Author’s response to reviews

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

Authors:

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

Thank you very much for your offer of the opportunity again 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.

We have prepared a “Response to the Editor’s Requests” to state clearly on a point-by-point basis the changes made in accordance with the comments. We have also check the revised manuscript to make sure that it conforms to the journal style. We believe that all the requests made by the Editor 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
Responses to the Editor’s Requests

1.) Please upload English language versions of all questionnaires developed specifically for use in this study as additional files. If the questionnaires are already available, please supply references and/or links to them.
  Response: We are attaching the file as requested.

2.) Please add the details the questionnaire validation procedure to the Methods section.
  Response: We added the details to the Data Collection subsection of the Methods in the revised manuscript.

3.) Please provide a formal consent statement in the Methods section, stating whether consent to participate was verbal or written.
  Response: We added the statement to the end of the Ethics Statement subsection of the Methods in the revised manuscript.
Response to the Reviewer’s Comments

Reviewer 2

Comment 1. Please insert as Table one a description of the distribution of the subjects with number in each age interval, number with VV, and number without VV to give the reader an overview of the findings. Give age-strata prevalence and whatever other age-stratified information you wish.
Response: The data were in fact available in Table 3 of the original manuscript, but we did not report the age-strata specific prevalence. In response to the reviewer’s comment, we added age-strata specific prevalence to Table 2 of the revised manuscript. We did not add the data to Table as the reviewer suggested because Table 1 is for continuous variables. To accommodate this change, we also changed the percentages in Table 2 from column percentage to row percentages in the revised manuscript.

Comment 2. List items in the same order in the text and in the tables. See Table 1.
Response: We did report the variables in the same order in the text as in Tables but presented variables with and without statistical significance separately. For example, the variables in Table 1 are work history, age, body mass index, monthly standing work hours, number of childbirths, and number of hours doing housework in standing position, and therefore we presented work history, age, and monthly standing work hours (significant variables) first, followed by body mass index, number of childbirths, and number of hours doing housework in standing position (insignificant variables). There are at least two good reasons for doing this instead of reporting the variables in the exact same order as in the table. First, it is generally discouraged to repeat the table contents in the text, and we reorganized them according to statistical significance. Second, putting significant variables ahead of insignificant variable brings the attentions of the readers to significant findings.

Comment 3. Number of pregnancies should be a categorical variable, not a continuous one.
Response: While we agree with the reviewer’s concept that number of childbirths (not pregnancies) should be a categorical variable, we analyzed it as a continuous variable and reported its means and standard errors as many papers did. We also tried analyzing it as a categorical variable, but it did not appear to be a significant predictor, either. Therefore, in response to the reviewer’s comment, we added the following statement to the last sentence of the third paragraph of the Results in the revised manuscript: “We also tried analyzing the number of childbirths as a categorical variable (0, 1, 2, 3, and >3), but it still did not appear to be a significant predictor.”
Comment 4. Why is constipation a variable? Is that current constipation or ever constipation, or what? It is not mentioned in the introduction as an a priori risk factor.
Response: It is “frequent constipation.” While we did not mention it in the Introduction, we mentioned it in the Gender, Body Mass Index, Constipation, Pregnancy, Exercise, Smoking, and Drinking section of the Discussion as “other reported factors included… trauma or injuries to lower limbs [9], constipation [8, 16]…” in response to the reviewer’s comment, we added the item to Introduction in the revised manuscript and change the order of references.

Comment 5. The percentages in the abstract and text about prevalence of doing housework in a standing position should also be in the table. That variable is confusing. Isn’t all housework done standing up? Give the specific wording of the question answered.
Response: Some housework can be done in sitting position, such as ironing, sewing, bookkeeping, feeding children, etc. The question was “Do you need to do housework in standing position after work at home?”

Comment 6. If the number of monthly standing work hours is supposed to be quintiles, the cut at 168 should be higher in Table 4. If the strata were set in Table 5, say so.
Response: The variable was presented as overall quintiles, and therefore the cutoffs did not divide the participants into exact quintiles when the participants were separated as two groups according to their age (Tables 4 and 5).

Comment 7. In Table 5, the difference in number of years working as a hairdresser of 31-42 and 43-57 is no difference, therefore do not emphasize it.
Response: The data were mentioned only once in the Abstract as “…working as a hairdresser for >30 years (for 31-42 years, OR=10.9, 95%CI=1.6-73.8; for ≥43 years, OR=12.0, 95%CI=1.6-88.5)” and twice in the text as “…longer history of working as a hairdresser (31-42 years, OR= 10.9, 95% CI= 1.6-73.8; 43-57 years, OR= 12.0, 95% CI= 1.6-88.5)…” and “…more work years was a significant risk factor in the older age group…”; none of them emphasized a difference between 31-42 vs. 43-57 years, even though there was a difference in the point estimates (OR 10.9 vs. 12.0) and the test for trend was significant. Instead, as shown in the Abstract, we emphasized that “working as a hairdresser for >30 years” (combining 31-42 years and 43-57 years as a whole) as risk factor. In response to the reviewer’s comment, we changed the two statements in the text as “working as a hairdresser for >30 years” and “a long work history (>30 years)” respectively in the revised manuscript.
Comment 8. What are the limiting factors such that the multiple regression analyses include only 121 of the 182 study subjects.
Response: “Monthly standing work hours” is the limiting factor; 135 participants provided their estimates.

