Monitoring and diagnosis of intermittent arrhythmias: evidence-based guidance and role of novel monitoring strategies

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Mafalda Carrington was born in Coimbra, Portugal in 1991. She graduated in Medicine from the Faculty of Medicine, University of Porto in 2015 (MD) and completed 1 year of general residency training at Centro Hospitalar Universitário Lisboa Central in 2016. She performed her

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Abstract

Technological advances have made diagnosis of heart rhythm disturbances much easier, with a wide variety of options, including single-lead portable devices, smartphones/watches to sophisticated implantable cardiac monitors, allowing accurate data to be collected over different time periods depending on symptoms frequency.

This review provides an overview of the novel and existing heart rhythm testing options, including a description of the supporting evidence for their use. A description of each of the tests is provided, along with discussion of their advantages and limitations. This is intended to help clinicians towards choosing the most appropriate test, thus improving diagnostic yield management of patients with suspected arrhythmias.

Keywords: ECG Monitoring; Holter; Implantable Cardiac Monitors; smartphones; smartwatches; external loop recorders

Introduction

Heart rhythm monitoring options have expanded beyond the classic 12-lead surface electrocardiogram (ECG) and Holter monitors, now including portable devices, wearable continuous ECG monitoring patches, smartphones, and smartwatches (**Graphical abstract**). Knowledge of the benefits and limitations of each type of test may help improve its diagnostic yield and management of arrhythmias. Prolonged out-of-hospital heart rhythm monitoring is a key component of assessment of atrial fibrillation (AF) burden, as well as other suspected arrhythmias in patients who present with unexplained symptoms such as syncope or palpitations, or who have 12-lead ECGs that show rhythm disturbances. In this report, we summarize the available novel tests and their supporting evidence.

1. Electrocardiogram

The 12-lead ECG is a cost-effective and widely available test with proven reliability and validity in many populations to detect cardiac disease.(1) Resting ECGs can provide significant information about atrial and ventricular arrhythmias (VA), as well as heart rhythm disturbances, but only depict ~10 seconds of cardiac activity; hence, they usually miss transient symptomatic arrhythmias (**Table 1**). On the other hand, ECG analysis provides other important information, such as signs of ischaemia or prior myocardial infarction (MI),(2) implications for tendency to supraventricular arrhythmias (SVT) or VA or localisation of accessory pathways and premature ventricular complexes.(3) In elderly patients, in whom the incidence of asymptomatic arrhythmias increases, normal resting ECG decreases the likelihood of abnormal 24-hour Holter monitoring,(4) raising a possible need for longer monitoring options in this population.

Furthermore, in-hospital ECG monitoring by telemetry can be used for diagnosis of different aetiologies underlying cardiac syncope and palpitations, or to detect asystolic responses during provocation tests (e.g. cardiovascular autonomic testing for unexplained syncope (US) or orthostatic intolerance), or during EEG and video recording for unexplained seizures and psychogenic attacks.

2. Exercise ECG

Exercise stress testing includes electrocardiographic, blood pressure and clinical monitoring during exercise on a treadmill or exercise bicycle, and at rest immediately following exertion which should be performed in settings where resuscitation equipment and trained personnel can promptly intervene, particularly in patients with a history or risk for potential life-threating VA (**Table 1**).(5)

Exercise stress testing can be important in assessing symptoms such as chest pain, tiredness, pre-syncope and syncope that occur during or immediately after exertion, and might correspond to myocardial ischaemia, but also to chronotropic competence or exercise-induced arrhythmias or atrioventricular (AV)-block (**Table 2**).

When syncope is reproduced after exercise, during recovery, and it is concomitant with severe hypotension, a reflex mechanism is suggested.(6) On the other hand, syncope during exercise in adults is probably of primary cardiac origin, as may be evident in the exercise ECG tracing showing VA, with or without signs of ischaemia. Cardiac syncope can also be confirmed, albeit rarely, when 2nd or 3rd-degree AV-block develop during exertion, even in absence of transient loss of consciousness during the test. Electrophysiology studies (EPS) have demonstrated that, in

these cases, when atrial rate increases, there is an infra-nodal block,(7) that may be explained by abnormality, usually fibrosis, of the His-Purkinje system, indicating that increased sympathetic tone fails to enhance conduction during exercise.(8)

