Regarding “Aneurysmal iliac arteries do not portend future iliac aneurysm enlargement after endovascular aneurysm repair for abdominal aortic aneurysm”

The article by Kirkwood et al, “Aneurysmal iliac arteries do not portend future iliac aneurysm enlargement after endovascular aneurysm repair for abdominal aortic aneurysm,”1 raises a pertinent question. I believe there are two methodological issues that may affect the study’s validity.

1. The main outcome is “common iliac artery (CIA) dilation ≥ 5 mm.” This event is clearly a time-dependent outcome: the risk of a patient having one of its CIs dilating beyond a certain threshold depends on the time such patient is exposed. In this case, on the follow-up time after aneurysm repair. Although details on subject follow-up time were not reported, by the type of study one may infer that we are dealing with staggered data (patients entering the study at different time-points, thus being followed during uneven lengths of time). This clearly implies that one cannot compare the frequency of this outcome between both groups simply by calculating proportions and testing differences with Fisher exact test, as reported. The use of survival analysis techniques (usually Kaplan–Meier curves, testing for differences with the log-rank test) is mandatory. Reporting a similar mean follow-up time between both groups of exposure does not justify using a methodology appropriate for time-independent outcomes. Other outcomes (secondary interventions and aneurysm-related mortality) were rightfully analyzed.

2. The objective was stated as “...examine the fate of aneurysmal iliac arteries during endovascular aneurysm repair...” Two groups were defined (with or without baseline iliac aneurysms) and compared. Iliac management was not uniform, although some patients had hypogastric embolization with graft extension to the external iliac artery, while in others, a flared limb extension was used. Furthermore, the frequency of such techniques was significantly different between both groups of exposure (with or without ectatic baseline iliacs), P < .01. When defining two groups for comparison, one should ensure they remain as uniform as possible, except for the variable at stake. Such comparability should be especially checked for variables presumably associated with the studied outcome.

After considering both these issues, I do not think we can easily accept the conclusion “...current techniques for endovascular management of concurrent CIA aneurysms do not predispose to future growth of these vessels” as a valid one. I would much appreciate the authors’ feedback.

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**Reply**

We appreciate the letter by Dr Sampaio and agree that if the study had been run in the manner stated in his letter, then the assertion regarding the statistical analysis would be correct; however, in this trial, each patient in the study came back for evaluations at regularly scheduled time intervals, scheduled after each individual’s aneurysm repair. Since each patient was observed at the same intervals, the comparison performed is appropriate in this case. The mean follow-up was provided not as a justification for the analysis method, but as another element of homogeneity between the groups of interest. To address Dr Sampaio’s second point regarding the nonuniformity of iliac artery management, the authors agree that those patients treated with external iliac extensions could have been removed from the calculations; however, with such a small proportion of patients in the study to whom this would apply, it was felt best to analyze the two groups as a whole.

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Regarding “A meta-analysis of clinical studies of statins for prevention of abdominal aortic aneurysm expansion”

Our previous meta-analysis1 of five studies showed that statin therapy was associated with lower expansion rates in patients with small abdominal aortic aneurysm (AAA) (pooled random-effects standardized mean difference, −0.50; 95% confidence interval [CI], −0.75 to −0.25; P = .0001; P for heterogeneity = .03), which suggests that statins may reduce AAA expansion. The major limitation of our study, however, was that we combined only observational studies. Because the treatment strategy was not based on randomized assignment, our findings were subject to selection bias and confounding. To minimize these biases, Schlosser et al2 and Schouten et al3 used a multivariate linear regression model and provided not unadjusted but adjusted mean differences (MDs) of AAA expansion rates with 95% CIs between statin and control groups. From the other three studies, we were able to abstract only crude means and standard deviations in both groups. In nonrandomized observational studies, it is always necessary to adjust for confounding, otherwise, the results are subject to some degree of bias. We performed herein an updated meta-analysis pooling only adjusted MD of AAA expansion rate between statin and control groups.

We searched literature through April 2011 with the same strategy and inclusion criteria as those of our previous meta-analysis.2,3 Our search identified four risk-adjusted observational studies.2-5 Pooled analysis demonstrated statistically significant lower expansion rate with statin therapy relative to control (pooled random-effects MD, −0.72 mm/y; 95% CI, −1.41 to −0.04 mm/y; P = .04; P for heterogeneity = .03; Table). Despite debates in their Letters to the Editor by Hurks et al6 and Ferguson et al7 regarding our previous meta-analysis,1 we found that, based on a meta-analysis of only risk-adjusted observational studies, statin therapy is associated with less expansion rates in patients with small AAA, which is strengthened by the results of the most recent meta-analysis by Twine and Williams8 of seven observational studies. Nevertheless, hidden bias may remain be-