Reviewer’s report

Title: Autonomic neuropathy in Fabry disease: a prospective study using the Autonomic Symptom Profile and cardiovascular autonomic function tests.

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Reviewer: Carlos Luciano

Reviewer’s report:

In this manuscript, Biegstraaten et.al. present their findings on autonomic symptoms and cardioautonomic testing in 48 and 36 patients, respectively, with proven Fabry disease.. This is an important study that provides additional information about the frequency and types of autonomic symptoms and cardiac autonomic dysfunction in a rare disease that is known to affect small myelinated and unmyelinated fibers but with limited information available. The study is of interest because it uses validated instruments and given the rarity of the disease, shows data from a respectable number of patients. The following are some comments:

1) Major Compulsory Revisions: The authors propose that in view of the low frequency and degree of abnormalities for autonomic symptoms and cardiac autonomic testing, some of the observed autonomic dysfunction may represent end-organ damage and not necessarily autonomic fiber involvement. However, they provide no objective data on this cohort for the presence or absence of abnormal end-organ function and its relation to autonomic symptoms or abnormal autonomic testing. Additional objective data supporting the absence of presence of end-organ dysfunction would be needed to support this argument or it should be modified.

2) Minor Essential Revisions: Since most patients were mildly or moderately affected based on the MSSI, it is possible that autonomic neuropathy is more prevalent in severely affected patients. The question of severity should be addressed by the authors.

3) Discretionary Revisions: It is not clear why the authors only used non-parametric tests for statistical analyses and whether these were always appropriate. Additional information for this choice would be of interest.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests