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Nestor Gahungu

Afsin Shariar

David Playford

Christopher Judkins

Eli Gabbay

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Transfer Learning Artificial Intelligence for Automated Detection of Atrial Fibrillation in Patients Undergoing Evaluation for Suspected Obstructive Sleep Apnoea: A Feasibility Study.

Nestor Gahungu[a,b], Afsin Shariar[b], David Playford[a], Christopher Judkins[a,c], Eli Gabbay[a,d]

[a] School of Medicine, The University of Notre Dame Australia, 21 Henry St., Fremantle, WA, 6160, Australia

[b] Department of Medicine, Royal Perth Hospital, 197 Wellington Street, Perth, WA 6000

[c] Department of Cardiology, Mount Hospital, 150 Mounts Bay Rd, Perth, WA, 6000, Australia

[d] Chair, Bendat Respiratory Research and Development Fund, SJOG Subiaco, WA, 6008, Australia

Corresponding author

Dr. Nestor Gahungu

The University of Notre Dame, School of Medicine

21 Henry St., Fremantle, Western Australia 6160, Australia

Email: nestor.gahungu@gmail.com

Telephone: +61 8 9433 0228

Fax: +61 8 9433 0250

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Abstract

Background: Individuals with obstructive sleep apnoea (OSA) experience a higher burden of atrial fibrillation (AF) than the general population, and many cases of AF remain undetected. We tested the feasibility of an artificial intelligence (AI) approach to opportunistic detection of AF from single-lead electrocardiograms (ECGs) which are routinely recorded during in-laboratory polysomnographic sleep studies.

Methods: Using transfer learning, an existing ECG AI model was applied to 1839 single-lead ECG traces recorded during in-laboratory sleep studies without any training of the algorithm. Manual review of all traces was performed by two trained clinicians who were blinded to each other's review. Discrepancies between the two investigators were resolved by two cardiologists who were also unaware of each other's scoring. The diagnostic accuracy of the AI algorithm was calculated against the results of the manual ECG review which were considered gold standard.

Results: Manual review identified AF in 144 of the 1839 single-lead ECGs (7.8%). The AI detected all cases of manually confirmed AF (sensitivity = 100%, 95% CI: 97.5 - 100.0). The AI model misclassified many ECGs with artefacts as AF, resulting in a specificity of 76.0 (95% CI: 73.9 - 78.0), and an overall diagnostic accuracy of 77.9% (95% CI: 75.9% - 97.8%).

Conclusion: Transfer learning AI, without additional training, can be successfully applied to disparate ECG signals, with excellent negative predictive values, and can exclude AF among patients undergoing evaluation for suspected OSA. Further signal-specific training is likely to improve the AI's specificity and decrease the need for manual verification.

Key words: Atrial Fibrillation, Machine learning, Artificial Intelligence, Transfer Learning, Obstructive sleep apnoea.

INTRODUCTION

AF is the most common clinically significant cardiac arrhythmia encountered in clinical practice [1]. It is associated with a 5-fold increased risk of stroke, a 3-fold increased risk of heart failure, reduced quality of life and increased mortality [2-5]. Paroxysmal AF (PAF) is often asymptomatic and therefore not diagnosed until the occurrence of thromboembolic complications, such as stroke [6]. AF-related strokes are nearly twice as likely to be fatal as non-AF strokes, and are associated with more severe functional deficits, higher mortality and higher risk of recurrence [7]. Recent studies have shown that up to 20% of patients with AF remain undiagnosed [8, 9]. Of more concern is that half of older individuals with undiagnosed AF are in the high-risk category for stroke [10]. While anticoagulation has been shown to decrease embolic risks in the setting of atrial fibrillation, more than 20% of patients who experience an AF-related stroke have not received guideline-directed preventative anticoagulation therapy due to delayed diagnosis [6]. As such, there has been a growing interest in opportunistic as well as structured screening strategies to improve early detection of AF in high-risk groups to reduce the risk of AF-related complications.