Exercise stress testing is also of interest for non-invasive risk stratification of patients with cardiomyopathies, inherited primary arrhythmic syndromes or myopericarditis. An example is standardized clinical evaluation for SCD-risk stratification of patients with hypertrophic cardiomyopathy (HCM) which implies a symptom-limited exercise test beside 48-hour-Holter monitoring. Similarly, exercise stress testing is recommended to achieve diagnosis/risk stratification in patients with VA who have intermediate to high probability of coronary artery disease (CAD), or in those with suspected exercise-induced VA, monomorphic ventricular tachycardia (VT) or polymorphic VT. In the context of catecholaminergic polymorphic VT (CPVT) and in long QT syndrome (LQTS),(5) where stress testing can provoke arrhythmia and unmask the syndrome by showing paradoxical QTc prolongation during recovery. This finding is relevant to LQTS 1 patients, where exercise may trigger arrhythmias.(9) In addition, the appearance of high-grade premature ventricular complexes (PVCs) (defined as either frequent (>10 per minute), multifocal, R-on-T type, or ≥2 PVCs in a row) occurring during recovery of an exercise stress test was associated with long-term risk of cardiovascular mortality in asymptomatic individuals, whereas PVCs occurring only during exercise were not associated with increased risk.(10) Exercise testing and ambulatory ECG monitoring are also indicated for non-invasive risk stratification of asymptomatic patients with pre-excitation on ECG, such as Wolff-Parkinson-White syndrome. Induced or intermittent loss of pre-excitation on exercise testing, resting electrocardiogram and Holter are low-risk features favouring clinical follow-up

instead of accessory pathway catheter ablation.(3) Finally, after myopericarditis, athletic patients should not resume training and competition until 24-hour Holter and exercise stress testing confirm absence of clinically relevant arrhythmias.(11)

3. Smartphones and smartwatches

At present, ambulatory single-lead devices incorporated in smartphones/watches can be used intermittently to monitor heart rhythm and send ECG strips to treating physicians through integrated mobile transmitters (**Table 1**).

Using electrodes

AliveCor®KardiaMobile® system is a Food and Drug Administration (FDA)-approved handheld ECG portable device. It allows the patient to record single-lead ECGs by placing two fingers, one of right and left hand, and/or the wrist on two electrodes incorporated in a handheld device, iPhone® case or Apple Watch® wrist band.(12) Finger contact activates ECG recording of bipolar lead I to be interpreted by an algorithm in an iPhone® or Android™app, which has been validated as reliably differentiating AF from sinus rhythm,(13) especially when supported by physician review.(14) After exclusion of unclassified recordings (28%), KardiaMobile® algorithm for automatic interpretation of rhythm strips yielded 97% sensitivity and 94% specificity for AF detection, compared with physician-interpreted 12-lead ECGs (kappa 0.85).(15) In a randomized controlled trial of AF screening, using AliveCor®KardiaMobile® twice weekly comparing with routine care in patients aged more than 64-years and with CHADS-VASc≥2,(16) AliveCor® increased AF diagnosis by 4-fold, at a cost per diagnosis of

$10,780 (£8,255).(16) In a cohort with the same age-range, the SEARCH-AF study demonstrated the value of AliveCor® algorithm for AF screening in a 'real-world' primary care setting, yielding high sensitivity and specificity, compared with general practitioner review of the tracings or 12-lead ECG.(17) Interestingly, the AliveCor®KardiaMobile® device may also record atrial flutter waves by placing the electrodes on right hand and left knee, similar to lead II of a traditional 12-lead ECG.(18) For patients presenting to the emergency department with palpitations and pre-syncope, the AliveCor®KardiaMobile® device in addition to standard care allowed a 6-fold increase in symptom-ECG correlation compared with standard care at 90 days.(19) In addition, in patients presenting with intermittent palpitations, a specific diagnosis was possible in the majority with AliveCor®KardiaMobile® device, which was non-inferior to simultaneous external loop recorders (ELR) in revealing symptomatic arrhythmias.(20) Recently, AliveCor®KardiaMobile® launched a six (limb) leads device, incorporating a third electrode on its underside to contact the skin of the patient's left leg. Interestingly, it received FDA-clearance for AF burden assessment and for the calculation of the corrected QT interval, a utility that can potentially change the paradigm of the monitoring of acquired or congenital changes to this interval, by identifying those at a higher risk of potentially life-threatening arrhythmias.

CardioSecur® is another option of mobile-based ECG that uses 4-electrodes and a cable that connects to a tablet or smartphone equipped with a software that depicts 22 reconstructed ECG-leads. This system is portable and less prone to error in placement on the patient's chest. *Spaich et al.* demonstrated that the implementation of CardioSecur® is more feasible, user-friendly and has similar diagnostic yield in the prehospital emergency setting, comparing to conventional 12-lead ECG.(21) Similar results were obtained during maximal exercise when compared to 12-lead

ECG (22) and also improved diagnosis in patients with cardiovascular symptoms in the primary care setting.(23)

Using photoplethysmography sensors

Likewise, recent smartphones can also detect pulsatile signals related to cardiac-induced variations in tissue blood flow in fingertips placed over the camera lens or in facial video recordings.(24) These smartphones incorporate photoplethysmographic (PPG) sensors on their cameras that measure changes in blood flow based on the reflected light intensity from light-emitting diode flashes. These signals generate pulse intervals (tachograms) which can be classified as regular or irregular, based on the pulse interval variation. So far, several smartphone camera applications have also been created for diagnosing AF.(12) In a systematic review and meta-analysis which included 3,852 participants and four applications (Cardiio Rhythm, FibriCheck®, Heartbeats Preventicus, Pulse-SMART), combined sensitivities and specificities were 94% and 96%, respectively.(25) Although negative predictive value was also high for all analyses, the positive predictive value in asymptomatic individuals aged≥65-years was modest (19-38%), suggesting that using these applications in an asymptomatic population may generate a high number of false-positives.(25) These smartphone applications analyse regularity of PPG signals and the diagnosis is made if it reaches a threshold of irregular timing (usually measured by the Root Mean Square of Successive Difference (RMSSD) of RR intervals) and a consecutive period (typically >30 seconds) of non-identical morphology.(25) Therefore, sinus bradycardia and ectopic beats during regular sinus rhythm are potential causes of false detection of AF (false-positives). The ectopic beats can been minimized by specific algorithms that detect the typical

