Reviewer’s report

Title: Clinically-evident tophi are associated with reduced muscle force in the foot and ankle in people with gout: a cross-sectional study

Version: 0 Date: 08 May 2017

Reviewer: Gordon Hendry

Reviewer’s report:

Manuscript number: JFAR-D-17-00043

Thank you to the authors for the opportunity to review this manuscript. The authors should be commended on the concise nature of the manuscript, however in some areas there is a need for further expansion of the arguments presented. I have provided itemised suggestions for major and minor revisions below.

MAJOR SUGGESTED REVISIONS:

Background, lines 34-36. In addition to the sentence on "mechanism responsible", perhaps it would be prudent to add details on how this study is the first step in determining whether or not tophi may play a role? In its current form, this study design is unable to address the hypothesis concerning tophi involvement in the mechanism responsible for muscle weakness.

Discussion, p8, lines 14-19. Need for some caution and expansion of the discussion here. Measurement of pain was same day single-time point with a visual analogue scale. Discrete pain measurements may be a poor indicator of previous pain history over preceding months/years and it is possible that cumulative pain over time may have been the main driver of pain avoidance which may have led to muscle weakness. This needs to be expanded upon with reference to pain measurement literature and other studies of pain and muscle weakness. It seems as though the authors are rejecting the pain-avoidance muscle weakness theory in favour of a theory which seems to suggest that presence of tophi cause muscle weakness by some other mechanism. I would urge more caution as longitudinal studies are required.

Discussion p8, lines 26-29. Greater discussion about the limitations of dynamometry and construct validity relative to dynamic muscle forces during gait are required here.

Discussion, p8, lines 31-36. Is there any evidence for restricted ankle joint sagittal plane RoM in gout in those with tophi? If so, are you suggesting that limitation of ankle RoM with tophi then results in a cascade of events which cause reduced muscle force for inversion, eversion and dorsiflexion?

Discussion p8, line 39. The limitations section needs to be expanded upon. In particular I'd like to see a statement declaring that the study cannot infer causation. Also, perhaps more caution
should be taken not to discount the cumulative role of pain based on a discrete measurement of pain which was used to adjust in the final statistical model.

Discussion, p8, lines 53-56. The authors correctly identify the limitation of dynamometry. However I'd like to see more discussion around the implications of this for the results. For the benefit of the reader, it would make sense to state up front that it is possible that muscle function during gait may not have been affected, unless the authors can provide a strong argument that dynamometry measurements are strongly correlated with muscle function during gait in gout.

Discussion, p9, lines 2-5. The authors declare the lack of blinding. I would like to see this expanded upon with a statement also declaring that this makes the study highly vulnerable to assessor bias.

Discussion, general comment. There seems to be a need for additional discussion about the clinical relevance of muscle weakness observed between groups. The authors focus on the statistical significance but fail to discuss how important the levels of muscle weakness observed may be in terms of function/mobility etc.

Conclusion, p9, line 33. Please change "foot pain" to "current foot pain" here and throughout.

Conclusion, p9, line 41-43. I've remove the 2nd half of the final sentence as this hints that functional measurements of muscle force during gait were altered which was not measured in the present study.

MINOR SUGGESTED REVISIONS:

Background, general comment. There needs to be a paragraph on the potential clinical relevance of this work.

Background, lines 13-14. Inflammation and joint effusion are not symptoms. Perhaps revise to state "contribute to clinical signs and symptoms"

Methods, p5, lines 13-15. Please provide details of the reliability/validity of this method of tophi assessment with a citation.

Methods, p6, lines 10-12. Can you confirm that all the assumptions of your statistical tests were met?

Results, p6, lines 47-48. What was the mean tophus count for participants (i.e. not by foot)?

Results, p6, line 50. For Achilles tendon, how many participants had tophi (i.e. not by tendons)?

Discussion, line 50. Please change to "…at the Achilles tendon may play".
Discussion, p9, lines 12-20. Also, longitudinal studies are required to determine whether or not tophi are involved in the mechanism of muscle weakness in gout.

Table 2. Please check the Diff value for pf force.

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