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Atrial Fibrillation and the Role of Thumb ECGs

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Abstract

Atrial fibrillation (AF) may be underdiagnosed, and there is much that remains unknown about this prevalent and potentially life-threatening arrhythmia. AF epidemiology has been thwarted in part by the fact that about a third of patients with AF have no symptoms, those with symptoms may experience them intermittently or have vague symptoms, and it can be challenging to capture an episode on a 12-lead ECG, which is required for diagnosis. There are many significant knowledge gaps in our understanding of AF etiology and progression. A new user-friendly device that allows for frequent self-monitoring of the heart rhythm has been introduced. With the thumb ECG, patients can record a tracing multiple times a day. A smartphone app will soon allow them to interact with their healthcare providers about these ECG recordings. An ECG parser will allow for an algorithm-directed, rapid, automatic interpretation of these recordings with high specificity and sensitivity. This may help researchers learn more about the so-called *silent AF*, AF progression (and possible remission), and risk factors for AF. This technology holds great promise for patient care as well as for research into AF.

Keywords: arrhythmia, atrial fibrillation, thumb ECG, Coala heart monitor, stroke

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia and associated with a fivefold increased risk of stroke and a threefold increased risk of heart failure; thus, AF is a major cause of cardiovascular morbidity [1–3]. The European Society of Cardiology (ESC) recognizes five main types of AF: first diagnosed episode, paroxysmal, persistent, long-standing persistent, and permanent [3] (see **Table 1**). It had long been thought that *AF begets AF* and the arrhythmia followed a linear forward progression from short, infrequent, self-terminating episodes to more persistent forms of AF, but that paradigm has been challenged in that about 3% of patients seem to have paroxysmal AF that never advances to more persistent forms [4]. It is now recognized that AF may plateau, remit/relapse, and one patient can simultaneously have multiple types of AF [5]. The ESC has also identified seven clinical types of AF, as the etiology of AF may relate to any of multiple mechanisms (see **Table 2**). In addition to types and categories of AF, the arrhythmia burden is frequently used as a metric to describe the amount of time an individual spends in AF [6].

Types of AF	Definition	Treatments
First diagnosed	Newly identified AF of any type	Varies, depending on how severe the AF is and if the patient is symptomatic
Paroxysmal	Sudden onset, self-terminating episodes that typically last a few moments to as long as 48 h; recurrent	Episodes terminate with or without intervention; may be asymptomatic
Persistent	AF that lasts more than 7 days but can be converted with medical intervention	Pharmacological or electrical cardioversion
Long-standing persistent	AF that lasts a year or more and for which treatment is available	Catheter-based ablation, open ablation, drug therapy
Permanent	AF that has lasted more than a year and which is accepted by patient and medical team	Rate control

These distinctions are based primarily on the duration of AF.

Table 1.
Main types of AF as set forth by the European Society of Cardiology [3].

Clinical type	Characteristics	Comments
AF secondary to structural heart disease	May occur in patients with left-ventricular systolic or diastolic dysfunction or other forms of structural heart disease	Treatment approaches vary; anticoagulation therapy
Focal AF	AF paroxysms associated with localized triggers, such as the pulmonary veins	Pulmonary vein ablation may be considered; anticoagulation therapy
Polygenic AF	Genetic, early onset	Much remains to be elucidated about this type of AF; anticoagulation therapy
Postoperative AF	Occurs following cardiac or other surgery in patient without prior history of AF	This AF may remit on its own, may persist or progress; treatment varies
AF with atrial remodeling	AF typically associated with mitral stenosis and/or mitral valve surgery or other forms of valvular disease	Atria remodel in response to arrhythmic burden; anticoagulation therapy
Athlete’s AF	AF, often paroxysmal, that occurs during intense athletic training	Appears to be related to intensity of exertion
Monogenic AF	Associated the cardiomyopathy and channelopathy	Anticoagulation therapy

Therapeutic interventions, when appropriate, are typically grouped as those involved rate control (allowing AF to continue but preventing a rapid ventricular response) or rhythm control (converting to sinus rhythm when possible).

Table 2.
Clinical types of AF as defined by the European Society of Cardiology [3].

Despite the vast healthcare resources required to manage AF, little epidemiological research has been conducted for this arrhythmia. AF can be an elusive arrhythmia and short episodes can be difficult to capture on conventional ECGs. New technological innovations, including the thumb ECG, may offer tools to help better understand this arrhythmia. The thumb ECG opens up new technological abilities to benefit patients and individual cases of AF as well as to benefit research to better understand the epidemiology and natural history of AF in real-world populations.

2. The challenge of AF epidemiology studies

The classic diagnostic assessments of AF require that documentation of the arrhythmia on a 12-lead ECG. An irregular pulse may cause a clinician to suspect AF, but the ECG is considered necessary for a diagnosis [7]. AF is characterized by irregular R-R intervals without discernible P-waves (except when the patient has concomitant atrioventricular third-degree block). About a third of all individuals with AF are asymptomatic, with silent AF or subclinical AF [8]. Even when symptoms occur, they may be infrequent or diffuse. Historically, early efforts to quantify the incidence and prevalence of AF and to better understand its potential relationship to stroke, heart failure, and other conditions were hampered by the limitations of standard ECG technology, the episodic nature of AF, and the large proportion of patients who had vague or no symptoms. Unfortunately, the first manifestation of AF may be stroke.

