Author's response to reviews

Title: Varicose Veins in Hairdressers and Associated Risk Factors: A Cross-sectional Study

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Author's response to reviews: see over
Dear Editor,

Thank you very much for your offer of the opportunity to revise the manuscript “Varicose Veins in Hairdressers and Associated Risk Factors: A Cross-sectional Study” for your consideration for publication in BMC Public Health. My colleague and I are very excited to have this privilege and appreciate very much the valuable comments and suggestions from the referees.

We have prepared a “Response to Referees’ Comments” to state clearly on a point-by-point basis the changes made in accordance with the comments. In addition, we changed the format of the references according to the Journal’s requirement. We believe that all the comments made by the referees have been addressed and hope that this manuscript is acceptable to you.

If you have any further requests or questions, please do not hesitate to contact me.

Sincerely,

How-Ran Guo, MD, MPH, ScD
Response to Referees’ Comments

Referee 1

Major Compulsory Revision

Comment 1. Since participants with and without VV significantly differed by age, all other comparisons between these two groups should be age adjusted (variables presented in Tables 1 and 2) and after that, variables significantly associated with VV at a level of \( p < 0.1 \), should be included in the multivariate analysis.

Response: As a general practice of data analyses, multivariate analyses are performed according to the results of univariate analyses, and therefore performing univariate analyses without adjustment as shown in Table 1 (for continuous variables) and Table 2 (for categorical variables) at the beginning is appropriate. Table 3 is for age itself, and so there is no need for age adjustment. We agreed with the Referee’s argument that variables significantly associated with VV should be included in the multivariate analyses, and that was exactly what we did. Specifically, we postulated age as an effect modifier and identified it as a potential confounder from Table 1 \((p = 0.032)\), and therefore we used it as a stratification variable for Tables 4 and 5. In addition, we identified “work history” \((p = 0.005)\) and “monthly standing work hours” \((p = 0.008)\) from Table 1 and “family history of VV” \((p = 0.011)\) and “standing housework” \((p = 0.042)\) from Table 2 as variables significantly associated with VV in the univariate analyses. So, we included these variables in the multivariate analyses as shown in Tables 4 and 5. Although we applied a two-tailed significant level of 0.05, no variables in Table 1 or Table 2 were associated with a \( p \) value between 0.05 and 0.10.

Comment 2. Taking into account relatively small number of participants, especially when they are divided into two age subgroups, and consequently imprecise estimate of OR (broad confidence interval), it would be better to perform one multivariate analysis with all participants. Age should be included in the multivariate model.

Response: In this study, we identified age as an effect modifier of VV, which means effects of other risk factors depend on age. Therefore, it is appropriate to perform separate analyses according to age (as we did), so that the effect modification can be identified and demonstrated. While adding age as a variable in the regression model can adjust its effect and thus control for confounding, it cannot demonstrate the effect modification. Besides, as far as statistical power is concerned, the inclusion of a binary variable for age in the regression model, as suggested by the Referee, is similar to separating the population into two subpopulations by age, as we did. In response to the Referee’s comment, we changed the description of the stratified analysis in the
Data Analysis subsection to “we divided the participants into two age groups (≤ 45 years old and > 45 years old) and conducted separate analyses to adjust for the effects of age and demonstrate its effect modification of other risk factors” in the revised manuscript.

Comment 3. In line with the above proposed changes in data analysis, Table 3 should be deleted and Tables 4 and 5 should be replaced by a single one presenting the results for the whole study group.
Response: As explained above, we observed effect modification by age, and Table 3 is to show its modification of the effects of work history. Furthermore, it shows the rationale of setting the cutoff at 45 years old in the further analyses. Therefore, in response to the Referee’s comment, we added the following statement to the last sentence of the third paragraph of the Results in the revised manuscript: “indicating effect modification, and therefore we conducted further stratified analyses by age and use 45 years old as the cut-off.”

Minor Essential Revisions

Comment 1. In the Background section, line 4, from the beginning of the sentence “We conducted a study is to identify...” the word “is” should be deleted.
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

Comment 2. In the Conclusion section, line 1, “…is a major risk factor of developing...” should read “…is a major risk factor for developing...”
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

(Introduction)
Comment 3. The second sentence of the first paragraph should be corrected. Age has been considered not only as “an aggravating factor”, but also as a risk factor for VV.
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

Comment 4. In the first paragraph, line 6, the first part of the sentence “Prolonged standing at work had been suspected as an aggravating...” should read “Prolonged standing at work has been suspected as a risk factor or an aggravating ....” At the end of this sentence additional references should be added.
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

(Method)
(Data collection)
Comment 5. At the end of the second sentence ”Data on demographic....were collected from each participants.” add “by the use of self-administered questionnaire”.
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

(Results)
Comment 6. In the second sentence of the first paragraph “The average age was 45.8 years old...” the words “years old” should be deleted.
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

Comment 7. At the end of the second paragraph, text in bracket “(all with p< 0.05)” should read “(all with p> 0.05).”
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly. [It should be referring to the third paragraph.]

(Discussion)
(Family history of Varicose Veins)
Comment 8. Please, do not repeat the results in detail in the Discussion section.
Response: We thank the Referee for the suggestion and made changes in the revised manuscript accordingly.

