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Wearable Devices for Cardiac Arrhythmia Detection- A New Contender?

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Contributions

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Wearable devices are increasingly popular with more than 325 million devices sold in 2016 alone and a projected yearly growth of approximately 18%[1]. Consumer grade devices are rapidly bridging the gap to providing medical grade services, due to progressive improvements in technological capabilities combined with the ability to wirelessly transfer

data for remote analysis. This has culminated in the endorsement, by the Food & Drug Administration (FDA), for several wrist worn consumer smart device platforms (SDPs) for cardiac rhythm analysis, including the latest Apple Watch[2, 3]. The ascension of the 'quantified-self' movement, with continuous acquisition of cardiac physiological data, has potential to be translated into actionable information for the clinician.

Improving cardiovascular health outcomes has recently become a prominent goal for consumer SDP manufacturers. The current generation of SDPs have in-built photoplethysmography, gyroscopes and accelerometers. These can measure heart rate (HR) and encourage physical activity through continuous biofeedback. The miniaturisation and incorporation of photoplethysmography (PPG) facilitates estimation of HR based on pulsatile blood volume changes within the microvasculature. Initial efforts were focussed on developing systems for accurately detecting heart rate in sinus rhythm for the fitness and wellbeing enthusiast. Medical grade PPG systems have demonstrated excellent accuracy in estimating HR in sinus rhythm, with a significant correlation coefficient of 0.96[4]. However, limitations of PPG include the underestimation of heart rate during sinus tachycardia and reduced accuracy during physical activity[4]. Similar to medical grade PPG systems, two early iterations of SDPs with integrated consumer grade PPG, Fit Bit Blaze (Fitbit Inc., San Francisco, USA) and Apple Watch Series 1 (Apple Inc., Cupertino, USA), demonstrated strong agreement with concurrent ECG derived HR in sinus rhythm[5].

Utilizing PPG-based smart watches for detection or chronotropic assessment of arrhythmias, particularly atrial fibrillation (AF), has garnered interest from both clinicians and patients. However, there was only weak to modest agreement during AF with marked HR underestimation when compared to a criterion standard ECG[5]. This is similar to the pulse

deficit identified during manual pulse check in patients with AF. Nevertheless, a HR of ≥ 100 bpm during atrial arrhythmia closely correlated with an ECG HR ≥ 100 bpm and may warrant consideration of clinical review[5]. The demonstrated accuracy is likely to deteriorate further in a real-world setting. Notably, factors such as darker skin pigmentation and ambulation have been shown to impede the accuracy, due to the attenuation of the light wavelength by melanin and a reduction in device to skin contact[6]. While PPG based technology ranks highly for ease-of-use, its technical limitations may limit its use in isolation for prolonged HR assessment.

The incorporation of SDP based automated rhythm analysis systems that acquire single-lead electrocardiograms have overcome many of the limitations faced by PPG technology. Although these FDA-approved devices provide both ECG tracings and a presumptive diagnosis, clinician verification is recommended through various paid subscription models. Automated algorithms have demonstrated excellent accuracy in interpreting single lead ECGs when compared with contemporaneous 12-lead ECG as the reference standard (Table 1). However, between 15% and 33% of the traces were deemed unclassified by the automated algorithm, with baseline artefact being the primary reason for this classification[7, 8]. Clinicians were able to interpret recordings deemed unclassified by the device, with 100% sensitivity and 80% specificity[8]. A hybrid approach that utilised device proffered automated diagnosis in conjunction with clinician over read limited to the unclassified tracings offered excellent diagnostic accuracy (Table 1).

Opportunistic screening for AF is recommended by the European Society of Cardiology guidelines, by conducting a pulse check or by obtaining an ECG rhythm strip in patient ≥ 65 years of age[9]. A randomised control trial using an SDP was conducted in patients ≥ 65

years of age to screen for subclinical AF. The study compared routine care, with participants who acquired weekly single lead ECGs over a 12-month period, overread by an automated algorithm and a cardiologist[10]. Unsurprisingly, more patients were diagnosed with AF in the treatment arm compared with routine care, with a hazard ratio of 3.9 (p=0.007). However, this study raised a number of issues. Firstly, there was an unexpectedly low positive predictive value of 5%. The large number of false positives will invariable lead to heightened concern for the patient and unnecessary downstream testing. Another potential limitation of SDPs includes the significant degradation in the quality of single lead ECGs obtained without medical supervision. This was reflected by the large proportion of unclassified tracings in this study. Lastly, economic analysis revealed a cost of $10,780 per AF diagnosis, which is significant. However, in this study all tracings were over read by a clinician, rather than limiting this to the unclassified tracings. Regardless, the poor positive predictive value observed in this study necessitates a clinician over-read of all positive AF diagnosis, to reduce unnecessary downstream testing.

The prevalence of AF in an unselected adult population is approximately 2%, which rises to 5% in patients aged 65 – 84 years[11]. In a patient ≥ 65 years using an SDP for rhythm analysis, we estimate the post-test probability of a positive diagnosis of AF to be 14%, which is only modest (Figure 1). Non-invasive screening strategies, utilising conventional medical grade systems such as Holter monitors and event monitors, are limited by the intermittent nature of monitoring and by the need to 'return to base' for data download. Utilising SDPs as a 'rule out' strategy may be of greater clinical utility, as a negative result demonstrates very low likelihood of underlying AF (Figure 1). This approach is particularly suited for wrist worn SDP based screening of paroxysmal arrhythmias, as these devices are designed for almost continuous use with wireless upload of data for remote analysis.