Recording AF on a standard 12-lead ECG assumes both that the clinician suspects that the patient has AF and that the AF will occur during the ECG recording. ECG monitoring is too elaborate and expensive for use in routine population testing, such as for epidemiological studies. Continuous ECG monitoring can be obtained in individual patients by a wearable Holter monitor, but such systems are cumbersome to patients and generate vast quantities of tracings that can be a burden to analyze. Holter monitors are typically used for 24 h or for a specific number of days, such as 7 days. Event recorders may also be used. The advent of diagnostic counters in cardiac implantable electronic devices (CIEDs) allowed physicians to monitor device-detected arrhythmias, including AF. CIED monitoring offered the advantage of beat-by-beat analysis. Clinicians could program a cutoff rate for *high rate events* on the atrial channels, usually in the lower range of 170–220 beats per minute. This led to a shift in terminology in that these devices obtained data on atrial high-rate episodes (AHRE), which included ectopic atrial tachycardia, atrial flutter, as well as AF. Current dual-chamber CIEDs offer mode-switching algorithms, which can essentially turn off ventricular tracking during episodes of AHRE. Mode-switching algorithms in conventional pacemakers can identify AHRE with 98% sensitivity and 100% specificity [9]. The value of this beat-by-beat monitoring first emerged in the Mode Selection Trial (MOST) in which 313 patients (median age 74 years) with pacemakers to treat sinus node dysfunction were followed for 27 months, during which their pacemakers recorded AHRE when atrial activity occurred at a rate > 220 beats per minute for more than 5 minutes [10]. More than half (51.3%) had AHRE, which in turn could be associated with elevated morbidity (stroke, permanent AF) and mortality [10]. The asymptomatic atrial fibrillation and stroke evaluation in pacemaker patients and atrial fibrillation reduction atrial pacing trial (ASSERT study) evaluated 2580 patients over age 65 with hypertension but without a history of AF who had a pacemaker or ICD with an atrial lead. In the first 3 months of follow-up, 10.1% of patients had documented subclinical AF lasting over 6 min; at 2.5 years, subclinical AF occurred at least once in 34.7% of patients. The patients with subclinical AF had a 2.49-fold increased risk of stroke compared to patients who did not have subclinical AF, irrespective of any other atrial arrhythmias [11]. In a study of 356 pacemaker patients with continuous atrial-channel monitoring, 88.2% had paroxysmal AF and 50.3% had at least one episode of persistent AF [12]. A study of 678 pacemaker patients (411 without AF and 267 with known AF) were followed over 38 months, and it was found that 30% of those with no history of prior AF had silent AF [13]. Of course, the patient populations for these studies were limited to those with specific device indications (and in some cases other inclusion criteria), and therefore, these findings are not generalizable to the population as a whole.

As might be intuitively expected, the accuracy of AHRE detection improves with more continuous monitoring [14]. The high prevalence of AHREs detected by device diagnostics gave rise to the implantable loop recorder (ILR). The ILR relies on a detection algorithm to identify AF typically based on R-R interval stability as evidenced by consecutive QRS complexes. AF detection algorithms in ILRs are undergoing refinement and may change in the future to improve specificity and sensitivity. As with a CIED, an ILR would be implanted only in patients who are suspected of having AF or other arrhythmias. The TRENDS study was an observational trial (n = 2486), which followed patients with an ILR for a mean of 1.4 years and analyzed them for atrial tachycardia and AF burden and thromboembolic events and found 45% of patients with no prior history of AF (n = 1988) had subclinical episodes of atrial tachycardia [15].

The incidence and prevalence of AF may be vastly underestimated because there was until recently no reliable and accurate way to monitor patients who were not at specific risk for AF or who did not have a device or ILR indication. In other words, till now, AF data were gathered mainly from people with or at an elevated risk for arrhythmias. Epidemiological information on AF progression (from paroxysmal to persistent and permanent), risk factors for AF, and AF associations remain to be elucidated. Statistical analyses and meta-analyses have allowed certain risk factors for AF to emerge, such as hypertension, heart failure, coronary artery disease, valvular disease, diabetes mellitus, obesity, and chronic renal failure [16–18] as well as risk factors for AF progression, including older age and hypertension [19]. The thumb ECG offers an excellent opportunity to gather real-world data on AF from general and specific populations. Some important questions about AF remain to be elucidated:

- What is the actual incidence and prevalence of AF in the general population?
- Are there specific subpopulations with a higher prevalence of AF, for example, patients with diabetes, myocardial infarction, and cancer patients?
- What is the association between silent AF and stroke, for example, how many patients with silent AF are needed to have one patient suffer a stroke?
- What is the trajectory of AF—does it always progress? Can we define its course in clinically meaningful ways?
- Can patients with a low AF burden plateau for a long period of time at that level or does AF typically advance to increase the AF burden?
- What can be known about the population who has more than one type of AF at the same time (for example, both paroxysmal and persistent long-standing AF)? Do multiple types of concurrent AF confer worse morbidity and mortality?
- Can we better identify risk factors for AF?

In addition to these questions, it would be important to be able to better evaluate treatment strategies for AF by monitoring patients following drug therapy, ablation, or other procedures.

3. The thumb ECG

The thumb ECG is a small-format, patient-friendly device that lay persons can use to monitor their heart rhythm. After reading the instructions or a brief training,

individuals can use the thumb ECG on their own quickly and conveniently many times over the course of a day. The thumb ECG is a miniaturized and digital descendant of the original ECG technology that was available around 1900. Patients can monitor their heart rhythm by pressing the device to the chest or by placing their thumbs on pads at the top of the device for a reading (see **Figure 1**). Several thumb ECG devices are available, and it is likely more are in development. Among them, the Coala Heart Monitor™ has been approved for use in Europe to individual patients in 2016 as a Class IIa medical device and to professional organizations in 2017. The device is connected to a cloud-based service to which users subscribe. When information is uploaded from the thumb ECG to the cloud, it is automatically analyzed for AF or other arrhythmias using proprietary algorithms. Devices are available for use by multiple patients at a clinic but may also be purchased direct-to-consumer (the Coala Heart Monitor Pro™ and the Coala Heart Monitor™, respectively). The Coala device is connected via wireless Bluetooth connectivity to a smartphone for use with a proprietary Coala app. In this way, the thumb ECG dispenses with chest electrodes or other adhesive patches. An ECG may take up to 60 s.

