Reviewer’s report

Title: Dynamic Predictive Accuracy of Electrocardiographic Biomarkers of Sudden Cardiac Death within a Survival Framework: The Atherosclerosis Risk in Communities (ARIC) study

Version: 0 Date: 25 Jun 2019

Reviewer: Daniel Morin

Reviewer's report:

Abstract: What ECG markers were measured? What does "traditional" mean when discussing ECGs and science?

ROC and AUC are ineffectively stated/abbreviated. Please address.

How can an ECG predict non-SCD? This seems implausible, except that some ECG finding(s) may indicate low risk for SCD, and maybe very weakly something like heart failure, and then by substitution non-SCD is thereby "predicted," but this is a logical fallacy. Recommend removing this claim of association.

The description of reclassification ("18% SCD reclassified up") is unclear.

Background: "… an estimated 356,461" doesn't sound so "estimated."

Methods: Patients with AF (I presume at baseline) were excluded. What happened to patients who developed AF over the period of the study? Were they included?

The adjudication of SCD is confusing. At first there's a committee of 5, then a committee of 11, then in case of disagreement "a third reviewer" is used? This implies that each death was actually reviewed by only 2 reviewers (with a maximum of 3). If this is the case, the size of the committees is irrelevant and should be deleted. How often was a third reviewer required?

Agreement between reviewers is a RESULT, not a METHOD.

Page 10, line 31 says "meat" instead of "beat."

Nearly a page of text is spent to discuss electrode placement, but procedures related to ECG measurements are treated briefly. At least a paragraph or two should have been offered discussing the authors' novel ECG approach to risk assessment. What is GEH and why did the authors suspect that it would work for SCD risk stratification? Why might it work better than other, more established, ECG measurements?

Only HR, QRSd, and QTc were examined as "traditional" metrics. Other more recently examined metrics should be examined as well… e.g., T-peak to T-end (Tpe), or Tpe/QT ratio, or HRV, or HRT...
Lots of statistical tests were performed. Were P values corrected for multiple measurements, in any way (e.g., Bonferroni correction)?

Results: The fact that no ECG measurement predicted SCD within 3 months is the #1 major finding in this examination of the ability of repeatedly measured ECGs to predict SCD. This result belongs front and center, including in the Abstract. It's also important to note that only 11 patients out of the thousands of patients suffered SCD within 3 months of ECG acquisition. This is a very small number, which raises the likelihood of spurious findings.

Some of the AUCs are presented in an odd way: the AUCs are significantly >0.5, but are described in a "positive" way. I realize that this is mathematically equivalent, but readers are used to seeing "good" ROC curves above the 50% line. I recommend constructing all of the ROC curves in the positive.

Discussion: How might these data be used next?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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 recommend additional statistical review

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