Reviewer’s report

Title: Brief episodes of rapid irregular atrial activity (micro-AF) are a risk marker for atrial fibrillation: A prospective cohort study

Version: 1 Date: 23 Dec 2019

Reviewer: Sotirios Nedios

Reviewer's report:

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This is a case-control study evaluating the association of micro-AF (sudden irregular bursts of ≥5 APCs with <30 sec. duration) with undiagnosed silent atrial fibrillation. Out of 3,763 participants of the STROKESTOP II trial in Sweden (75-76 years old, NT-proBNP ≥125 ng/L) with intermittent ECG screening (4x30 sec./d over two weeks) 221 had micro-AF, 196 were followed with continuous ECG monitoring and 26 were finally diagnosed with AF. The micro-AF patients were compared with a control group without micro-AF (n=250), were continuous monitoring detected 7 new AF cases. Thus the authors conclude that micro-AF is associated with higher AF risk (13% vs. 3%, p<0.001). Thus individuals with micro-AF may benefit from extended and early AF screening.

The authors are commended for their elaborate work and the data provided. The manuscript is well written. However, there are several issues that need to be addressed prior to considering publication in the BMC Journal for Cardiovascular Disorders.

Specific comments:

1. Methods/Results: The authors define "micro-AF" as sudden onset irregular bursts of ≥5 APCs with ≤30 sec. duration. Since most participants with micro-AF had an average of only 6 beats (IQR 5-8), this term should not be interpreted as reflecting a higher thromboembolic risk. The study reports a five-fold higher risk for AF related with "micro-AF", but it did not evaluate the increase in thromboembolic risk and the clinical implications for "micro-AF" warrant further studies. Please comment.

2. Methods/Results: Duration between two ECG screenings was zero for the control group. How (based on what criteria) were patients selected to undergo a continuous ECG monitoring?

3. Methods/Results: Participants in the micro-AF group were taller, younger, had lower CHA2DS2-VASc scores and higher often diabetes mellitus than the control group. Additionally, individuals diagnosed with AF were taller compared to individuals free from AF and had longer duration of analyzed signal time during continuous event recording. The authors though use logistic regression with 2 different multivariable models for the development of AF: one adjusting for height & analyzed signal time and one for age, hypertension, heart failure & stroke. Why use two different models? What precluded the use of all variables in one model? Why was there no adjustment for CHADS-VASc score? Was micro-AF the only predictor or AF? Did any other predictors remain significant after adjustment in the model?

4. Methods/Results: What is the predictive value of SVEBs when used as a continuous variable? What is the cut-off value that combines the best sensitivity and specificity? In other words, would
changing the cut-off better predict AF (including control pts.)?

5. **Methods/Results:** What was the average duration of diagnosed AF? How many patients were symptomatic?

6. **Figure 3:** Report p values

7. **Supplementary Table 1:** Report per group

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**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?**
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