Author’s response to reviews

Title: Migraine and Increased Risk of Developing Open Angle Glaucoma: A Population-Based Cohort Study

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Version: 1 Date: 05 Jan 2019

Author’s response to reviews:

January 4th, 2019

Guangde Tu
Editor
BMC Ophthalmology


Dear Editor-in-Chief:

I, along with my coauthors, would like to re-submit the attached manuscript entitled “Migraine and Increased Risk of Developing Open Angle Glaucoma: A Population-Based Cohort Study” as an Original Research article. The manuscript ID is MS No.: BOPH-D-18-00734.
We appreciate the reviewers’ comments on our paper. The manuscript has been carefully rechecked and appropriate changes have been made in accordance with the reviewers’ comments. The responses to the reviewers’ comments have also been prepared. All authors have reviewed and concur with each of the changes made to the manuscript, and to the order their names listed in the authorship.

We hope that the revised manuscript is now suitable for publication in your journal.

I look forward to your reply

Sincerely,
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Editor Comments:

Your manuscript "Migraine and Increased Risk of Developing Open Angle Glaucoma: A Population-Based Cohort Study" (BOPH-D-18-00734) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Ophthalmology.

Their reports, together with any other comments, are below. Please also take a moment to check our website at https://boph.editorialmanager.com/ for any additional comments that were saved as attachments.
In particular, as pointed out by reviewer 1, there is a previous report derived from a same database (Chen, Lin and Kao. Does Migraine Increase the Risk of Glaucoma? A Population-Based Cohort Study. 2016: Medicine Volume 95 (19)), and hence, the reason why the current study was conducted, following the previous study, should be very clearly detailed. Furthermore, the obtained results do not agree. This point is not entirely clear in the current manuscript. This manuscript will be otherwise rejected.

We appreciate the editor’s comment and have revised the manuscript to clarify this point. We have compared the previous report conducted by Chen et al and have pointed out the purpose of the current study and the differences between our current findings and those of the previous study.

(Introduction section, Page 6 )

In a previous report, Chen and colleagues utilized Taiwan’s National Health Insurance Research Database and investigated whether migraine influence the risk of OAG. In their report, the risk of POAG was not significantly higher in the migraine cohort than in the comparison cohort (adjusted hazard ratio [aHR] = 1.15, 95% confidence intervals [CIs] = 0.93–1.42). However, there was a borderline significant trend for increased risk of POAG in young patients (age ≤ 34 years) (aHR = 1.67, 95% CIs = 0.96–2.90) [23]. In one recent study, young migraineurs with no overt cardiovascular disease were found to have increased aortic stiffness and enhanced pressure wave reflection, which may represent one possible mechanism underlying the increased cardiovascular risk in migraine patients [24]. The manner by which migraine poses a risk for OAG in patients of different age groups and comorbidities may differ. To address this question, we conducted the present study using a population-based dataset. The purpose of our study was to investigate the likelihood of OAG development after diagnosis of migraine, by using the age-adjusted Charlson comorbidity index (ACCI) score. We further assessed the hazard ratio for OAG in migraineurs with different degrees of comorbidity.

(Discussion section, Page 13)

Compared to a previous report based on the same database [23], the age and sex distributions in the migrainous and non-migrainous populations was similar. Since the present study applied stricter criteria and selected patients with the same diagnostic code on at least three, rather than one, recorded visits, the frequencies of comorbidities in both the migrainous and non-migrainous groups were less than that reported in the previous study. Nonetheless, the migrainous population had a significantly higher proportion of hypertension, hyperlipidemia, and coronary artery
disease than the non-migrainous population in both our own and the previous study. Both studies demonstrated that the prevalence of DM did not differ between the migrainous and non-migrainous groups.

(Discussion section, Page 14)

The present finding was also similar to those of a previous study that used the same database [23], which found that the incidence of OAG was significantly higher in the migraine cohort than in the non-migrainous cohort (log-rank test, P = .04).

(Discussion section, Page 15,16)

The current finding was similar to that previously reported in a study utilizing the same database: the risk of POAG was not significantly higher in patients with migraine than in non-migrainous controls after adjustment for all relevant confounding factors [23]. In contrast to the previous study, which categorized the patients into different age groups and the presence or absence of comorbidity, we evaluated patients with different ages and different levels of comorbidities simultaneously, and found that migraine was associated with a higher risk of OAG in patients without comorbidities, who were under the age of 50 years.

In the present study, comorbidities may have been under-diagnosed or not well-treated in patients with migraine in this age subgroup, as indicated by subjects with an ACCI score of 0. This finding is similar to a recent study, in which young migraineurs with no overt cardiovascular disease were found to have increased aortic stiffness and enhanced pressure wave reflection, which may represent one possible mechanism underlying the increased cardiovascular risk in migraine patients [24].

Comments from reviewer 1:

Riham Allam (Reviewer 1): The study is a retrospective analysis for the association between migraine and POAG in Taiwan

Analysis:

1. The study question and idea: the idea has been studied before in the same population for both POAG and PACG by Chen et al., 2016 (Chen, Lin and Kao. Does Migraine Increase the
We appreciate the reviewer’s comment and have compared our findings with those of the previous report. We have edited the manuscript according to the editor’s suggestion and have listed the revised sections above.

2. The study design and methodology: a well conducted study regarding data analysis and collection, statistical analysis and data presentation

We appreciate the reviewer’s comments.

Impression:

The study is not novel. A prospective cohort study to see the relation between glaucoma progression and migraine severity would have been of more interest from my point of view

We appreciate the reviewer’s comment and have added this viewpoint as a limitation of the study.

(Discussion section, Page 17 )

The severity of glaucoma and migraine were not indicated in the current database and therefore, the relationship between glaucoma progression and migraine severity could not be investigated. Furthermore, surveillance bias might also have been present, because patients with migraine might be more likely to visit a clinic than would non-migrainous individuals.

Comment from reviewer 2:

Sarah Atkinson (Reviewer 2):

This a well-written and well described paper, there are some minor spelling mistakes which need to be corrected before publication but nothing else of note.
We appreciate the reviewer’s comment and have carefully checked and corrected the spelling throughout the manuscript.

Comment from reviewer 3:

Junyi Chen (Reviewer 3): This study investigated the risk for OAG in migraineurs using a 10-year follow-up study that employed a nationwide population-based dataset in Taiwan. The results showed that migraineurs had a significantly higher cumulative incidence rate than patients in the comparison cohort. The results of this study have certain clinical implications.

We appreciate the reviewer’s comments.