Obstructive sleep apnoea (OSA) has been recognised as an important risk factor for development of AF. Patients with OSA are four times more likely to develop AF compared to the general population and the risk of AF is influenced by the severity of OSA [11]. The burden of both AF and OSA is increasing with an ageing population and increased rates of cardiovascular comorbidities such as obesity, hypertension, metabolic disease, and heart failure [12-14]. The coexistence of AF and OSA represents a significant public health burden due to shared risk factors and associated complications. As with AF, previous studies have shown that OSA is also an independent risk factor for stroke [15-17]. However, it remains unclear to what extent this increased risk is due to undiagnosed AF in patients with OSA.

Currently, there are no established strategies for the detection of AF in patients with confirmed or suspected OSA, beyond what is available to the general population, which also remains under active investigation [18, 19]. Previous studies have shown that PAF is seventeen times more likely to occur during respiratory disturbances than during normal breathing [20], suggesting that the rate of detection of PAF in patients with OSA could be higher during sleep compared to daytime. AF can be “opportunistically” detected in patients undergoing sleep studies using traditional sleep apnoea diagnostic methods with abilities to acquire ECG data. However, the ability to detect AF with this strategy is currently limited by

the lack of automated arrhythmia detection technology, as manual interpretation requires extensive resources and appropriate clinical training.

Artificial Intelligence (AI) is a novel method of ECG analysis that uses machine learning (ML) to detect patterns within electrical waveforms and may potentially be ideally suited for automated application to the ECG component of overnight sleep studies. AI has the potential to improve the early detection of PAF by providing efficiency gains (through automation) and improved accuracy of detection [21]. Recent data have demonstrated great promise in AI being able to classify AF from other cardiac arrhythmias with an accuracy that is superior to that of physicians [22]. Unlike most current AF-detection technologies, which have limited abilities to analyse large datasets, AI-based technologies are robust and are well suited to large amounts of ECG data, including those obtained from Holter monitors, implantable arrhythmia devices. Our study aimed to test the feasibility of utilising transfer learning of a previously trained AI technology, for opportunistic detection of atrial fibrillation from polysomnographic ECG traces.

MATERIALS AND METHODS

Population and data collection

One hundred and ninety patients who underwent an in-laboratory polysomnographic evaluation for suspected obstructive sleep apnoea between 2012 and 2017 were identified from a sleep clinic's database. This included 75 consecutive patients who had a final diagnosis of moderate to severe OSA (Apnoea-hypopnoea index, AHI > 15), 50 consecutive patients with mild or no OSA (AHI <15), and 65 patients with a previously documented history of atrial fibrillation, irrespective of the final OSA diagnosis. Selection of these patients was based on OSA and AF diagnosis only and did not consider the quality of the ECG traces. There were no specific exclusion criteria. For each patient, 7 to 11 single-lead ECG traces were retrieved from the database. This resulted in 1839 single-lead ECG traces that were analysed in the study. Ethical approval was granted through the University of Notre Dame Australia Human Research Ethics Committee (Ref # 019028F) and the study complied with the ethical guidelines of the 1975 Declaration of Helsinki [23].

Training and validation of the AI

The project was conducted within a framework of concurrent training and validation of a flexible ECG waveform analysis AI, which is currently under development. The goal of this

strategy is to develop a model that is capable of being deployed to many different types of ECG signals acquired using differing methodologies, including short term single lead ECG traces ("event" recorders), 12-lead surface ECGs, 24-hour continuous ECG recordings ("holter" monitors), subcutaneous implanted event recorders ("loop" recorders), intracardiac ECGs obtained during electrophysiology studies, and single-lead ECGs from polysomnograms. Prior to the commencement of the current study, the AI model had undergone two levels of training. The first was with >18,000 individual 12-lead ECGs using a single training technique (multilayer convolutional neural network producing a single connected layer). The results of the base AI model 12 lead ECG analysis showed a sensitivity of 95%, specificity of 94%, and a PPV of 92% for the detection of atrial fibrillation (unpublished data). The second level involved transfer learning (a method by which an existing machine learning AI model is applied to a disparate data set) [24], where the AI model was further trained on >700 individual ECGs from implanted loop recorders (these devices generate a single channel ECG signal). This newly trained model was then applied directly (without further training) to the single-lead ECGs recorded during in-laboratory polysomnographic sleep studies for the detection of AF.