short-long RR sequence, used in the Pulse-SMART application.(26) As previously stated, false-negative rates in the diagnosis of AF are negligible.(15)

Smartwatches also have PPG sensors incorporated in their case, on the side that is in contact with the wrist. These sensors intermittently and passively measure changes in blood flow at the wrist while during rest and can measure pulse rate and regularity. In the Apple Heart Study, among participants who received irregular pulse notifications from their watches, 34% had AF on subsequent ECG patch readings and 84% had concordant notification on the Apple Watch® application.(27) In the WATCH AF trial, although PPG-based automated AF detection algorithms using smartwatch' recordings have high diagnostic accuracy when compared with blinded cardiologists' assessment of these devices tracings, its applicability may be limited by uninterpretable recordings, which may be present in up to 20% of cases.(28) The accuracy of heart rate measurements using three different smartwatches was compared in patients undergoing EPS for SVTs and/or palpitations. The accuracy (within ±10 bpm of an ECG) was 100%, 90%, and 87% for the Apple Watch® Series 2, Samsung Galaxy Gear S3, and Fitbit Charge 2, respectively.(29) A case series of symptomatic patients with palpitations using smartwatches to document VT was recently published.(30) Therefore, these technologies may be useful for diagnosing both SVT and VT, although the existing evidence is limited to case reports and small case series.

4. Extended rhythm recording using patches and wearables

These are lightweight, water-resistant adhesive patches, which allow patients to have light showers. They are easy to self-apply and enable up to 14-days continuous single-lead rhythm

monitoring, with better compliance than traditional 3-lead Holter (**Table 1**).(31) A button can be pressed by patients to annotate symptoms, thus facilitating symptom-ECG correlation in those with possible arrhythmia.(31)(32) In a cross-sectional study including 26,751 patients referred for heart rhythm monitoring for various reasons, the Zio® patch (iRhythm Technologies©, San Francisco, USA) had high patient compliance, high analysable signal time (99% of total wear time that had a mean of 7.6±3.6 days), and an incremental diagnostic yield beyond 48-hours for all arrhythmia types.(31) Furthermore, in patients referred for cardiac arrhythmia evaluation and undergoing simultaneous monitoring with Zio® patches and 24-hour Holter, the ECG patches were more effective in detecting clinically relevant arrhythmias.(32) Similarly, validation of 24-hour recordings of Cardiostat™ patches with simultaneous 24-hour Holter monitoring for AF detection showed that the Cardiostat™ patches had excellent correlation (kappa 0.99) with Holter. However, Holters were superior in discriminating premature atrial and ventricular beats as 3-lead systems offer a vector-based approach.(33) Other options include smart clothes embedded with single-lead ECG devices for heart rhythm monitoring and other wearable biosensors allowing breath, temperature and sweating analyses, as well as monitoring of posture changes with 5G geolocation and real-time alert allowing immediate assistance in case of emergency. T-shirts, gloves, headbands wristbands or insoles are washable making them suited to young/physically active individuals (e.g. symptoms during sports activity)(https://accyourate.com/pages/accyourate).(34)

5. Holters, event monitors and telemetry

Holter monitors (**Table 1**) are small, lightweight devices that typically record three leads of continuous ECG data from electrodes placed on the patient's chest, although 12-lead devices are also available. Holters are relatively inexpensive, and they are appropriate for patients experiencing frequent arrhythmias, especially daily or more than once weekly episodes (**Table 2**),(6) and for the assessment of chronotropic incompetence during daily living activities. Although 24-hour Holter monitoring is more frequently available, extended arrhythmia assessment is also possible with 48, 72-hours and even 7 days Holter monitors. However, diagnostic yield in patients presenting with non-daily symptoms is relatively low. *Kühne et al.*(35) showed that the diagnostic yield of 24-hour Holter monitoring in 826 patients with syncope was only 8.6%. Though slightly higher in subgroups with structural heart disease and advanced age, authors demonstrated a low additional impact of Holter diagnosis on device implantation. Holter monitoring often coincides with lack of symptoms during recordings and should be regarded as useless in syncope patients. In a prospective trial, Sivakumaran *et al.*(36) demonstrated that 1-month loop recorders had a much higher diagnostic yield than 48-hour Holters in patients referred for monitoring due to syncope or presyncope (56%vs22%,$p<0.001$). A cost-effectiveness analysis of this trial has shown that loop recorders tripled diagnostic yield of Holters,(37) without increasing cost per diagnosis. Conversely, in a systematic review of studies dedicated to AF screening, the detection rates of multiple ECG recordings on portable handheld devices (AliveCor®, Zenicor™, MyDiagnostick™, Omron Heartscan HCG-801™, Remon RM-100™) were comparable with 24-hour Holter monitoring.(38) Upon patient activation, these devices with two to three electrodes typically generate 30-seconds tracings that can be stored for

posterior review by the treating physician. In the STROKESTOP trial, Svennberg *et al.* screened for AF individuals aged 75-76 years with a handheld Zenicor™ device used twice daily for 2 weeks, and showed a small net benefit in terms of ischaemic or haemorrhagic stroke, systemic embolism, bleeding leading to hospitalisation, and all-cause death, compared with standard of care.(39)

Event monitors are also small, lightweight devices that typically record one to two lead-ECGs but are more expensive than Holter monitors as they have more sophisticated equipment and can be used for two to four weeks (**Table 2**). There are two types: 1- post-event recorders (non-looping) that can be placed on the patient's chest at the onset of symptoms and store the rhythm for 30-150 seconds after a button has been pushed, 2- loop event recorders that continuously record for a pre-specified period and will save the data only when trigger to do so. In those with symptomatic arrhythmias, manual-activation can be done by the patient who pushes an event-button for rhythm recording. In contrast, more recent equipment also allows an auto-trigger recording and storage of asymptomatic arrhythmias at preselected rhythm thresholds. Modern event monitors allow ECG data for triggered events to be sent to the monitoring station for review in real-time by physicians. Nevertheless, failed activation is a common problem, most frequently occurring in patients who live alone, are unfamiliar with technology and have a low motivation.(40) In a registry enrolling 395 individuals, ELRs were diagnostic in 25% of patients with US and in most (72%) patients with unexplained palpitations.(41) Diagnostic yield increased with early referral and use, history of SVT and frequent episodes.(41)

Finally, continuous ambulatory cardiac telemetry monitoring offers hybrid solution with event recording and real-life monitoring up to 30 days, such as PocketECG™. This is a 3-lead ECG

portable device that provides online telemetry and immediate feedback from a 24-hour monitoring centre when arrhythmia is detected.(42) Similarly, Mobile Cardiac Outpatient Telemetry (MCOT) 2-leads system monitors rhythm during a period of up to 30 days and, in symptomatic patients, can lead to higher diagnostic yield, comparing with standard patient-activated single-lead ELR (88%vs75%,p=0.008).(43) Although unmonitored periods are easily identified with MCOT, a total of 7% of the patients did not comply with the protocol that required a minimum of 25 days of monitoring. Patients reported difficulties in using the devices, interference with their work or travel and skin irritation from the electrodes.(43) Similar to event monitors, continuous ambulatory telemetry can be equipped with algorithms for automatic arrhythmia detection and can also be patient-activated. Other options include beat-to-beat hybrid blood pressure and ECG monitoring for hypotensive episodes along with bradycardia.

6. Implantable cardiac monitors

Implantable cardiac monitors (ICMs) are devices measuring between 45 to 78mm long and 7 to 9mm wide (**Table 1**), typically inserted subcutaneously in the left parasternal region. ICMs store events automatically according to programmed criteria or when triggered by the patient. Stored events can be relayed to the physician using home downloads, allowing remote analysis. Their batteries may last beyond three years, and they are MRI-conditional. European Society of Cardiology (ESC) recommendations on ICM implantation are described in **Table 2**.

Based on two real-world, prospective registries,(44)(45) ICMs were most frequently implanted because of US (91%), and 38-48% of patients experienced an episode of syncope, presyncope, palpitations or significant arrhythmia after ICM implantation. After an average follow-up of

10±6 months, the ICM-guided diagnosis was possible in around 30%; most cases showed bradyarrhythmia. In a meta-analysis of five studies,(6) patients with syncope randomized to either ICM or conventional strategy with ELR, tilt testing and EPS, those with prolonged ICM monitoring had a 3.6-fold higher probability of diagnosis, with higher cost-effectiveness than conventional strategy. In addition, microeconomic analysis of the PICTURE registry identified an opportunity to reduce costs associated with both number and types of diagnostic tests used in the initial phase of syncope investigation, before ICM implant.(46) In a study of 50 patients with unexplained, infrequent, sustained palpitations, Giada *et al.* also demonstrated higher diagnostic yield of ICM compared to conventional strategies including a 24hour-Holter, a 4-week ELR and a EPS (73%vs21%,p<0.001), with lower cost per diagnosis.(47) In addition, a recent retrospective real-world study showed a diagnostic yield of 51%, 60% and 40% in patients with ICM implanted due to US, palpitations and suspected AF, respectively.(48)

