

## Drug Protects Against Kidney Injury from Imaging Dye in ACS Patients



High doses of a popular cholesterol-lowering drug significantly reduced the rate of acute kidney injury caused by dye used in imaging in acute coronary syndrome patients who underwent a coronary procedure, according to research presented today at the American College of Cardiology's 62nd Annual Scientific Session. This group of patients is at high risk for kidney damage related to contrast agents used in imaging tests.

Previous studies have demonstrated the kidney-protective value of various statins administered before patients undergo angioplasty. Rosuvastatin was chosen for this phase IV study because inflammation is involved in development of both acute coronary syndrome and kidney injury, and the drug has anti-inflammatory properties and reported clinical benefits in preventing events that can harm the heart. U.S. and European guidelines recommend statins for all acute coronary syndrome patients, regardless of cholesterol levels, within one to four days after admission.

A total of 504 patients were randomly assigned to the statin or control group. None of the patients had taken statins before; all were slated for diagnostic angiographic imaging with intent to perform angioplasty, had iodixanol injected for imaging and had non-ST elevation acute coronary syndrome, which carries high risk for heart attack. The statin patients received one 40-mg dose of rosuvastatin as soon as they were admitted to the coronary care unit plus a single 20-mg dose daily until they were discharged, then continued with post-discharge rosuvastatin at 20 mg/day or 10 mg/day, depending on kidney function determined by creatinine clearance. The control group received atorvastatin at 40 mg/day after discharge and no statin before then.

On the primary endpoint — contrast-induced acute kidney injury, defined as a rise in creatinine of at least 0.5 mg/dl or at least 25 percent from baseline within 72 hours — the statin group had significantly better results (6.7 percent vs. 15.1 percent). Rosuvastatin showed comparable benefits with other definitions of kidney injury as well: creatinine increase of at least 0.3 mg/dl from baseline within 48 hours (3.6 vs. 8.7 percent) and within 72 hours (4.4 vs. 10.7 percent).

"The beneficial impact of statin pre-administration was consistent in all subgroups and in particular in patients with kidney dysfunction shown by creatinine clearance less than 60 ml/min, where kidney injury incidence was 8.6 percent compared with 20.9 percent in the control group," said Anna Toso, MD, clinical and interventional cardiologist with the Division of Cardiology, Misericordia e Dolce Hospital, Prato, Italy, and the study's principal investigator.

The number of ACS patients who undergo angiographic procedures is growing and includes a population that's getting more elderly and has more risk factors, she noted.

The statin group also demonstrated superior results for 30-day adverse clinical events of death, dialysis, heart attack, stroke and persistent kidney damage, with cumulative incidence of 3.9 percent compared with 7.9 percent for the control group.

"Our study shows that early administration of high-dose statin has a protective effect against kidney damage due to contrast medium in patients with ACS," Dr. Toso said. "The results help define better the timing of early administration of statins, which should be given as soon as possible after admission and always before the angiographic procedure, to reduce kidney complications and achieve clinical benefits, even before hospital discharge."

This research is part of the larger PRATO-ACS clinical project to explore rosuvastatin's pleiotropic effects — actions other than those for which the drug was developed (in this case, lowering cholesterol) — on a number of targets, including contrast-induced acute kidney injury.

"It would be interesting to compare the effects of lipophilic and hydrophilic statins," Dr. Toso said. "We are now planning the PRATO-ACS 2 project, a head-to-head comparison between high-dose rosuvastatin [hydrophilic] and high-dose atorvastatin [lipophilic] administered on admission to statin-naïve ACS patients scheduled for early invasive strategy."

Researchers say a multicenter study is needed. The PRATO-ACS study was supported by the nonprofit Centro Cardiopatici Toscani. Dr. Toso indicated no conflict of interest to disclose.

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