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Statistical Issues on Evaluating Association Between the Cilioretinal Artery and Age-Related Macular Degeneration

Gui-shuang Ying, PhD

Scheie Eye Institute, Department of Ophthalmology, Perelman School of Medicine, University of Pennsylvania, Philadelphia

To the Editor I read with great interest the article by Snyder et al¹ evaluating association between the cilioretinal artery and age-related macular degeneration (AMD). The article provided interesting results showing that the presence of cilioretinal artery is significantly associated with lower rate of both prevalence and incidence of choroidal neovascularization (CNV) but is not associated with central geographic atrophy. However, after reading the article, there were a few statistical questions for which clarification would be of value, as described here:

1. In Table 3, numbers in last 2 columns (crude odds ratio [OR] and *P* value) would not seem to be consistent with numbers presented as text in the Results section. In text, eyes with a cilioretinal artery were reported to be associated with lower rate of progression to CNV (OR, 0.75; *P* = .05), but in Table 3, it showed OR, 0.83; *P* = .35 for CNV. Similar potential inconsistencies were noted for central geographic atrophy and no late AMD. Should the crude OR and *P* value in Table 3 be 1.28 (95% CI, 1.00–1.64); *P* = .05 for no late AMD; 0.75 (95% CI, 0.56–1.00); *P* = .05 for CNV; and 0.83 (95% CI, 0.56–1.23); *P* = .35 for central geographic atrophy?
2. In Tables 2, 3, and 4, the reported OR (95% CI) are crude (ie, not adjusted by age, sex, and smoking status), but the *P* value was adjusted by these variables. It might be more appropriate to report the adjusted OR (95% CI) so that they are consistent with the *P* value.
3. In the last paragraph of the Results section, the numbers in sentence of “the change of AMD severity score (1.35% vs 1.50%; *P* = .18)” appear to be wrong. Based on Table 4, these percentages are actually the standard deviation. Should the correct sentence be “change of AMD severity score (0.51 vs 0.59; *P* = .18)”?
4. The AMD severity score was correctly analyzed as a continuous measure by using linear regression model. However, the OR was reported in Tables 2, 3, and 4 for this continuous outcome measure. This does not seem correct because OR is only applicable and meaningfully interpretable to the categorical outcome measure. By examining the eTable 2 in the Supplement, it seems the OR for

Corresponding Author: Gui-shuang Ying, PhD, Scheie Eye Institute, Department of Ophthalmology, Perelman School of Medicine, University of Pennsylvania, 3535 Market St, Ste 700, Philadelphia, PA 19104 (gsying@pennmedicine.upenn.edu).

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AMD severity score was calculated by taking natural exponential of the linear regression coefficient from the multivariate linear regression model. The OR calculated this way from linear regression model is not interpretable, because only OR from logistic regression model for the categorical outcome can be meaningfully interpreted. For the AMD severity score outcome, would it be more appropriate to present with the mean difference (95% CI) between eyes with cilioretinal artery and eyes without cilioretinal artery?

I look forward to the responses.

References

1. Snyder K, Yazdanyar A, Mahajan A, Yiu G. Association between the cilioretinal artery and choroidal neovascularization in age-related macular degeneration: a secondary analysis from the age-related eye disease study. *JAMA Ophthalmol.* 2018;136(9):1008–1014.doi:10.1001/jamaophthalmol.2018.2650 [PubMed: 29978186]