Response to Letters by Cook and Hessel, and Kramer

Response:

We are not surprised at the comments expressed in the letters by Cook and Kramer. Although it is true that meta-analysis in the past have led to erroneous conclusions, we feel that the results of this study are too promising to ignore. Cook and Kramer identify two recent articles which failed to find benefit with the use of statins for SAH. Although interesting, these studies were not randomized controlled trials (RCT). The article by Kramer and colleagues cannot be deemed conclusive given that the cohorts were different in the before versus after groups including aneurysm size and primary treatment (coiling versus clipping).1 These significant differences in groups are just two of the variables collected. As is the problem with comparing groups without randomization, there may be many other factors which were not collected which account for the different outcomes (ie, ischemic heart disease, diabetes, etc). It is impossible to correct all these factors, even by using advanced statistics, as done in the other article mentioned by both Cook and Kramer by Moscovich and colleagues, who performed a rigorous retrospective study with advanced statistical analysis.2 Although they did find a benefit in patients previously on statin therapy before their SAH, it was not statistically significant. Although this was indeed a very rigorous retrospective study, it still falls short of a RCT for the same reasons.

We agree with some of the points raised in the letter to the editor by Kramer. We agree that in the article by Lynch that what is referred to as “vasospasm” in the article is actually a clinical deficit with confirmation of vasospasm by diagnostic imaging, thus it should have been included in our figure b (see revised Figure 2). This would maintain a significant RR of 0.40 (95% CI: 0.23 to 0.70) for vasospasm-related ischemic clinical deficits. Removing this study from the radiographic vasospasm group would alter the results to a RR of 0.83 (95% CI: 0.60 to 1.14) (Figures 1 to 3). Although the result still favors statin treatment, this result is no longer statistically significant. The more objective, definitive clinical outcomes of clinical deficit and death remain statistically significant.

Kramer suggests comparing the modified Rankin Score (mRS) of 3 to 6 (moderate disability to death). Although we agree that this could also be examined, this was not part of our planned analysis, and the results of Lynch are also not reported for this outcome. I disagree that lumping all the patients together with a mRS score of 3 to 6 is clinically reasonable. Although patients with a score of 3 had a moderate disability, requiring some help, they are able to walk independently which I would argue is a much better outcome than severe disability, chronic vegetative state, or death. Because we are only given the mRS stratified in two groups (1 to 2 versus 3 to 6), I disagree that this is a better assessment than the harder clinical outcome of death. We have updated all three figures below, changing the previous Ogilvy information to that of Chou, who was the first author of the full manuscript.3

We stand by our initial conclusions and continue to encourage the use of Statins for patients with SAH. With good evidence for benefit, and the main down side of their use being a slight increase in costs, there is little reason to withhold this treatment. We agree that given the small size of these studies, that larger studies would strengthen and verify our conclusions. Large well conducted studies will always improve the body of evidence. Furthermore, further studies are required to determine what is the optimal statin, when this therapy should be initiated, and whether certain subgroups benefit greater than others (ie, clipping versus coiling).

Disclosures

None.

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