Innovations in big data analysis with machine learning has culminated in development of deep neural networks to identify patients with AF based on PPG guided R-R variability alone[12]. Furthermore, the latest iteration of wearables now employs a hybrid system that prompts the user to acquire a single lead ECG, when their HR deviates from a personalised R-R variability and physical activity template generated from their PPG data. These systems are likely to compete with conventional medical grade devices, given the ease with which biometric indices can be recorded. However, clinical data pertaining to their use in such a manner is currently lacking.

With increasing prevalence of AF in the population, the prospect of readily available screening via SDPs appear attractive. However, a fundamental question still remains largely unanswered; subclinical AF may not confer the same risk for stroke as manifest AF and several studies have shown an apparent lack of temporal association between cardiac implantable device detected atrial high rate episodes and subsequent stroke[13]. However, meta-analysis of these studies demonstrate that, while subclinical AF appears to confer a lower risk for ischaemic stroke than manifest AF, it remains higher than in patients without subclinical AF[14]. The absolute annual stroke risk was 1.89 (95% CI 1.02 – 3.52) compared with 0.93 (95% CI 0.58 – 1.49) per 100-person years[14]. However, the overlapping confidence interval makes this comparison problematic. Furthermore, trials have shown significant heterogeneity on what constituted an episode of subclinical AF[14]. As such uncertainties remain regarding the duration of subclinical AF that is required to derive benefit from oral anticoagulation for thromboembolic prevention. Further, a large AF screening study based on single lead ECG acquisition demonstrated that less than 25% of eligible patients subsequently received oral anticoagulation[15]. At present, there are no trials addressing the

net clinical benefit and cost of oral anticoagulation for stroke prevention using these screening techniques.

Technological limitations notwithstanding, potential patient specific barriers may impede widespread screening using SDPs. However, attitudes to SDP based arrhythmia detection remain favourable compared with conventional Holter monitoring system for symptomatic arrhythmia[16]. In one study, SDPs were deemed to be more convenient by 98% of the patients, while 90% were likely to utilise the device to determine cardiac rhythm during symptomatic episodes[16]. Further, patients do not report anxiety and on the contrary appear extremely or very comfortable using SDPs and in sharing clinical and personal information they generate for medical purposes[10]. However, these findings may lack generalisability, as participation bias could attribute for the high level of acceptance noted in these studies. Older patients have markedly higher prevalence of atrial arrhythmias and have the potential to derive the most benefit from SDPs, but conversely may exhibit reluctance in utilising SDPs. The feasibility of SDPs in such high-risk patient cohort, requires further assessment. With the consolidation of numerous patient biometrics tagged to social and demographic data by commercial entities, privacy remains a central concern. There is a growing need for data privacy laws to keep abreast of the rapid innovations in this nascent field.

Despite the limitations, consumer grade SDPs are increasingly prevalent and are undergoing rapid iterative improvements. The gap between conventional medical grade devices and the SDPs continues to narrow. Clinicians should be open to reviewing data generated by these platforms, as they may provide valuable individualised information to aid patient management. However, a regulatory framework for standardising and incorporating this data into routine clinical practice is currently lacking. These devices have the potential to generate

vast amounts of biometric data that could lead to unnecessary and expensive downstream diagnostic testing, with significant implications for the individual and the wider healthcare system. The adoption of SDPs with incorporated arrhythmia detection, must be carefully balanced against the variable accuracy of these devices and current gaps in evidence pertaining to the optimal management of conditions such as subclinical AF. Therefore, we as clinicians should be wary of turning the person into a patient.

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Figure Legend

Figure 1.

Fagan's nomogram for the confirmation of atrial fibrillation (AF) by the current generation of single-lead ECG platforms. This is a Bayesian graphical tool that estimates how much the result of a diagnostic test changes the probability of a patient having a condition. A line drawn from the pre-test probability through the likelihood ratio of interest intercepts the new post-test probability for the patient. This assumes a 5% population prevalence (pre-test probability) of AF for a patient ≥65 years of age with likelihood ratios used from previously published research. If a patient tests negative, the post-test probability of not having AF would be approximately 2% (blue line). Alternatively, if the patient tests positive, the post-test probability of AF would be approximately 14% (red line).

LR_Negative= negative likelihood ratio; LR_Positive= positive likelihood ratio; Post_Prob_Neg= negative post-test probability; Post_Prob_Pos = positive post-test probability.

Tables

Table 1. Sensitivity and specificity of smart device platforms and their underlying technology in analysing cardiac rhythm.

Study	SDP and Technology	Patients n	Uninterpretable tracing	Sensitivity	Specificity
Desteghe et al. 2017[17]	Kardia Mobile *Single lead ECG*	265	na	54.5%	97.5%
Desteghe et al. 2017[17]	MyDiagnostick *Single lead ECG*	265	na	81.8%	94.2%
Bumgarner et al. 2018[8]	Kardia Band *Single lead ECG*	100	33.7%	93%	84%
Koshy et al. 2018[7]	Kardia Mobile *Single lead ECG*	102	15%	100%	95%
Koshy et al. 2018[7]	Kardia Mobile *Single lead ECG + clinician over read of unclassified tracings.*	102	2.9%	93%	92%
Tison et al. 2018[12]	Cardiogram + Apple Watch *PPG + neural network*	51	-	98%	90.2%

PPG = photoplethysmography, na = not available.

Kardia Mobile & Kardia Band (AliveCor Inc., Mountain View, CA), MyDiagnostick (Applied Biomedical Systems BV, Maastricht), Cardiogram (Cardiogram Inc), Apple Watch Series 1 (Apple Inc., Cupertino, CA)