Lead-I ECG for detecting atrial fibrillation in patients with an irregular pulse using single time point testing: a systematic review and economic evaluation

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Scientific summary

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Background

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia and is associated with conditions such as hypertension, heart failure, coronary artery disease, valvular heart disease, obesity, diabetes mellitus and chronic kidney disease. The National Institute for Health and Care Excellence (NICE) clinical guideline CG180 [NICE. *Atrial Fibrillation: Management. Clinical Guideline CG180*. 2014. URL: www.nice.org.uk/guidance/cg180/chapter/Introduction (accessed January 2018)] recommends that, after positive manual pulse palpation (MPP), the diagnosis of AF should be confirmed based on the results of an electrocardiogram (ECG). People who present to primary care with signs or symptoms of the condition (e.g. palpitations, dizziness, shortness of breath and tiredness) and who have an irregular pulse should receive a referral for a 12-lead ECG in the days following their initial primary care appointment if a 12-lead ECG is not available in the practice. Lead-I ECG devices are handheld instruments that can be used in primary care to detect AF at a single time point in people who present with relevant signs or symptoms and who have an irregular pulse.

Objectives

The aim of this study was to assess the diagnostic test accuracy (DTA), the clinical impact and the cost-effectiveness of using single time point lead-I ECG devices for the detection of AF in people presenting to primary care with signs or symptoms of the condition and who have an irregular pulse compared with using MPP followed by a 12-lead ECG in primary or secondary care (prior to initiation of anticoagulation therapy). To achieve this aim we:

- conducted systematic reviews of the diagnostic accuracy and clinical impact of lead-I ECG devices for (1) detecting AF in people presenting to primary care with signs or symptoms of the condition, or, if evidence was not available for this population/setting, for (2) detecting AF in an asymptomatic population, defined as people presenting to any setting without symptoms of AF, with or without a previous diagnosis of AF
- developed an economic model to assess the cost-effectiveness of using single time point lead-I ECG devices compared with using MPP followed by a 12-lead ECG in primary or secondary care (prior to initiation of anticoagulation therapy) in people presenting to primary care with signs or symptoms of AF who have an irregular pulse.

Methods: assessment of clinical impact and diagnostic test accuracy

Electronic databases [MEDLINE, MEDLINE Epub Ahead of Print and MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, PubMed, Cochrane Databases of Systematic Reviews (CDSR), Cochrane Central Database of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment Database] were searched from inception up to March 2018. Eligible studies assessed the diagnostic accuracy or clinical impact of specified lead-I ECG devices [i.e. imPulse (Plessey Semiconductors Ltd, Ilford, UK), Kardia Mobile (AliveCor Inc., Mountain View, CA, USA), MyDiagnostick (MyDiagnostick Medical B.V., Maastricht, the Netherlands), RhythmPad GP (Cardiocity, Lancaster, UK) and Zenicor ECG (Zenicor Medical Systems AB, Stockholm, Sweden)] in people presenting with signs or symptoms of AF and who have an irregular pulse. Studies that assessed the diagnostic accuracy of lead-I ECG devices used at a single time point to detect AF in an asymptomatic population were considered for inclusion owing to the non-existence of studies in symptomatic populations. We considered an

asymptomatic population to comprise people not presenting with symptoms of AF, with or without a previous diagnosis of AF.

Two reviewers independently screened the search results, extracted data and assessed the methodological quality of the included diagnostic accuracy studies using the QUality Assessment of Diagnostic Accuracy Studies–2 (QUADAS-2) tool. The methodological quality of cross-sectional and case–control studies evaluating the clinical impact of lead-I ECG devices was assessed using the Newcastle–Ottawa quality assessment scale.

The sensitivity and specificity of each index test were summarised in forest plots and plotted in receiver operating characteristic space. Pooled estimates of sensitivity and specificity with 95% confidence intervals (CIs) were obtained using bivariate models. When there were few studies, the bivariate model was reduced to two univariate random-effects logistic regression models by assuming no correlation between sensitivity and specificity across studies. Judgement of heterogeneity, and hence the choice of more simple hierarchical models, was informed by the visual appearance of forest plots and summary receiver operating characteristic plots, in addition to clinical judgement regarding potential sources of heterogeneity. The analyses were stratified by whether a diagnosis of AF was made by a trained health-care professional interpreting the lead-I ECG trace, or by the lead-I ECG algorithm. For both sets of analyses, the reference standard was an interpretation of the 12-lead ECG trace by a trained health-care professional. When studies reported data for two types of lead-I ECG device and two different interpreters, one data set was chosen and sensitivity analyses were performed using the alternative data sets. Clinical impact outcomes were synthesised narratively.

Methods: assessment of cost-effectiveness

The literature was reviewed to identify published economic evaluations on the use of lead-I ECG devices for the detection of AF in people presenting to primary care with signs or symptoms of the condition and who had an irregular pulse. Electronic databases (MEDLINE, MEDLINE Epub Ahead of Print and MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, PubMed, EconLit and the NHS Economic Evaluation Database) were searched from inception up to April 2018. Additional searches were carried out to identify supporting information on costs and health state utility data.

A de novo economic analysis was undertaken that followed the diagnostic pathway for patients presenting to primary care with signs or symptoms indicative of AF and an irregular pulse. The sensitivity and specificity of the different lead-I ECG devices were taken from the results of the review DTA. The probabilistic sensitivity analysis results were presented to reflect uncertainty in the model inputs; extensive deterministic sensitivity analysis and scenario analysis were also undertaken to assess the impact of uncertainty in model assumptions. This study reports the total costs of the annual number of symptomatic patients with positive MPP seen by a single general practitioner (GP), total quality-adjusted life-years (QALYs) for these patients, incremental costs and QALYs, and incremental cost-effectiveness ratios (ICERs). Several scenario analyses were undertaken to investigate the impact of varying some of the base-case assumptions on the size of the ICER per QALY gained. Costs and outcomes of future years over a lifetime time horizon were discounted at an annual rate of 3.5%.