Analysis of the ECG traces

All 1839 ECG traces, irrespective of their quality, were individually uploaded as EDF (European Data Format) files to a web Holter system. This system allows the investigator to specifically upload the cardiac component of a full sleep study while eliminating the noise generated by other sleep study parameters. Each uploaded ECG recording was analysed by the rhythm AI model and beat-detection algorithm, which subsequently generated the associated rhythm and beat events.

Following automated AI analysis, each individual ECG trace was manually reviewed by two independent clinicians using the process outlined in figure 1. The first reviewer analysed each individual ECG trace and classified the ECG as either "AF" or "no AF". A second investigator reviewed the same ECG traces who reported the same classifications. Both reviewers were blinded to the diagnosis scored by the sleep scientists and each other but had access to the diagnosis scored by the AI model. The first 500 ECG traces were used to calculate the inter-rater agreement between the two investigators. Discrepancies were adjudicated by a panel comprising of two cardiologists who reviewed the ECG traces independently, blinded to each other's review. The protocol allowed for discrepancies

between the two cardiologists to be resolved in a meeting between the adjudication panel that included a third cardiologist, external to this process. The final diagnosis scored by the manual review process was used as the gold standard against which the performance of the AI model was compared.

Statistical analysis

Cohen's Kappa statistic was used to determine the interobserver correlation coefficients. The diagnostic accuracy of the AI system for the detection of AF was evaluated in all 1839 traces. The analysis of the diagnostic accuracy of the AI algorithm was performed using the method previously described by Šimundić [25] where the manual ECG review by the investigators was considered as gold standard (i.e. true positive; true negative). Using this method, we determined the sensitivity and specificity, and the positive and negative predictive values of the AI algorithm for the detection of AF. The sensitivity was calculated as the percentage of true positives (true positive/(true positive + false negative)) and the specificity as the percentage of true negatives (true negative/(true negative + false positive)). The positive predictive values (PPV) and negative predictive values (NPV) were calculated as the percentages of patients with positive test (PPV = true positive/(true positive + false positive)) and negative results (NPV = true negative/(true negative + false negative)). Where appropriate, MedCalc statistical software for Windows version 18 (MedCalc Software, Belgium) was used for statistical analysis.

RESULTS

ECG analysis by manual review

A total of 190 patients undergoing evaluation for suspected OSA were included in this retrospective study. Each patient contributed 7 to 11 traces, resulting in 1839 single-lead ECG traces. The mean duration of recording of the ECGs was 57.43 ± 9.61 minutes (range: 4 minutes to 60 minutes).

Manual review of the ECGs identified AF in 144 ECG traces (7.8%). There was an excellent agreement between the first and second reviewers (k = 0.97). Disagreements occurred on 10 traces, which were subsequently evaluated by two independent cardiologists, who provided the final diagnosis (Figure 1). There were no disagreements between the two cardiologists that required involvement of a third cardiologist.

ECG analysis by the artificial intelligence

The AI model performed a beat-by-beat analysis of the uploaded ECGs and provided a rhythm diagnosis within seconds. For each segment of the ECG that was analysed, the AI model determined the duration of the detected arrhythmia (or sinus rhythm) and recorded it below the ECG trace (Figure 2). For each ECG trace, we recorded the duration of the longest segment that was detected as AF by the AI model. For example, if a 60-minute ECG trace had 6 segments of AF (30 seconds; 2 minutes; 5 minutes; 10 minutes; 20 minutes; 25 minutes), the duration of the longest segment with AF (i.e., 25 minutes) was recorded.