But ICM indications are progressively expanding beyond US, and many studies have proven its efficacy in the diagnosis of underlying arrhythmias in other clinical situations such as in cryptogenic stroke, unexplained recurrent falls or high arrhythmic risk in post-MI patients (**Table 2**). In the 6-12 months following a cryptogenic stroke, the authors of the CRYSTAL-AF and PER DIEM trials demonstrated that ECG monitoring with ICM was 3 to 6-fold superior for AF detection, compared with conventional strategies of in-hospital telemetry, 24-hour Holter and ELR for 30 days.(49)(50) However the benefit of early AF diagnosis is not clear. In the PER DIEM trial, although AF was significantly more diagnosed in patients with ICMs and all patients with AF initiated oral anti-coagulation, there were no significant differences for the secondary outcomes of recurrent ischaemic events, death or haemorrhagic events.(50) Also, in the LOOP

study, which included individuals aged 70-90 years and with at least one additional stroke risk factor, ILR screening resulted in a 3-fold increase in AF detection and anticoagulation initiation compared to usual care, but there was no significant reduction in the risk of stroke or systemic arterial embolism in this population.(51)

In addition, an ICM may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective and in patients with unexplained falls, in whom pooled analysis has shown that ICM monitoring can document and attack in 62% and 70% of patients and allow the identification of an arrhythmic cause in 26% and 14% of them, respectively.(6)

Another area of expanding interest for ICM indications is autonomic dysfunction after MI. Cardiac autonomic function can be assessed using a 20-minute high-resolution digital ECG that allows calculation of 2 novel biosignals (periodic repolarisation dynamics and abnormal deceleration capacity of heart rate) that identify a high-risk group of post-MI patients with left ventricular ejection fraction>35%, as they are strong and independent predictors of all-cause and cardiovascular mortality at 3-5 years.(52)(53) In such patients, ICM monitoring allowed the detection of a 6-fold higher rate of serious arrhythmic events, including AF ≥6 minutes (23%), 2nd degree Mobitz II AV-block or higher (7%) and sustained VT or ventricular fibrillation (4%), compared with conventional clinical follow-up.(54)

Complications related to monitoring are low, ranging from 1.7-3.3%.(45)(48)(55) In an observational study including 540 patients, implant site infection was observed in 1.5%, pain requiring device removal or revision in 1.5%, hypertrophic scar in 0.2% and device malfunction in 0.2%. In addition, Lim *et al.* demonstrated that the Reveal LINQ^{TM} (Medtronic©, Minnesota,

USA) could be safely implanted in the outpatient setting by nurses,(56) leading to significant cost reductions compared with physician-implants in the electrophysiology laboratory.

Here we have reviewed the advantages and limitations of contemporary rhythm monitoring options, as well as current ESC recommendations on the role of prolonged heart rhythm monitoring in symptomatic and asymptomatic patients (**Table 2**). We have included 27 indications, 15 with class of recommendation I, 8 with class IIa, 5 with level of evidence A and 8 with level C. Although it is essential to grade the level of evidence and strength of recommendation according to predefined scales, some of the indications are still supported by weak evidence (e.g. single cohort studies or simple review articles that do not fulfil the criteria for level B). This highlights the fact that heart rhythm monitoring options deserve future study. Despite the large range of available diagnostic tools, their application in clinical practice is frequently limited due to increased workload (specially in devices requiring longer monitoring such ELR, MCOT and ICMs), lack of authorities' clearance for medical use and reimbursement. Artificial intelligence (AI) is fast evolving and may help to decrease the burden of tracing analysis for remote monitoring teams.(57) In addition, with recent advances in big data analytic platforms, artificial intelligence methods to combine clinical data and the tracings obtained by rhythm monitoring devices will help predict which patients may develop AF in the future.

Conclusions

Technological advances have made diagnosis of heart rhythm disturbances much easier, with a wide variety of options that allow accurate data to be collected over different time periods depending on symptoms frequency. A more personalized form of healthcare is possible as

clinicians have at their disposal many options, including continuous *versus* intermittent monitors, that can be wirelessly remote and of varying durations. Choosing the most appropriate test will improve diagnostic yield and facilitate management of patients with suspected arrhythmias.

Learning points:

- Technological advances have amplified the options for heart rhythm monitoring
- Optimum choice of test depends on symptom frequency and improves diagnostic yield
- More precise arrhythmia diagnosis will lead to better management of patients
- Advantages and limitations of contemporary rhythm monitoring options exist
- ESC recommendations on heart rhythm monitoring options are provided

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1 **Table 1 – Test available for assessing heart rhythm**
2