Comment 9. On page 9, lines 4-6, the sentence “Some other studies also showed that a family history of VV was a major risk factor [8-11], and a study demonstrated that the risk increased dramatically in relation to the number of morbid parents [12].” should read “Some other studies also showed that a family history of VV was a major risk factor [8-11], and a study conducted by Cornu -Thenard et al. demonstrated that the risk increased dramatically in relation to the number of parents with VV [12].
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.
Comment 10. In this section relatively small number of participants should be mentioned as a study limitation.
Response: We thank the Referee for the suggestion and added the limitation in the revised manuscript accordingly.

Comment 11. In the first line “...a major risk factor of developing...” should be replaced by “...a major risk factor for developing.”
Response: We thank the Referee for the correction and made the change in the revised manuscript accordingly.

Comment 12. When presenting the results of multivariate analysis, OR and 95% confidence interval are sufficient. Do not present numbers of participants.
Response: We thank the Referee for the suggestion, but the number of participants in each stratum was not reported in anywhere else in the manuscript, and therefore we believe the information should be helpful to the readers. Nonetheless, if the Editor also wishes to omit this part of the data, we will agree to delete them.

Referee 2

Major Compulsory Revision

Comment 1. Childbirth numbers should be presented as a categorical rather than a continuous variable.
Response: Besides the fact the difference in the number of childbirth between participants with and without varicose veins did not reach statistical significance, the magnitude of difference was small (2.46 vs. 2.14). Even though it is not well justified, we tried to analyzed the data treating childbirth it as a binary variable (ever vs. never) as suggested by the Referee, and the difference still failed to reach statistical significance.

Comment 2. It seems strange that 25% do no standing housework. Is the average duration of standing housework for all participants or for those who do any standing housework?
Response: It was for those who do any standing housework. In response to the Referee’s comment, we added a footnote “for those who do any standing housework” to Table 1 in the
Comment 3. There is no description of the questionnaire indicting whether this is a validated questionnaire, whether it had been piloted.
Response: The questionnaire had been validated but not used in any pilot studies. In response to the Referee’s comment, we added the following statement to the Data Collection in the revised manuscript: “The questionnaire had been validated before its use.”

Comment 4. The questionnaire apparently did not include inquiries on smoking and alcohol history as other studies of varicose veins risk factors have.
Response: We do have data on smoking and alcohol history. The main reason why we did not include them in the original manuscript was that the vast majority of hairdressers in Taiwan (and thus of our participants) are women, and the prevalence is very low in Taiwanese women for both habits; therefore, they are not likely to have a remarkable impact on our study results. In addition, the scientific evidence on their roles in the etiology of varicose veins was much weaker than the other risk factors we evaluated in the original manuscript. In response to Referee’s comment, we presented the data in Table 2 and added related descriptions to the main text of the revised manuscript. Differences in the prevalence of these two factors between participants with and without varicose veins were small (6.8% vs. 9.7% for smoking and 6.8% vs. 11.2% for drinking), and as expected, neither of the differences reached statistical significance.

Comment 5. Table 3 should be testing whether duration of work history is an independent risk factor separate from age, and it doesn’t.
Response: As explained in the response to Referee 1 (Major Compulsory Revision Comment 3), Table 3 is to show age as modifier of the effects of work history. Therefore, it did test whether duration of work history is an independent risk factor separate from age, as suggested by the Referee. The results showed that work history was a risk factor separate from age and that the effect of work history pended on age—an effect modification by age.

Comment 6. Multivariate logistic regression is stratified as <= 45 y/o (Table 4) and > 45 y/o (Table 5). The rationale for this separation is not clear. For both those <= 45 y/o and those > 45 y/o, the average duration of work history for those with varicose veins is 1.19 that of those without varicose veins. Yes, the prevalence differs for an age-related phenomena [20% in <= 45 y/o; 29% in > 45 y/o], but the real break is at <= 35 y/o. Rather age should have been added as a stratified variable in a single multivariate analysis.
Response: The rationale for separating the population by age at 45 years old was clearly stated in the Data Analysis of the original manuscript as “According to the results of initial analyses, we divided the participants into two age groups (≤ 45 years old and > 45 years old) and conducted separate analyses to adjust for the effects of age.” In response to Referee 1 (Major Compulsory Revision Comment 2), we elaborated this further as “According to the results of initial analyses, we divided the participants into two age groups (≤ 45 years old and > 45 years old) and conducted separate analyses to adjust for the effects of age and demonstrate its effect modification of other risk factors.” in the revised manuscript. In the Work History subsection of Discussion in the original manuscript, we also explained “Aging has been recognized as a major risk factor of VV[2,3,8-10,14,18], but it usually correlates well with the length of work history. In our study, we tried to solve this problem by using stratified analyses according to age. We found the lengths of work history were similar (2 years apart or less) between participants with and without lower limb VV in the two younger age groups (≤35 years and 36-45 years), but the difference was statistically significant in the 46-55 year-old group (a difference of 4.6 years). In the oldest group (≥55 years), while a larger gap (5.4 years) was observed, the difference did not reach statistical significance, most likely due to the larger SE because of the larger age range covered in this group (Table 3). Therefore, in the multivariate analyses, we put the two older groups together and combined the two younger groups.” This part of the original manuscript provides the rationale of setting the cutoff at 45 years old in the further analyses. As shown in Table 3 and the description above, the break was at 45 years old. The main reason for not adding age as a stratified variable in a single multivariate analysis is that we had identified age as an effect modifier, and the effect modification cannot be demonstrated by a single multivariate analysis; we have explained this in the response to Referee 1 (Major Compulsory Revision Comment 2).