Of the 1839 single-lead ECGs that were uploaded to the online platform, the AI algorithm detected AF in 551 traces (30%). All ECG traces that were classified as AF by the manual review were accurately detected by the AI algorithm, resulting in a sensitivity of 100% (95% confidence interval [CI]: 97.5 - 100.0). The AI algorithm misclassified 407 ECG traces as AF (table 1), resulting in a specificity of 76.0 (95% CI: 73.9 - 78.0). The misclassification was predominantly due to the presence of artefact, predominantly due to muscle motion (figure 3). Furthermore, many short segments of normal sinus rhythm were also misidentified as AF by the AI algorithm (An example is shown in figure 4). Indeed, of the 407 ECGs that were incorrectly classified as AF by the AI, the majority (73%) were short segments of artefacts or sinus rhythm of less than 30 seconds (table 2). The overall positive predictive value of detected AF by the AI algorithm was 26.1% (95% CI: 24.5 % to 27.8 %).

DISCUSSION

To our knowledge, this is the first study to uniquely examine the feasibility of using transfer learning techniques for application of a novel machine learning AI algorithm for automated detection of AF from ECG traces, recorded during in-laboratory polysomnographic studies. Using a robust method of manual adjudication for AF, the AI model achieved 100% sensitivity but with frequent AF classification of artefact and short-duration sinus rhythm. Since the model was applied directly without specific AI training on a PSG-derived ECG signal, the results confirm two important findings: First, without further training, an ECG AI system can be applied to disparate ECG signals, and Second: An AI-based approach to AF detection during PSG for sleep apnoea is technically feasible. Due to its high NPV, the current AI model would be most suitable as a means for excluding a diagnosis of AF, and AI-detected positive would require manual review. We expect that false positive rates would improve with transfer learning and additional PSG ECG-specific training.

The ability to accurately detect AF from PSG-derived ECG signals using a robust AI algorithm would have major clinical implications. From a logistical point of view, it could be used to highlight possible AF for review, which would improve the workflow in the sleep clinic and reduce the costs associated with manual review of large ECG data. Furthermore, the anticipation, as suggested by recent data, is that AI may be able to classify AF from other arrhythmias with an accuracy that is similar or greater to that of physicians [22]. This would be a great advantage in the sleep clinic where PSG-derived ECGs are interpreted by sleep physiologists whose primary focus is on respiratory scoring. Evidence suggests that the accuracy of AF detection from single-lead ECGs is very low among non-clinical personnel [26]. As such, it would be expected that AI-based ECG review would optimise the detection of AF in the sleep clinic though this would require further prospective studies for confirmation. Such an advancement could have major implications on the overall care of the patient, such as leading to the timely initiation of anticoagulation for stroke prevention.

However, the application of AI in clinical medicine remains challenging. First, the training phases of AI algorithms are limited by the lack of standardised training protocols, and availability of large datasets [27]. In addition, the validation of new AI models is often performed against diagnostic rather than clinical outcomes, and the performance generalisability is limited by overfitting. Because AI models are trained for specific tasks, many such algorithms perform well on datasets that are most closely related to the datasets used in the training phase [28]. Consequently, poor performance is often observed when such algorithms are applied to datasets that are less representative of the training datasets [28]. It is therefore unsurprising that our AI algorithm, which had not been trained on sleep ECGs, had a low specificity for AF detection in this group. Therefore, before any AI model can be applied to clinical practice, it must overcome these limitations [27]. In addition, robust evidence of clinical utility needs to be demonstrated in prospective clinical trials prior to AI's application in routine clinical practice.We also acknowledge several limitations specific to the current study. First, this is a single-centre proof-of-concept study, and whilst our data are promising, larger studies are required to confirm the results. Secondly, an inherent limitation of using single-lead ECG recordings is that the accuracy of AF identification from these recordings is generally only moderate when compared to 12-lead ECGs [29]. This is often due to the confusion created by artefacts, which may be even greater in PSG as ECG recording in this setting is not the primary objective. Our study included all eligible ECGs irrespective of their quality and as such, it is highly likely that artefactual ECGs were major