Test	Examples	Description	Benefits	Limitations
ECG	Non-applicable	12 lead ECG	Ability to accurately diagnose arrhythmia. Provides other important information (e.g. ischaemia, focus of arrhythmia, accessory pathway localisation).	Difficult to obtain outside of hospital setting. Abnormal heart rhythm may be transient and may be missed at the time of having ECG.
Exercise ECG	Exercise stress test	ECG recorded whilst exercising on a treadmill or exercise bike. Blood-pressure and symptoms are also monitored during exercise and during recovery period.	Supervised assessment for diagnosis. Tries to reproduce arrhythmia, syncope or chronotropic incompetence as they would occur during ambulatory activity. Risk assessment for accessory pathways.	Not all patients are able to manage the treadmill (e.g. advanced arthritis). Needs equipment which is associated with a cost and requires trained staff which may not be readily available.
Smartphones and smartwatches	KardiaMobile®(Alivecor®) Phones applications (e.g. Cardiio Rhythm, FibriCheck, Heartbeats Preventicus, Pulse-SMART)	Detect atrial fibrillation, bradycardia, tachycardia, and normal sinus rhythm.	Practical and versatile. Ability to check at any time. Can be purchased for personal use. Higher chance of picking up arrhythmia.	May have a cost to the individual (~£100). May cause anxiety and frequent checking. Uninterpretable recordings. High number of false positives. Limited evidence of benefit from treating incidental, asymptomatic abnormal heart rhythms. No specific diagnosis provided.

				of irregular arrhythmia – requires further assessment to confirm.
Extended rhythm recording using patches and wearables	Cardiostat™ (Icentia), Zio® patch (iRhyhthm) YouCare™ (ZTE© and AccYouRate©)	Up to 30 days	Self-applied High patient compliance Continuous prolonged monitoring Button for symptom annotation	Single-lead ECG Limited capacity of discriminating atrial or ventricular ectopic beats.
Holters, event monitors and telemetry	24-to-72-hour and 7 days Holter monitoring, Handheld devices (e.g. MyDiagnostick ™, Zenicor ™), External Loop Recorders (ELR) and Post-Event Recorders (non-looping), Ambulatory continuous cardiac telemetry monitoring (e.g. PocketECG ™)	A continuously or intermittently recording ECG, for variable periods of time, to help diagnose the cause of symptoms, such as palpitations, which usually are not constant and rarely happen at time of resting ECG.	Holters: can pick up arrhythmia occurring on a frequent basis; Handheld devices and Post-event recorders: can pick up symptomatic arrhythmia, even when rare; ELR: can pick up arrhythmia occurring more rarely, either symptomatic or asymptomatic; Ambulatory continuous telemetry: possibility of wireless transmission of rhythm strips.	Holters: often non-diagnostic due to limited period for testing; anxiety or false reassurance when no arrhythmia is detected; Handheld devices, event monitors and ambulatory continuous telemetry: more expensive than Holters; failed diagnosis of the symptoms is common in patients who live alone or are unfamiliar with technology.

Implantable Cardiac Monitor (ICM)	BioMonitor III™ (Biotronik©), 78x8mm CONFIRM Rx™ (Abbott©), 49x9mm Reveal LINQ™ (Medtronic©), 45x7mm LUX-Dx™ (Boston Scientific©), 45x7mm	About the size of a small USB stick. Battery lasts over five years. Insertion of ICM is a simple and quick procedure done in a normal clinic room environment, with current models being injected to the subcutaneous tissue on the chest	Good option if other cardiac event recorders fail to reveal anything. Useful in infrequent symptoms (e.g. recurrent syncope, especially in the presence of red flags) Possibility of detecting serious arrhythmias during sleep. Possibility of remote monitoring with serious arrhythmic events quickly detected and leading to immediate patient assessment.	Costly (device ~£2400 + implantation in the procedure room ~£100 (58)) Requires minor invasive procedure in hospital for initial implant and removal. Local complications such as implantation site infection, pain requiring device removal or revision or hypertrophic scar (low rates).

Table 2. Summary of recent guideline recommendations on the role of heart rhythm assessment

ESC Guidelines recommendations	Class	Level	Evidence	Guideline
Electrocardiograms				
ECG documentation is required to establish the diagnosis of AF.	I	B	1 cohort study	AF (2020)
Resting 12-lead ECG is recommended in all patients who are evaluated for VA.	I	A	Expert consensus document	VA and prevention of SCD (2015)
Exercise stress testing				
Exercise stress testing is indicated in patients who experience syncope during or shortly after exertion.	I	C	Expert opinion	Syncope (2018)
Exercise stress testing is recommended in adult patients with VA who have an intermediate or greater probability of having CAD by age and symptoms to provoke ischaemic changes or VA.	I	B	Expert consensus document	VA and prevention of SCD (2015)
Exercise stress testing is recommended in patients with known or suspected exercise-induced VA, including CPVT, to achieve a diagnosis and define prognosis.	I	B	Systematic review article	VA and prevention of SCD (2015)
Exercise testing is recommended in patients who experience symptoms suspicious of bradycardia during or immediately after exertion.	I	C	Expert opinion	Cardiac pacing and CRT (2021)
In patients with suspected chronotropic incompetence, **exercise testing** should be considered to confirm the diagnosis.	IIa	B	1 cohort study	Cardiac pacing and CRT (2021)