The patient can view the individual ECG recordings and results from automated analysis directly on their smartphone app. Messages from the clinic to the patient can also be viewed directly on the app for feedback. ECG recordings can also be stored or printed by the patient to keep on hand for their next appointment. Patients can also add a special *heart report* service to their smartphone to discuss their ECG recordings with trained nurses for recommended actions. In this way, one centralized and highly specialized healthcare function may provide first-line primary cardiac healthcare coverage for a large and geographically spread-out population.

Clinicians monitor the results from their patients' thumb ECG devices by accessing a secure portal via an ordinary laptop computer. The proprietary algorithms for ECG analysis are based on the ECG Parser, an algorithm system. The ECG Parser identifies specific beats and patterns of beats and groups them into classes by

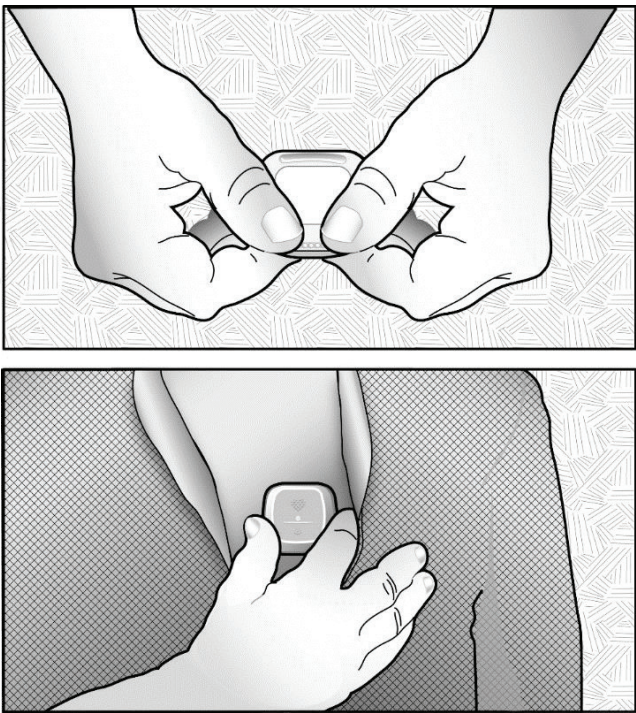


Figure 1.
The Coala Heart Monitor™. Device sensors detect the heart rhythm when the device is placed on the chest or when the device is grasped with the thumbs on top of the two sensors on the device. Drawing: Courtesy of Todd Cooper.

Category	Description	Does this indicate AF?
0	Poor quality	No
1	Normal	No
2	Atrial fibrillation	Yes
3	Pause/AV block II	No
4	Fast, regular	No
5	Long-short sequences	No
6	Bigeminy	No
7	Trigeminy	No
8	More than 5 supraventricular extrasystoles	No
9	More than 5 ventricular extrasystoles	No
10	Irregular rhythm with P-waves	No

Table 3.
The Coala Heart Monitor™ system is based on an ECG parser with a proprietary and algorithmic system to help categorize arrhythmias automatically (Category 2 events indicate AF based on R-R interval dispersion and the absence of P-waves).

morphology; using the sequence of beats, the algorithm applies markers to ranges, measures intervals based on averaged beats, and then categorizes each signal or signal segment into one of the 12 different categories to facilitate their use in large databases (see **Table 3**).

4. The role of the thumb ECG in AF research

The ability to easily and inexpensively obtain ECG data has opened up new avenues to advance research into AF and other arrhythmias.

4.1 The role of premature atrial contractions and premature ventricular contractions in arrhythmogenesis

It has long been suspected that premature atrial contractions (PACs) and premature ventricular contractions (PVCs) may be associated with arrhythmias. However, since PACs and PVCs typically occur without warning and as isolated events, there has been no way to obtain appropriate data to investigate this question without generating an overwhelming volume of tracings. A study published in 2012 attempted to explore the relationship of PACs and PVCS to AF by evaluating 428 patients without structural heart disease and with no history of AF using 24-h Holter monitoring [20]. This study found that frequent PACs were indeed significant predictors of AF ($p < 0.001$). However, the study required patients to wear Holter monitors and the investigators had to analyze hundreds of hours of ECGs. A similar study was undertaken using thumb ECG technology that could analyze 40,000 measurements over a span of 500 days. This second study was able to likewise confirm that frequent PACs were indeed highly significant predictors of AF ($p < 0.001$) [21] (see **Figure 2**).

Furthermore, with thumb ECG technology, it was relatively straightforward to confirm that the rate of VES and SVES events increased as AF developed [21] (see **Figure 3**).