drivers of the AI's low specificity. This is an important limitation because the AI model used in our study had only been trained to perform a binary classification (AF vs no AF – primarily sinus rhythm). As such, a high prevalence of ECGs with artefacts, other non-AF atrial arrhythmias, sinus pauses, and supraventricular and ventricular ectopics, which are frequently observed in patients with OSA [30-32], potentially contributed to the reduced specificity resulting from a misclassification of these non-AF arrhythmias and artefacts as AF by the AI model. Indeed, artefacts and traces of short-duration sinus rhythm accounted for most AF misclassifications. This could be addressed by performing a PSG ECG signal specific training of the AI model and by introducing new classes for the classifier to include categories for noise/unreadable, as well as specific non-AF cardiac arrhythmias. In addition, the AI model had only been previously trained on 12-lead ECGs and implanted loop recorders, both of which have relatively low artefact compared with the ECGs in the present study.

Finally, the current study utilised the default system probability threshold of 0.5 for AI's binary classification of AF vs no AF. This likely led to a bias towards a high sensitivity and NPV at the expense of specificity and PPV. Future work could analyse the AI's performance for classification of AF across a range of probability thresholds, which may identify the optimal probability threshold setting for this population. This could form basis for future signal specific AI training on PSG-derived ECGs.

In spite of these limitations, the performance of the ECG AI algorithm that has never been trained on this type of data is encouraging, suggesting that AI-based approach to AF identification in a sleep clinic is feasible. This approach is likely to be more robust than existing automated algorithms, which often perform well in training and validation phases but poorly in real-life scenarios. This was previously demonstrated in the REHEARSE-AF trial (Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation) where only 5% of AF detected by the AliveCor automated algorithm were true AF, despite the previously reported specificity above 90% in validation cohorts [9, 33]. The current automated AF-detection algorithms are also only suitable for short ECG strips and cannot be applied to PSG-derived ECG sets [34]. Therefore, AI algorithms offer a better chance of achieving the automation of ECG analysis and arrhythmia detection in the sleep clinic. A further advantage of the AI technology is the iterative ability of the deep learning (utilised by our AI model) to continue learning and thereby improving its processing speed and diagnostic accuracy over time, with and without explicit guidance [35-37]. It is

reasonable to believe that dedicated signal specific training of the AI using polysomnographic ECG datasets would result in significant improvement of the AI's ability to differentiate true AF from sinus rhythm, artefacts, and other cardiac arrhythmias. The clinical utility of the AI algorithm would require further prospective validation.

CONCLUSION

An ECG AI system, trained on completely different types of ECG data and applied to single lead PSG ECG data for the first time, achieved surprisingly good results in detecting AF with excellent negative predictive values. If confirmed in larger studies, this type of system could be used to exclude AF among patients undergoing evaluation for suspected obstructive sleep apnoea. The results suggest it is technically feasible to directly apply an ECG AI algorithm trained using transfer learning to PSG studies. Signal-specific training is required to improve the system's performance for potential clinical utility.

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Figure 1. Flowchart demonstrating the process utilised for manual and automated classification of electrocardiograms.

Figure 2. *Example of a single-lead ECG analysed by the artificial intelligence algorithm. Following an upload of an ECG trace, the AI performs a beat-by-beat analysis of the trace and generates an accurate diagnosis of Atrial fibrillation as demonstrated here. The AI algorithm also determines the duration of each arrhythmia that is detected. The online platform allows for manual review and/or overread (in case of training) by clicking on the forward and backward arrows as shown in the figure.*

Figure 3. Artificial intelligence's Analysis of two ECG traces with artefacts. In the first trace, the AI accurately identifies artefacts on ECG (labelled "A"). In the second ECG trace, the AI algorithm misclassifies artefacts as AF.

Figure 4. Example of a short segment of an ECG in sinus rhythm that was incorrectly identified as AF by the AI algorithm.