In patients with intraventricular conduction disease or AVB of unknown level, **exercise testing** may be considered to expose infranodal block.	I	C	Expert opinion	Cardiac pacing and CRT (2021)
Holter monitors				
Ambulatory ECG is recommended to detect and diagnose arrhythmias. **12-lead ambulatory ECG** is recommended to evaluate QT-interval changes or ST changes.	I	A	1 RCT	VA and prevention of SCD (2015)
Holter-monitoring should be considered in patients who have frequent syncope or presyncope (≥ 1 episode per week).	IIa	B	1 cohort study	Syncope (2018)
24 h (or multiday) ambulatory ECG monitoring should be considered for diagnosis of tachycardia-induced cardiomyopathy by identifying subclinical or intermittent arrhythmias	IIa	B	Review articles + 1 cohort study	SVT (2019)
In patients with acute ischemic stroke or TIA and without previously known AF, monitoring for AF is recommended using a **short-term ECG recording** for at least the first 24 h, followed by continuous ECG monitoring for at least 72 h whenever possible.	I	B	3 RCT + 1 cohort study	AF (2020)
Ambulatory ECG monitoring is recommended in the evaluation of patients with suspected bradycardia to correlate rhythm disturbances with symptoms.	I	C	Expert opinion	Cardiac pacing and CRT (2021)
External event monitors				
ELR should be considered, early after the index event, in patients who have an inter-symptom interval ≤4 weeks	IIa	B	1 RCT + 3 cohort study	Syncope (2018)

Cardiac event recorders are recommended when symptoms are sporadic to establish whether they are caused by transient arrhythmias.	I	B	1 cohort study	VA and prevention of SCD (2015)
Ambulatory continuous ECG monitoring (implantable or external) for 7-30 days or EPS should be considered for patients with new LBBB with QRS >150 ms or PR >240 ms with no further prolongation during the >48 hours after TAVI.	IIa	C	Expert opinion	Cardiac pacing and CRT (2021)
Ambulatory continuous ECG monitoring (implantable or external) for 7-30 days or EPS may be considered for patients with a pre-existing conduction abnormality who develop prolongation of QRS or PR>20 ms after TAVI.	IIb	C	Expert opinion	Cardiac pacing and CRT (2021)
Implantable Cardiac Monitors				
ICM is indicated in an early phase of evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria, and a high likelihood of recurrence within the battery life of the device.	I	A	5 RCT + 5 cohort studies	Syncope (2018)
ICM is indicated in patients with high-risk criteria in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment, and who do not have conventional indications for primary prevention ICD or pacemaker indication.	I	A	5 RCT + 4 cohort studies	Syncope (2018)
ICM should be considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal	IIa	B	1 RCT + 2 cohort studies	Syncope (2018)

episodes.				
Instead of an ICD, an **ICM** should be considered in patients with recurrent episodes of unexplained syncope who are at low risk of SCD, according to multiparametric analysis that takes into account the other known risk factors for SCD in HCM, AC, LQTS and BrS.	IIa	C	Expert opinion	Syncope (2018)
Instead of an ICD, an **ICM** should be considered in patients with recurrent episodes of unexplained syncope with systolic impairment, but without a current indication for ICD.	IIb	C	Expert opinion	Syncope (2018)
ICM may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective.	IIb	B	6 Cohort studies + 1 case report + 1 case series	Syncope (2018)
ICM may be considered in patients with unexplained falls.	IIb	B	1 RCT + 3 cohort studies	Syncope (2018)
ICM are recommended when symptoms, e.g. syncope, are sporadic and suspected to be related to arrhythmias and when symptom-rhythm correlation cannot be established by conventional diagnostic techniques.	I	B	1 cohort study	VA and prevention of SCD (2015)
In selected stroke patients (with cryptogenic stroke suggestive of embolic origin or at risk of developing AF: elderly, with CV risk factors or comorbidities, enlarged LA, high C2HEST score)	IIa	B	1 cohort study	AF (2020)

	without previously known AF, additional ECG monitoring using **long-term non-invasive ECG monitors** or **ICM** should be considered, to detect AF.				
	In patients with infrequent (less than once a month) unexplained syncope or other symptoms suspected to be caused by bradycardia, in whom a comprehensive evaluation did not demonstrate a cause, long-term ambulatory monitoring with an **ICM** is recommended.	I	A	5 RCT	Cardiac pacing and CRT (2021)

Legend: AF = Atrial Fibrillation; AVB = atrioventricular block; AC = Arrhythmogenic Cardiomyopathy; BrS = Brugada Syndrome; ECG = Electrocardiogram; C2HEST score = CAD/COPD (1 point each), Hypertension (1 point), Elderly (≥75 years, 2 points), Systolic heart failure (2 points), and Thyroid disease (hyperthyroidism, 1 point); CAD = Coronary Artery Disease; CPVT = Catecholaminergic Polymorphic Ventricular Tachycardia; CRT = Cardiac Resynchronization Therapy; CV = Cardiovascular; ELR = External Loop Recorder; EPS = Electrophysiology Study; ESC = European Society of Cardiology; HCM = Hypertrophic Cardiomyopathy; ICD = Implantable Cardioverter Defibrillators; ICM = Implantable Cardiac Monitor; LA = Left Atrium; LQTS = Long QT Syndrome; ms = milliseconds; RCT = Randomized Controlled Trial; SCD = Sudden Cardiac Death; TAVI = transcatheter aortic valve implantation; VA = Ventricular arrhythmias.
European Society of Cardiology (ESC) Guidelines: Class of recommendation I = Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective; II = Conflicting evidence and/or divergence of opinion about the usefulness/efficacy of the given treatment or procedure; IIa = Weight of evidence/opinion is in favor of usefulness/efficacy; IIb = Usefulness/efficacy is less well established by evidence/opinion; III = Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful; Level of evidence A = Data derived from

multiple randomized clinical trials or meta-analyses; B = Data derived from a single randomized clinical trial or large non-randomized studies; C = Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Graphical abstract – Illustration of novel monitoring technologies for the diagnosis of intermittent arrhythmias.