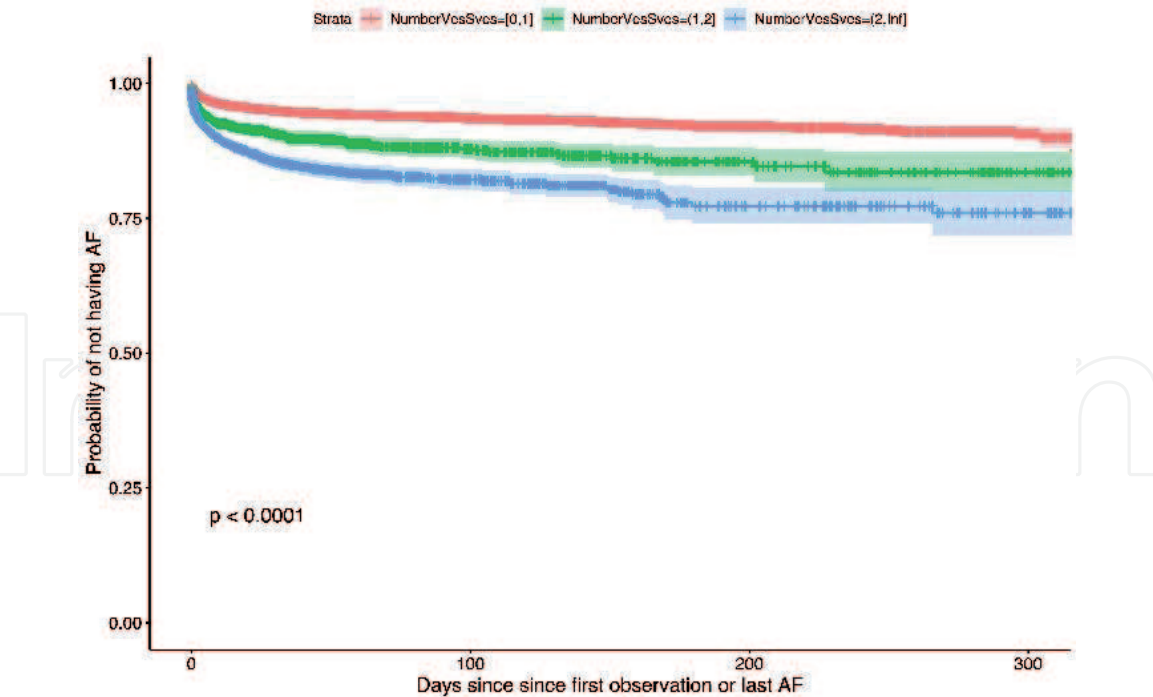


Figure 2.
The incidence rates for development of AF based on number of ventricular extrasystoles (VES) and supraventricular extrasystoles (SVES). Chart: Courtesy of Coala Life.

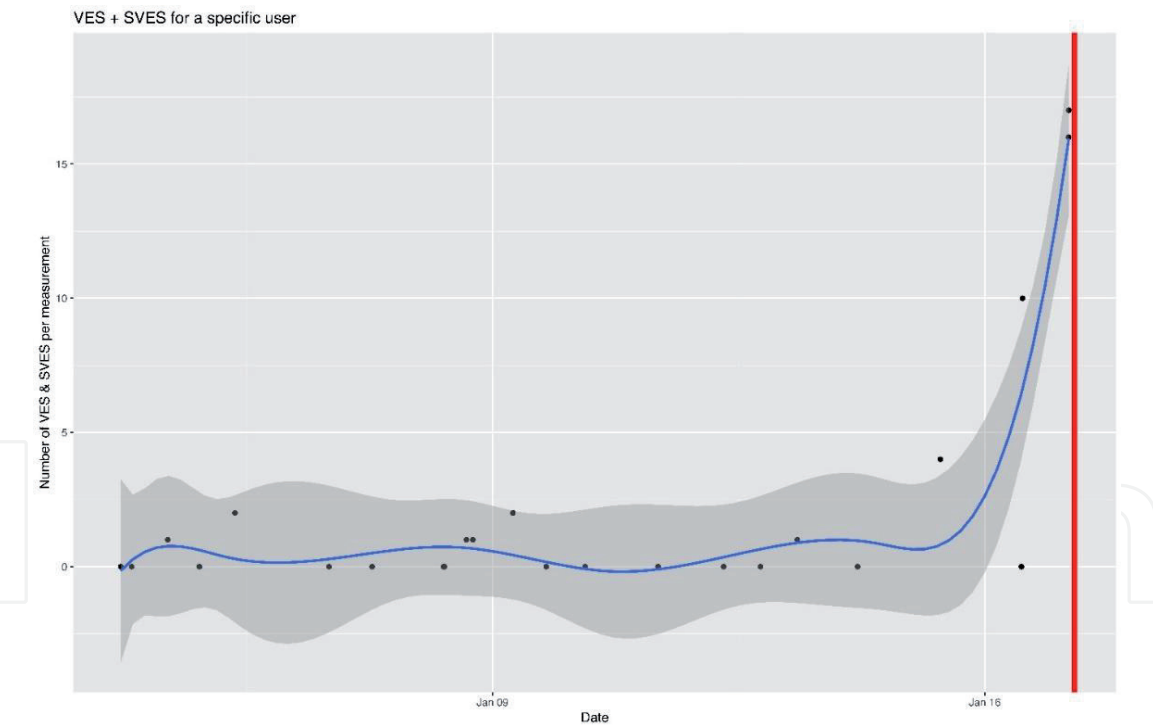


Figure 3.
As patients developed AF, the incidence of both ventricular extrasystoles and supraventricular extrasystoles increased sharply. Chart: Courtesy of Coala Life.

