Correlating ECG features with symptom burden in patients with atrial fibrillation using Markov modeling

Hamid Ghanbari[1], Kevin Wheelock[1], Kayvan Najarian[2], Jonathan Gryak[2], Brahmajee Nallamothu[1]
[1]Department of Cardiology, University of Michigan, Ann Arbor, MI, USA [2]Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA

Background.
Atrial fibrillation (AF) is the most prevalent major arrhythmia in the US. In many patients, AF is persistent and leads to symptoms that diminish health related quality of life (HRQOL). HRQOL is a comprehensive concept that takes into account symptoms, side effects of treatment, and perceptions about current and future risks of adverse outcomes. Improvements in HRQOL are an important therapeutic goal in patients with persistent AF.

The most common approach to improving HRQOL in persistent AF is controlling heart rate (HR), typically aiming for an average HR of <110 beats per minute at rest based on a 10 second electrocardiogram (ECG). Although this standard is widely accepted, nearly half of patients with persistent AF treated with this strategy are still symptomatic. A potential explanation for this poor treatment efficacy is that focusing on HR alone ignores novel features within the ECG that may further link electrocardiographic data with symptoms and HRQOL.

This question is relevant as long-term ambulatory ECG monitoring becomes more available. Many patients with persistent AF undergo continuous monitoring over an extended period of time using wearable devices. In addition, we have developed a mobile application (MiAfib) which allows patients to track symptoms and emotional state multiple times daily, increasing the data density of clinical outcomes in AF patients. Although these tools allow for more frequent evaluation of patient physiology and HRQOL, the clinical advantages of collecting this massive amount of data is uncertain and exceeds the limits of human capability for interpretation at scale. Machine learning may allow for analysis and interpretation of this data to provide novel insights that improve clinical decision making.

Methods.
In a preliminary study, we recruited 11 patients with persistent AF who underwent continuous ECG monitoring for 30 days. We developed an ECG analysis algorithm using a customized and extended Markov model, the details of which have been described elsewhere. Briefly, we filter the raw ECG signal, discretize it by a sampling frequency of 20Hz, and assign each sample a label based on amplitude. The label sequence is analyzed by the Markov model which then creates different states and learns the probability for transitioning among them. This model can predict development of AF with rapid ventricular rate (RVR), defined as HR >110 BPM, based on the preceding 2 minutes of ECG data. In the current study, we have a cohort of 22 patients with 1226 momentary symptom assessments from the MiAfib app. Additional HRQOL metrics we are obtaining include accelerometer data from the ECG monitor and GPS data from the MiAfib app. We will use our Markov model to classify symptomatic vs asymptomatic episodes using preceding ECG data. Symptoms tracked include shortness of breath, fatigue, chest pain, palpitations, and light-headedness.

Results.
In our preliminary analysis we identified 178 two-minute intervals which preceded development of RVR and 10517 intervals with controlled HRs. We trained the Markov model on 89 intervals preceding RVR and 2000 intervals preceding a controlled HR, then tested it using 89 intervals preceding RVR in the study cohort and 100 intervals of controlled HR obtained from a different patient group (Physionet). We correctly classified 66/89 (74.1%) of RVR-associated intervals as belonging to our study cohort and 90/100 (90%) as belonging to the Physionet cohort. The AUC and F1 scores were 0.92 and 0.88, respectively. Currently, we are using the Markov model on ECG data obtained 2,5, and 10 minutes prior to a symptom assessment from MiAfib app. Of the momentary symptom assessments, 293 are associated with an episode of AF, and 933 another rhythm.

Conclusion.
We have developed a Markov model to analyze signals obtained from continuous ECG monitoring in patients with AF. This model is able to predict development of RVR based on the ECG data preceding the event; in essence it uses a physiologic signal to make predictions about a later physiologic event. Our intention is to now use physiologic signal to predict patient-reported symptoms. Ultimately, our goal is to identify digital biomarkers that maybe used as new targets of therapy in patients with atrial fibrillation. This would dramatically improve on current clinical practice which focuses on controlling HR obtained from a 10-second ECG during a clinic visit and fails to alleviate symptoms in many patients.