Results

The electronic database searches identified 1151 citations (915 unique records). No studies were identified for the population of interest (i.e. people with signs or symptoms relevant to AF with an irregular pulse). Therefore, all of the studies included in the systematic reviews assessed the diagnostic accuracy and the clinical impact of using lead-I ECG devices at a single time point to detect AF in an asymptomatic population.

Diagnostic test accuracy

A total of 13 publications reporting on nine studies were identified. In these studies, the index test (lead-I ECG device) was interpreted by the device algorithm or by a trained health-care professional; trained health-care professionals included cardiologists, electrophysiologists and GPs. All studies used a 12-lead ECG device interpreted by a trained health-care professional as the reference standard.

Interpreter of lead-I electrocardiogram: trained health-care professional

Data from four studies contributed to the meta-analyses (two studies of Kardia Mobile alone, one study of Zenicor-ECG and one study of MyDiagnostick and Kardia Mobile). The main meta-analysis (AF cases, $n = 118$; total patients, $N = 580$) indicated that the pooled sensitivity of lead-I ECG devices was 93.9% (95% CI 86.2% to 97.4%) and the pooled specificity was 96.5% (95% CI 90.4% to 98.8%). Across the sensitivity analyses, the numerical results were similar; the pooled sensitivity values ranged from 88.0% to 96.2% and the pooled specificity values ranged from 94.4% to 97.4%.

Interpreter of lead-I electrocardiogram: algorithm

Data from four studies were included in the meta-analyses (two studies of MyDiagnostick alone, one study of Kardia Mobile alone and one study of MyDiagnostick and Kardia Mobile). The meta-analysis (AF cases, $n = 219$; total patients, $N = 842$) showed a pooled sensitivity of 96.2% (95% CI 86.0% to 99.0%) and pooled specificity of 95.2% (95% CI 92.9% to 96.8%). The numerical results were similar across the sensitivity analyses; the pooled sensitivity values ranged from 88.0% to 95.2% and the pooled specificity values ranged from 94.4% to 97.2%.

Clinical impact

A total of 24 publications reporting on 19 studies with a total of 33,993 participants were identified. The index tests that were evaluated included imPulse (one study), Kardia Mobile alone (12 studies), MyDiagnostick alone (four studies), Zenicor ECG (one study) and MyDiagnostick and Kardia Mobile (one study). Test failure rate was reported in nine studies and ranged from 0.1% to 9%. The results for test failure rate included both the failure of the lead-I ECG algorithm to produce a result and the poor quality of the lead-I ECG trace. Diagnostic yield was reported in 13 studies. The percentage of new patients diagnosed with AF ranged from 0.4% to 5.8%. Data for this outcome were considered too heterogeneous for a pooled estimate to be clinically meaningful. Only one study reported the concordance between different lead-I ECG devices (Kardia Mobile and MyDiagnostick) and observed no difference in agreement. Two studies reported a change in treatment management following the use of the Kardia Mobile lead-I ECG in new patients diagnosed with AF. The acceptability of lead-I ECG devices was reported in four studies, with generally positive views.

Cost-effectiveness

None of the studies identified assessed the cost-effectiveness of using single time point lead-I ECG devices compared with using MPP followed by a 12-lead ECG in people presenting to primary care with signs or symptoms of AF who had an irregular pulse.

A decision tree and two cohort Markov models were built in Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA). The decision tree describes the pathway followed by a patient presenting to primary care with signs or symptoms of AF and an irregular pulse during the initial GP consultation. The first Markov model captures the differences in the costs and benefits of treatment (standard diagnostic pathway vs. lead-I ECG pathway) during the first 3 months after the initial GP appointment. During this period, some patients will have a diagnosis of AF and start the relevant treatment and other patients will have further tests to diagnose, or to rule out, AF (where 'rule out' means no diagnosis of AF is recorded in the patient's notes and no treatment for AF is started). The second Markov model captured the differences in lifetime costs and benefits after patients have either received a diagnosis of AF or have had AF ruled out.

The de novo economic model yielded ICERs per QALY gained. The results of the pairwise analysis show that all lead-I ECG devices generate ICERs below the £20,000–30,000 threshold usually considered to be cost-effective by NICE. Kardia Mobile appears to be the most cost-effective option in a full incremental analysis and dominates both the standard pathway and the other lead-I ECG devices (costing less and generating more QALYs). The only exception to this is the generic lead-I ECG device, which generates a very small QALY gain but at a cost that produces an ICER well above £30,000 per QALY gained.

Conclusions

There is no evidence available to support the use of single time point lead-I ECG devices for the detection of AF in people presenting with signs or symptoms of AF and an irregular pulse. The results of this assessment, using data from asymptomatic patients as a proxy, suggest that the use of lead-I ECG devices is more cost-effective than MPP followed by a 12-lead ECG in primary or secondary care.

Currently, the standard pathway for the diagnosis of AF indicates that patients with signs or symptoms of AF and an irregular pulse are advised to have a 12-lead ECG test. The benefits accumulated during the time interval between the lead-I ECG tests and the confirmatory 12-lead ECG tests are sufficiently large for lead-I ECG devices to be considered as cost-effective in this specific population.

Study registration

This study is registered as PROSPERO CRD42018090375.

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This report

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