4.2 The real-world incidence and prevalence of AF

The StrokeStop I study was aimed at evaluating the risk of stroke in people with untreated AF. To accomplish the study, systematic ECG screenings would be needed from over 7000 patients. A thumb ECG system was used to obtain intermittent ECG recordings, which were then analyzed using a proprietary ECG

parser system. In the group of patients aged 75 or 76 years, AF prevalence was found to be 12.3% [22]. This differs markedly from medical records, which found that in that particular patient group, 9.3% had a prior diagnosis of AF. Thus, thumb ECG with the ECG parser technology was able to confirm a much higher AF prevalence than was previously determined. This suggests that the actual incidence and prevalence of real-world AF may be substantially underestimated, which has implications for public health and the healthcare system as well as for individual patients.

In the ongoing *Study of Men Born in 1943*, thumb ECGs were introduced in 2014 to help assess AF prevalence. After eliminating patients who had died, declined to participate, were lost to follow-up, or had known permanent AF, patients were evaluated twice daily by thumb ECG ($n = 479$). The thumb ECG in this study was able to diagnose a previously silent form of AF in 1.8% of patients ($n = 8$), and it found the overall prevalence of AF was 3.1% (95% confidence interval [CI], 1.83 to 4.98), but for men over the age of 71, the prevalence of paroxysmal AF was 9.9% [23].

In a study of 1510 patients aged 65 with risk factors for stroke, the use of thumb ECGs over a two-week period found undiagnosed AF in 0.9% of the population, which worked out for a total AF prevalence in the study group of 7.6% [24].

5. Thumb ECGs versus other types of monitoring

Ambulatory assessment using Holter monitors was previously the main way in which patients with suspected AF (and no implantable device) could allow the arrhythmia to *go on the record* for diagnosis. Holter monitors record ECGs from the patient around the clock and are typically set up to provide either 24 h or 7 days of data. Holter monitoring became the gold standard for arrhythmia analysis but had certain drawbacks: ambulatory monitoring utilizes a wearable technology that patients may find cumbersome, clumsy, and uncomfortable. Holter monitoring produces huge quantities of tracings to be analyzed. In a 7-day Holter monitoring program, each patient would yield 168 h of ECG tracings (over 10,000 min per patient) and even with automated systems, this represented considerable time and effort to analyze. Furthermore, in 168 h of ECG tracings, it was possible that only very short runs of AF would appear—for example, there might be 10 or 20 min of AF somewhere in 10,000 min of data.

Subclinical device-detected AF is defined as an AHRE (>190 beats/min for >6 min and <24 h) with lack of prior diagnosis and correlated symptoms in patients with devices that can produce continuous ECG monitoring [25]. Continuous ECG monitoring has been shown to increase the number of undiagnosed episodes of AF, especially in those with prior bouts of ischemia [26]. In fact, thumb (or handheld) ECGs have been shown to be significantly more sensitive in the detection of silent AF compared to conventional 24-h Holter ECGs [27, 28].

In order to determine whether Holter monitors offered comparable efficacy to thumb ECGs, a study of 95 patients (≥ 65 years) was initiated. Patients were excluded if they had a history of AF. All patients were monitored for 5 days using a Holter monitor and concurrently with a thumb ECG twice daily. Patients continued using the thumb ECG for 30 days. Paroxysmal AF was detected in 20 patients using the thumb ECG, in 17 patients using the Holter monitor, and by both systems in 10 patients [29]. The detection rates between the two methods did not differ in a statistically significant way ($p = 0.63$).

In a study of 108 consecutive patients with ambiguous symptoms of dizziness and heart palpitations, patients were monitored using a Holter monitor for 24 h and then twice daily using a thumb ECG for 28 days. The mean age of patients in this study was 54.1 years. In this study, the thumb ECG was significantly more effective over 4 weeks at identifying AF and paroxysmal supraventricular tachycardia than the Holter monitor [30].

In a study presented at the Cardiovascular Spring Meeting in Stockholm in April 2018, researchers took 1000 consecutive, anonymous printouts of waveforms captured from the chest and thumbs using the Coala Heart Monitor™ system. No exclusions were allowed. Each printout consisted of three 10-s tracings recorded at 25 mm/s. Algorithm analysis notation and patient information (except patient sex and age by 10-year groups) were removed from the strips. However, heart rate, R-R median values, and user-provided annotations were allowed. All strips came from real-world patients using the Coala monitor; subjects were given no special device training. All strips were then sent to a trained cardiologist who interpreted each one manually and then compared his interpretation to the automatic analysis offered by the Coala device. One cardiologist interpreted all of the rhythm strips. When comparing these 1000 real-world ECGs to the Coala algorithm's interpretation, it was found that the Coala was highly accurate with 97% sensitivity and 95% specificity. The estimated prevalence of AF from these recordings was 14.4% [31, 32].

In the StrokeStop I study, 80,149 tracings were recorded using the Zenicor™ thumb ECG system; tracings were obtained from 3209 patients aged 75 or 76 years. It was found to offer 98% sensitivity and 88% specificity, and the use of thumb ECG technology combined with an ECG parser reduced the workload in analyzing data by over 85% [22].

In a study of 100 patients with AF, a 12-lead ECG recording was followed by a thumb ECG assessment with the results compared by a blinded investigator. When the 12-lead ECG was compared to the thumb ECG, the thumb ECG had a sensitivity of 96% and a specificity of 92% versus the 12-lead ECG. As part of the same study, a second group of patients (n = 12) underwent effective cardioversion for AF and then used a thumb ECG to assess their rhythms twice a day for the next 30 days. In this group, 95% of cardioverted patients had tracings from the thumb ECG considered to be of sufficient quality for clinical diagnosis. A third group (n = 606) was screened for AF using the thumb ECG. Twelve people in this group were diagnosed with AF of whom six had no history of AF and no symptoms [33].

