reduction makes statin use imperative in this patient population. Therefore the question whether statins also have renoprotective effects will remain speculative as placebo-controlled trials will not be ethically justifiable in this patient population. Studies on statins and renoprotective effects in AAA patients should focus on the question whether type of statins, dosing of statins and timing of statin therapy initiation are of importance for the prevention of kidney injury in patients undergoing vascular surgery.

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