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LETTERS

The Reply:

We reviewed the letter by O'Connor and Love regarding our article, "Statin Therapy Reduces Contrast-Induced Nephropathy: An Analysis of Contemporary Percutaneous Interventions," published in ***The American Journal of Medicine.***[1] We note their concerns with the article, but respectfully disagree with their conclusions.

The use of the definition of postprocedural ≥0.5 mg serum creatinine increase for contrast-induced nephropathy (CIN) is well accepted in the literature.[2-4] We also have included results with ≥25% increase in serum creatinine for more sensitive analysis. We agree that this increase usually occurs over 48-72 hours. But it has been well documented that patients with significant CIN have this increase within the first 24 hours.[5] Therefore, if anything, our methodology underestimates the incidence of CIN in this population and possibly the effect of the primary treatment, and, therefore, further strengthens the conclusion. It is nearly impossible to tease out other etiologies of renal insufficiency other than CIN in this retrospective analysis in a complex group of patients undergoing percutaneous coronary interventions (PCI). All patients received contrast as a part of their PCI procedure, and prior studies have validated the use of postprocedure serum creatinine as accurate surrogate for CIN.[3]

As we describe in the article, there are significant baseline differences between the 2 large comparison groups. Some of these favor the "prestatin" group (eg, fewer patients undergoing emergent procedures) and others favor the "no prestatin" group (eg, less severe coronary artery disease). Overall, we think the risks are balanced in the 2 groups. However, understanding the limitation of these potential confounders, we performed robust multivariate analyses to adjust for these baseline differences and came to our conclusions. To further account for observed biases we used a propensity score to add to the multivariate model and showed that the results still remained conclusive. Only a randomized controlled trial will be able to eliminate the potential hidden biases.

O'Connor and Love have chosen our analysis to further a debate on propensity analysis. While we note the limitations of propensity analysis in a study like this, we disagree with their application in this situation. Bias by definition is both overt and covert. For the model for propensity of statin use, we have used variables believed to be related to treatment assignment.[6] We avoided candidate variables affected by exposure of interest in order to prevent bias.[7] Our model would suggest that fluoroscopy time, maximal contrast volume exceeded, and intra-aortic balloon pump are multivariately modestly associated with prestatin use. It is quite possible that these procedural variables, being indicators of patient severity, could show some association with administration of prestatins.

We consider that the rule suggested by O'Connor and Love of "means of the propensity scores of the 2 groups being compared must be <1/2 of 1 standard deviation" to use for propensity adjustment is only anecdotal.[8] In opposition to their suggestion that propensity matching would be a preferred choice of analysis, one reviewer to a recent manuscript submission criticized propensity matching when a large proportion of the subjects remain unmatched because of a possible source of residual bias. In our study data set, matching would result in about 7000 (24% of the total) patients unmatched, and various results are possibly contingent on the matching model chosen. We therefore maintain that the use of a propensity score for adjustment in our analysis is still valid and adds to the other statistical methods to adjust for confounders.[7]

Either way, even if we go with the references O'Connor and Love have used to criticize our methodology in the current article, our conclusions are still quite sound. In Table 5 of the original manuscript, model adjustment by propensity of statin use appears to yield models with better discrimination. However, if we follow the argument that propensity adjustment/matching is not necessary when the sample being studied is large and the outcome of interest (CIN) is not rare as in our case, traditional multivariate regression analysis is sufficient in such a situation.[8] In Table 5 of the manuscript, the odds ratio for CIN in patients treated with statins is quite favorable with the various multivariate adjustment models. We therefore stand by our conclusions that pretreatment with statins reduces CIN in patients undergoing PCI.

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References

1. Khanal S, Attallah N, Smith DE, et al. Statin therapy reduces contrast-induced nephropathy: an analysis of contemporary percutaneous interventions. *Am J Med* 2005;118:843-849.
2. McCullough P, Wolyn R, Rocher L, Levine R, O'Neill W. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med* 1997;103:368-375.
3. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;105:2259-2264.
4. Solomon R, Werner C, Mann D, et al. Effects of saline, mannitol, and furosemide to prevent acute decreases in renal function induced by radiocontrast agents. *N Engl J Med* 1994;331:1416-1420.
5. Guitterez NV, Diaz A, Timmis GC, et al. Determinants of serum creatinine trajectory in acute contrast nephropathy. *J Interv Cardiol* 2002;15:349-354.
6. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med* 1998;17:2265-2281.
7. Winkelmayer WC, Kurth T. Propensity scores: help or hype? *Nephhrol Dial Transplant* 2004;19:1671-1673.
8. Braitman LE, Rosenbaum PR. Rare outcomes, common treatments: analytic strategies using propensity scores. *Ann Intern Med* 2002;137:693-695.