6. Questions about silent AF

One of the primary reasons to suspect that AF incidence and prevalence is underestimated is the fact that as much as 40% of AF may be asymptomatic [34, 35]. Clinically silent AF may occur with paroxysmal AF, persistent long-standing AF, or permanent AF [36]. Asymptomatic AF is not benign; data from the EORP-AF study found that asymptomatic AF conferred on patients a higher 1-year mortality risk than symptomatic AF [35] although the AFFIRM study found no such difference between symptomatic and asymptomatic AF patients [37]. Early and accurate diagnosis of AF may help reduce the burden of AF on the healthcare system and may allow interventions to reduce morbidity and mortality associated with AF.

The classic AF symptoms may include any or a combination of the following: heart palpitations, sensations of a racing or pounding heart, dyspnea, chest pain or

discomfort, fatigue, lethargy, dizziness, malaise, anxiety, and syncope. Symptoms are thought to be caused primarily by rapid ventricular response to AF rather than by the atrial arrhythmia itself. It is thought that rapid ventricular activity, irregular rhythms, and the loss of the atrial contribution to ventricular filling might all contribute to reduced cardiac output, exacerbation of left-ventricular dysfunction, cardiac remodeling, and a general deterioration of overall health [36]. In addition to asymptomatic paroxysmal AF, some cases of AF may go unnoticed by patients because the AF episodes are brief and interspersed between long periods of normal sinus rhythm and symptoms may be very mild, diffuse, or overlooked by patients. Silent AF is typically an incidental diagnosis, which may occur during routine examinations or tests for other conditions.

The mechanical effects on the heart caused by fibrillating atria as well as the electrophysiological and neurological consequences of AF appear to be the same whether AF is clinically silent or symptomatic. Silent AF, like its symptomatic counterpart, is associated with silent or symptomatic emboli, heart failure, morbidity, and mortality [38].

Risk factors for silent AF include patients with cryptogenic stroke, hypertension, advanced age, obesity, diabetes mellitus, cigarette smoking, chronic kidney disease, or a history of cardiac disease [7, 35, 39–42]. Blood group type O appears to confer a protective effect against thromboembolism in persons with AF for reasons that remain unclear, but which may be associated with circulating von Willebrand factor levels [43].

7. Anticoagulation therapy

AF has been clearly associated with the catastrophic complications of thromboembolism and cerebral stroke, but the association between AHRE and thromboembolism/stroke is not well defined [44]. The thumb ECG, like CIEDs, can detect AHRE but it remains an open question as to whether and under what circumstances anticoagulation therapy is appropriate for patients with documented AHRE. AHRE is defined by two parameters: the atrial rate and the duration of the episode. However, it remains unclear as to how fast or how long an episode of AHRE must be to represent a risk of thromboembolism or stroke [45]. Thus, it remains to be elucidated at which point a patient with AHRE might benefit from anticoagulation therapy.

According to the ASSERT and TRENDS studies, the association between the formation of a thromboembolism and AHRE is challenged by the lack of a temporal relation between the two events [46, 47]. The current data are contradictory. In the ASSERT study, tachyarrhythmic episodes ≥ 6 min in duration have led to a higher embolic risk [11]. However, in the TRENDS study, tachyarrhythmic episodes ≤ 5.5 h were not associated with an increased thromboembolic risk [15].

With much to be elucidated about the potential role of anticoagulation therapy for patients with AHRE, thumb ECGs may play an important role. These devices may help uncover more about AHRE and its relationship to AF as well as its association to adverse events. A more refined understanding of the temporal relationship between AF and its comorbidities will help to create more effective anticoagulation therapies and better outcomes.

8. Knowledge gaps about AF

The incidence and prevalence of AF may correlate with gender, age, comorbidities (such as heart failure, atherosclerosis, hypertension, diabetes mellitus, and others),

and possibly other variables. The natural course of AF, once thought to be the linear progression from paroxysmal to persistent to permanent, remains to be elucidated and appears to be more fluid than originally thought, even allowing for remission and relapsing. While the association between AF and stroke is clear and ominous, it is not known if this risk is greater, lesser, or the same for symptomatic versus asymptomatic AF or different types or clinical presentations of AF. A meta-analysis of data on AF showed that while men generally had a higher incidence of AF than women, women and, in particular elderly women, were at a greater risk than men for stroke and thromboembolism associated with AF [48–50]. Whether or not AF in the elderly and oldest old populations is associated with more or more severe symptoms also remains unknown. Greater understanding of these matters could result in better, more targeted, and more effective clinical approaches and treatment.

It has been observed that patients implanted with CIEDs may experience brief, clinically silent episodes of paroxysmal AF when the device is initially implanted. The Automatic Interpretation for Diagnosis Assistance (AIDA) study found that half (50.6%) of patients with *de novo* pacemaker implantations experienced atrial arrhythmias in the first month following implant and these episodes were often asymptomatic [51]. In a study of 213 dual-chamber pacemaker patients, all of them had experienced at least one atrial arrhythmia at 3 years following implant [52]. This area has not been studied extensively and it is not known if this is clinically important or might resolve with time [53].

Other knowledge gaps occur in the treatment of AF and how patients respond. It has been suggested that pharmacological suppression of AF may simply convert symptomatic AF into clinically silent AF, but there is not much data to support or refute this notion. While it is known that AF incidence and prevalence increases with age, it is not clear whether geriatric patients are more likely to have symptomatic or asymptomatic AF, nor has it been fully elucidated whether certain types of AF (such as permanent or persistent long-standing AF) occur more often in elderly patients.

AF is thought to be more prevalent in industrialized nations compared to developing countries but this has not been extensively studied [54].