Comment 9. It is disturbing that the cases were interview by the physicians who got complete information and the non-cases were interviewed by others who got incomplete information. Along with drinking, the two critical variables – family history and standing hours – have the most missing information. Include that in your discussion.
Response: As stated in the Data Collection section of the original manuscript “For those with lower limb VV, a telephone interview was conducted by the same physician to collect detailed information on the illness....” The non-cases had no such data (information on the illness) to collect because they had no VV (illness) at all. Since the data were not reported in this paper, we deleted the description in response to the reviewer’s comment. As to missing data, we added discussion on this issue to the revised manuscript as suggested by the reviewer.

Comment 10. Why is standing house work both a continuous and a categorical variable?
Response: To see if it is a predictor for VV as a qualitative or a quantitative variable.

Comment 11. The methods section should include a detailed description of the standing housework variable. Table 1 indicates no difference in standing hours per week, yet significant difference in standing hours per month. That sounds like the real difference is the number of days worked per month. If the standing hours per week is 12 and the standing hours per month is 214, then each month must have 17 weeks. Something is not right here. This distinction should become perfectly clear. From a policy point, will one suggest fewer standing work hours per day or fewer work days per month, or what?
Response: We agree with the reviewer’s argument that the real difference is in the quantity, not just a yes/no (qualitative) issue. However, we don’t know it was the number of days worked per month that really mattered. [As explained in the response to Comment 6.] As described in the original manuscript, it was calculated as daily standing work hours multiplied by monthly work days. The working days per month and the number of hours standing at work varied a lot. For example, “168 hours” indicates 7 hours per day for 24 day a month (taking every Sunday and every other Saturday off as the maximum work days allowed by Taiwanese law: 30−4−2=23), and “120 hours” indicates 4 hours per day for 30 days a month (self-employed hairdressers in Taiwan usually don’t take days off except for the Chinese New Year holidays). Hairdressers
have their ways to do the same task. For example, some cut hairs in standing position most of the
time while others do it in sitting position most of the time. In addition, the job contents varied:
the entry-level hairdressers spend a lot of time in washing hairs while senior hairdresser (often
called “stylists”) spend most of the time cutting hairs. Furthermore, some hairdressers had good
business that worked more than 10 hours a day with little time to rest, while some hairdressers
sat in the shops for long hours waiting for customers. There were many combinations of the
number of work days per month and the number of hours standing at work per day, and we did
not have enough participants in each situation for further analyses. In other words, we were
unable to evaluate whether the number of work days per month, the number of hours standing at
work per day, or both really mattered.

In response the reviewer’s comment, we added a description to Materials and Methods as “To
evaluate the effects of prolonged standing at work, we calculated the hours of standing in
working each month as daily standing work hours multiplied by monthly work days. For example,
an employed hairdresser who worked in standing position about 7 hours a day for 24 day a
month (taking every Sunday and every other Saturday off as the maximum work days allowed by
law in Taiwan) had $7 \times (30 - 4 \{\text{Sundays}\} - 2 \{\text{Saturdays}\}) = 168$ hours of standing in working
each month. Likewise, a self-employed hairdresser who worked in standing position about 4
hours a day for almost every day (30 days a month) had $4 \times 30 = 120$ hours of standing in
working each month.” and discussions as “As the working days per month and the number of
hours standing at work varied a lot, the hours of standing in working each month had a wide
large. Hairdressers have different ways to do the same task. For example, some cut hairs in
standing position most of the time while others do it in sitting position most of the time. In
addition, the job contents varied: entry-level hairdressers usually spend a lot of time in washing
hairs while senior hairdresser often spend most of the time cutting hairs. Furthermore, some
hairdressers have good business and work more than 10 hours a day with little time to rest, while
some others sit in the shops for long hours just waiting for customers. Therefore, some
hairdressers worked 24 day a month and spent 7 hours per day on standing work (168 hours per
month), and some others worked almost every day and spent 4 hours per day on standing work
(120 hours). There were many combinations of the number of work days per month and the
number of hours standing at work per day, and we did not have enough participants in each
situation for further analyses. In other words, we were unable to evaluate whether the number of
work days per month, the number of hours standing at work per day, or both really mattered.” to
Discussion in the revised manuscript.

Comment 12. This paper should be publishable after the above issues are dealt with and no
other become apparent.
Response: We hope the reviewer and Editors find our responses satisfactory.
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 at a level of p < 0.1, should be included in the multivariate analysis,” 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, and included them in the multivariate analysis 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
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.

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.]

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.

(Conclusion)
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.

(Tables)
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 revised manuscript.
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).