Reviewer's report

Title: Clinical and molecular genetic risk determinants in adult long QT syndrome type 1 and 2 patients

Version: 1 Date: 28 Oct 2017

Reviewer: Michael Gollob

Reviewer's report:

The authors assert to report the largest cohort of untreated LQTS syndrome patients, and draw conclusions on associated risks for events and risk associated with specific mutations.

The data presented and detail to the analysis is appreciated. However, there are significant limitations to the paper, related to sample size and novelty.

1. For the most part, the large Registry data published by the Rochester LQTS registry is a more comprehensive and robust data set than that presented here. As well, most of those patients can be assumed to have been untreated (not noted in their papers).

2. The associated risk factors noted in the conclusion regarding risk are already well known.

3. Potential novelty comes from describing mutation-specific risks. But what is clear from Table 1 is that these risks are driven by QTc interval. The KCNQ1 D317N mutation carriers have QTc's in the 500 ms range, which would clearly drive their risk based on this already known risk factor. Similarly, the 'low risk' KCNH2 variants have QTc's less than 470 ms, which would be predictive of lower risk. In other words, the trends to events observed by the authors are predicted by the significant differences in the QTc intervals of the specific mutation carriers.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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