Thumb ECG studies can provide robust data to help answer these questions by allowing the inexpensive and straightforward acquisition of large amounts of ECG data annotated with patient-reported symptoms from selected populations and, together with algorithms to analyze the data, provide for fast and accurate interpretation of that data. The advent of thumb ECG technology will empower medical science and the healthcare system to obtain vital information crucial to the early and accurate diagnosis of AF, particularly paroxysmal and clinically silent AF.

Thumb ECG data may help better guide anticoagulation therapy. Anticoagulation therapy is frequently prescribed for AF patients. In CIED patients with diagnostic data revealing atrial high-rate activity, it is not clear despite this documentation whether patients would benefit from anticoagulation therapy [38].

The populations affected by AF are diverse and include patients with valvular disease, malignancy, inflammation, atherosclerotic coronary artery disease, plus those with genetic forms of AF, postoperative patients, patients following ablations, CIED patients, along with patients who are geriatric, obese, or who have heart failure and/or hypertension. These populations are diverse, some overlap considerably, and cross the lines between medical disciplines [40]. These factors contribute to the confusion that makes it hard to better quantify AF. A number of open questions remain and a high-level summary appears in **Table 4**.

Question	Obstacles	Comments
Which patient populations are at greatest risk from AF?	May require some kind of diagnostic algorithm to account for comorbidities; need to find definition of risk (risk of AF, stroke, mortality).	Likewise, an important unanswered question is which populations are at lowest risk? Why?
Can patients use thumb ECG technology to self-monitor and/or collect data?	Requires study parameters to be set up.	May be most helpful means to get more accurate and comprehensive AF data.
What is the normal trajectory of AF?	Requires more data, also it is not clear if the natural course of AF might vary by population (for instance, it might be different in older than younger patients, or in men versus women).	The old paradigm that <i>AF begets AF</i> may not be true or may be only partially accurate.
Are some types of AF associated with greater morbidity and mortality than others?	Requires more data and possibly stratification.	This question could lead to more individualized treatment courses.
Can we reach a consensus definition for AF burden?	This is a relatively new term that is typically well understood but imperfectly quantified; need consensus definition.	It is not clear if and in what ways AF burden may relate to AF risks/outcomes. Once it is defined, it can be more efficiently studied.
Is silent AF always without symptoms?	Evidence that quality of life decreases in patients even with asymptomatic AF suggests that AF is almost always symptomatic but not all symptoms are recognized.	Better diagnostic tools are needed to identify silent AF and then to measure quality of life.
What is actual incidence and prevalence of AF?	Correlations with clinical presentation, type, history, duration, and patient characteristics may be helpful but challenging to obtain.	Will allow for more effective and individually targeted treatments.

Table 4.
Key questions about AF that may be a good research topic with thumb ECG technology [40].

9. The AF burden and thumb ECG technology

In an effort to better grapple with the global effects of AF on a patient, the AF burden is often used to better describe the arrhythmia and its consequences. The AF burden may be defined as how much time the patient spends in AF per unit of time (such as what proportion of 1 day or 1 week) [6]. AF burden lacks a universally recognized consensus definition, has not been extensively validated as a measure, and is not often used when evaluating AF cases in terms of severity or risk. It is not known if a high AF burden exacerbates risk factors for stroke. It is strongly suspected that the AF burden is generally underestimated because of asymptomatic AF and the fact that conventional technologies have been used to assess the incidence and prevalence of AF [38]. A consensus definition would be helpful and would facilitate meaningful efforts to study how the AF burden affects the course of the arrhythmia, treatment options, and related morbidity and mortality.

10. An integrated approach to care for AF patients using thumb ECG technology

A knowledge deficit about AF may be observed even in patients provided specific, patient-focused oral, and/or written educational tools [55, 56]. Individualized,

educational interventions for AF have been proposed in order to address specific patient needs, for example, types of AF treatment, recommended lifestyle modifications, possible self-management tools, and drug therapy [57]. Thumb ECG technology may soon emerge as an important element in the care of AF patients. Patients who are considered appropriate candidates to monitor their hearts using a thumb ECG device should be given specific training on the use of the device; such training would likely be brief as these devices are designed to be easy to use for lay-people. The regular use of a thumb ECG can assist patients in arrhythmia detection and diagnosis as well as monitoring the course of treatment. The integration of the thumb ECG into AF patient care may empower the patient and be a cornerstone of a shared decision-making paradigm, in the event that multiple treatment options are considered. It is known that patient education, shared accountability, and individual empowerment drive improved adherence [58]. The use of a thumb ECG may also be helpful in linking AF episodes to specific symptoms [3]. Furthermore, the thumb ECG may reveal subclinical AF and may help better delineate the progression of AF over time.

AF is so pervasive and crosses so many disciplinary boundaries that a multidisciplinary approach to care is warranted, bringing together several healthcare disciplines, i.e., general practitioners, cardiologists, surgeons, and allied health professionals along with nonspecialists who may advise on diet, lifestyle modifications, physical and occupational therapy, and stroke prevention tactics. Moreover, patients with newly diagnosed AF may benefit from a comprehensive cardiovascular evaluation, including transthoracic echocardiography, as they are at risk for other cardiovascular conditions [59, 60].