Legend: 1. 12-lead resting electrocardiogram (ECG); 2. Treadmill exercise stress test; 3. Single-lead portable devices: A - AliveCor® KardiaMobile®, B - Smartphones and smartwatches; 4. A - Cardiostat™, B- Washable 5G smart T-shirt to monitor ECG and other biosignals: YouCare™ (ZTE© and AccYouRate©); 5. A- Holter and event monitors, B - Zenicor™Smart, C - MyDiagnostic ™; 6. A – Implant location of cardiac monitors, B - BioMonitor III™ (Biotronik©), C - CONFIRM Rx™ (Abbott©), D- Reveal LINQ™ (Medtronic©), E - LUX-Dx™ (Boston Scientific©).
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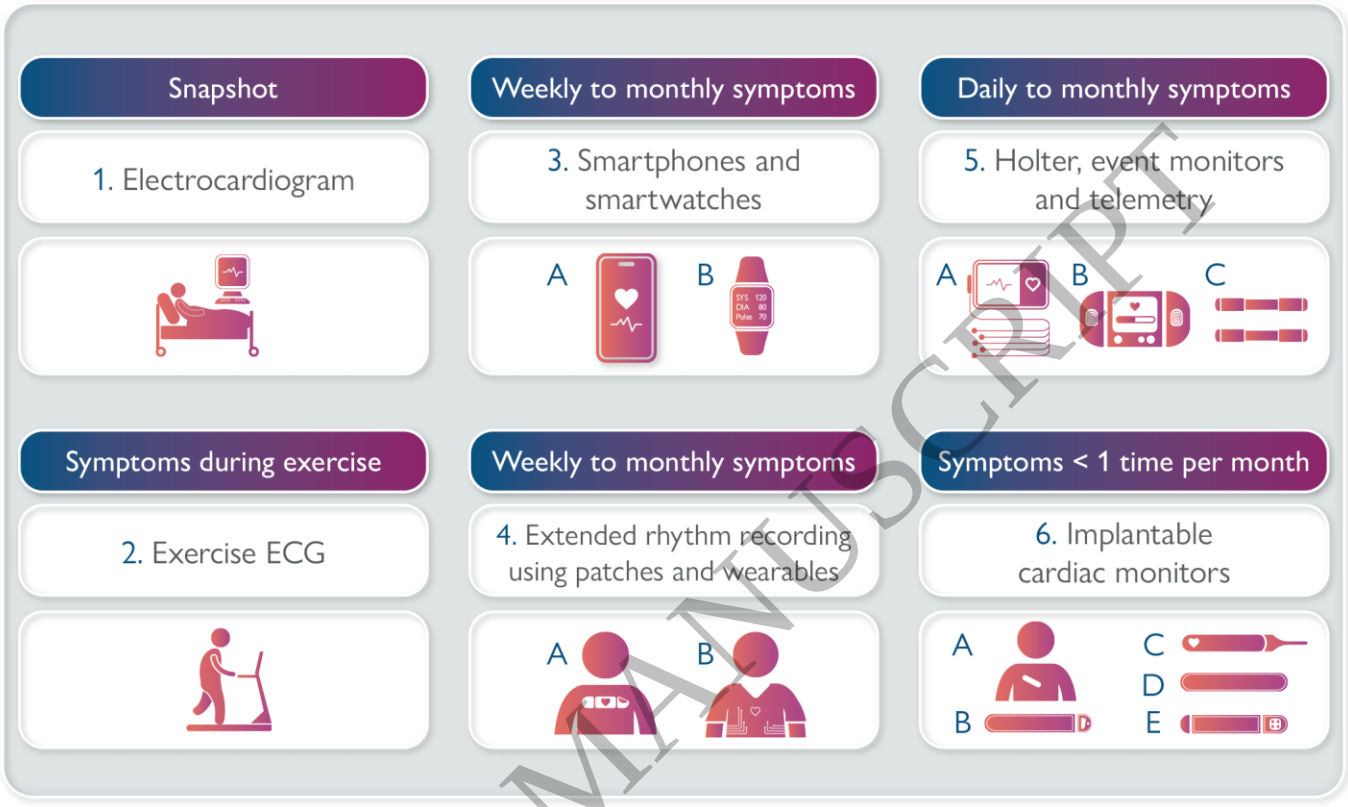

Graphical Abstract
180x109 mm (.90 x DPI)