AF treatment typically involves anticoagulation therapy (initiated early in appropriate patients), lifestyle modifications, and appropriate interventions, which could include the use of antiarrhythmic agents or other pharmacological treatments, catheter-based interventions, or surgical procedures (ablation, left-atrial appendage occluders, etc.) [3]. Growing understanding of how altered calcium homeostasis, atrial fibrosis, ion-channel dysfunction, autonomic imbalance, and oxidative stress may contribute to AF combined with new knowledge about the genetic underpinnings of arrhythmias should all be taken into account when structuring AF care programs [61]. As an example, pulmonary vein ablation has been recommended for some types of AF but would not benefit all AF patients. However, all AF patients are likely to benefit from regular, consistent, systematic care including routine follow-up visits, monitoring overall physical condition, arrhythmia assessments, pharmacological adjustments as needed, and assessments and encouragement to promote treatment adherence. Thumb ECG monitoring would be an integral part of that care paradigm.

AF care can be defined by three broad domains: stroke prevention (anticoagulation therapy), rate control (mainly aimed at symptomatic improvement), and rhythm control (arrhythmia conversion). Pharmacological therapy can be an important element of AF care and varies based on the individual characteristics of the patient (age, target for treatment, comorbidities, symptoms, symptom severity, left-ventricular ejection fraction, hemodynamics, other drugs the patient may be taking, and so on). Acute rhythm control can be achieved pharmacologically in up to half of all patients diagnosed with recent-onset AF by using antiarrhythmic agents. Antiarrhythmic drug therapy should be guided first by safety rather than effectiveness, and treatment goals should be established that seek symptomatic improvement with the foreknowledge that side effects with these drugs are common [3]. Dose reduction of antiarrhythmic agents may be needed for geriatric patients in that metabolism and the heart's electrical system slow down with increasing age [62]. Above all, it should be noted that many antiarrhythmic agents have seemingly paradoxical pro-arrhythmic effects. This requires regular ECG

monitoring to protect patients against the onset of a new drug-induced arrhythmia [63]. While there are to date no studies on the role of thumb ECG technology in this setting, it makes intuitive sense that a thumb ECG may be useful for patients on antiarrhythmic drug therapy.

11. Future directions

The usefulness of the Coala Heart Monitor™ needs further validation with regard to specific patient groups. Currently, the TEASE study is evaluating patients with cryptogenic stroke for 28 days using the Coala Heart Monitor™ [64]. The rationale for prolonged monitoring in this population is warranted in order to determine if anticoagulation is indicated. Furthermore, the Red Heart Study is an initiative using the Coala Heart Monitor™ exclusively among women with suspected AF or other arrhythmias [65].

While the thumb ECG has already proven its value as a tool for finding and following the progression of AF and other arrhythmias, it is beyond the functionality of this device to assess structural heart changes or impaired left-ventricular function. However, some thumb ECG devices already on the market, such as the Coala Heart Monitor™, have the capacity to record simultaneously both chest ECG and heart sounds through an electronic stethoscope membrane. This allows derivation of acoustic cardiographic parameters such as systolic time intervals (STI) along with the presence and intensity of S3 and S4 heart sounds. The use of STI has historically proven to be a highly sensitive method of assessment of changes in left-ventricular function, albeit with inconclusive findings as a diagnostic tool for differential diagnosis [66, 67].

The use of acoustic cardiographic parameters derived from repeated patient-engaged recordings performed in the home environment may, in this way, characterize and track changes in left-ventricular function at low cost and low burden to the healthcare system. Such indicative parameters of change in cardiac function may fully utilize the individualized data collected from many recordings over a period of time as a baseline rather than population-derived and regression-corrected baseline data for improved sensitivity and accuracy.

In the future, the automatic algorithm-driven detection and reporting of sudden deviations in the patient's heart rhythm may help reduce the human workload without compromising care, in that the healthcare provider at the clinic can be notified quickly about these deviations and take appropriate action, such as changing medications. It is plausible that this could all happen before the patient experiences any symptoms. In this way, small, highly specialized healthcare centers may provide first-line cardiac primary healthcare coverage with respect to AF or AF with left-ventricular dysfunction (e.g., decompensated heart failure) for a large and geographically widespread patient population. These centers would be centralized in terms of their function, but not necessarily geographically centralized.

Centralized data processing, ultimately with data from possibly millions of recordings, may provide for high detection accuracy and is an ideal application for machine learning or artificial intelligence, which could utilize pattern-recognition algorithms on these datasets to provide an early indication of any characteristic pathological developments, which can then be confirmed or ruled out in a traditional healthcare setting using conventional techniques and modalities. Continuous patient feedback through the smartphone, potentially even using *gamification* to

create a game-type application, may improve patient engagement and adherence to proposed lifestyle or dietary changes and pharmacological compliance. This platform may also be an ideal tool for running very large cost-effective clinical studies, in that data collection can take place using the thumb ECG. Patients can use the device and the smartphone app in the privacy of their own homes to track their own results and monitor symptoms. This could likely be done at a very low cost with few technical or logistical barriers. While visionary in concept, such a system may provide a unique solution for improved patient outcomes through early intervention and close follow-up of treatment with potential (and substantial) reductions in cost and resource utilization to the healthcare system.

12. Conclusions

AF is a prevalent arrhythmia that poses a significant burden on the healthcare system, but it is under-diagnosed in that it can be challenging to capture the arrhythmia on a 12-lead ECG (required for diagnosis), and up to a third of patients are asymptomatic. The thumb ECG offers an innovative, user-friendly approach to consistent cardiac self-monitoring that may provide new insights into the incidence and prevalence of AF. The use of pattern-recognition algorithms, artificial intelligence, and smartphone apps may allow the thumb ECG both to facilitate care for cardiac patients in the future and to make large studies of arrhythmias more cost effective.

Conflict of interest

MS is employed by Coala Life AB, Stockholm, Sweden. The other authors have no conflict of interests.

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