Estrategia de monitorización prolongada para detectar fibrilación auricular tras un ictus criptogénico: utilización de dispositivos Holter con electrodos integrados en camisetas elásticas

Título del documento	Estrategia de monitorización prolongada para detectar fibrilación auricular tras un ictus criptogénico, mediante monitorización por dispositivos Holter con electrodos integrados en camisetas elásticas.
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1. INTRODUCCIÓN

El ictus se clasifica en tres grupos en función de su origen: ictus isquémico, ictus hemorrágico e ictus sin clasificar o criptogénico. El ictus isquémico representa el 82,6% de los casos y dentro de él se encuentra el ictus criptogénico o de etiología desconocida, que representa el 30% de todos los ictus. Se trata de un diagnóstico de exclusión, por lo que la búsqueda de patología embolígena es fundamental.

Entre las causas de ictus isquémico, una de las más frecuentes es la fibrilación auricular (FA). La FA es la arritmia cardíaca más frecuente en la práctica clínica. Afecta al 1-2% de la población general; su prevalencia aumenta con la edad llegando a presentarse en casi el 10% de las personas de más de 80 años. Además es la responsable de uno de cada cinco ictus. Cada año hasta 3 millones de personas en el mundo sufren un ictus relacionado con la FA. En un individuo concreto la presencia de FA multiplica por 5 el riesgo de padecer un ictus.

La FA puede producir síntomas como palpitaciones, disnea o fatiga pero en muchas ocasiones permanece asintomática. Se estima que alrededor del 21% de los casos de FA son asintomáticos. La FA se sospecha a menudo durante un examen físico pero debe ser diagnosticada siempre mediante un electrocardiograma. Si la fibrilación auricular es paroxística (aparece y desaparece de forma espontánea) la realización de un electrocardiograma podría no ser suficiente y necesitaríamos otros medios diagnósticos como un Holter, que es un electrocardiógrafo portátil que puede ser llevado durante la rutina diaria hasta 24 horas, o incluso dispositivos de mayor duración como un registrador de eventos externos o implantables cuya vida útil puede llegar a los 3 años.

El ictus criptogénico puede tener, como causa subyacente, una FA no detectada por los electrocardiogramas convencionales. Ciertamente, la búsqueda activa de episodios de FA como posible etiología del ictus es un tema de actualidad, ya que el infradiagnóstico de fuentes cardioembólicas podría explicar un porcentaje significativo de episodios dentro del 30% de ictus considerados criptogénicos, por lo que la posibilidad de monitorizar el ritmo cardiaco por largos periodos podría permitir un número mayor de diagnósticos.

Ya en el años 2016, a raíz de la revisión por un grupo de expertos de la guía sobre Fibrilación Auricular de la Sociedad Española de Cardiología (1), se recomendaba la monitorización continua durante 72 horas tras un ictus isquémico y posteriormente monitorización ambulatoria cardiaca prolongada, sin aclarar duración, con electrocardiograma (ECG) no invasivos o grabadores de bucle para documentar la FA silente, aplicable especialmente al ictus criptogénico.

Se están investigando nuevas tecnologías de monitorización cardiaca externa, una de ellas consiste en un chaleco de tela elástica inteligente *Textile Wearable Holter (TWH*), que se adosa al cuerpo del paciente y registra su actividad cardíaca.

La empresa Nuubo, una compañía europea localizada en España, especializada en la medicina inalámbrica y la monitorización remota de parámetros fisiológicos, ofrece un sistema de monitorización de ECG para medio-largo plazo, sencillo, completo y eficiente.

La tecnología de electrodos textiles desarrollada por Nuubo simplifica enormemente los incómodos procedimientos tradicionales de conexión de electrodos, reduciéndolos al sencillo acto de vestir un peto. El tejido elástico se adapta a los movimientos del paciente, quien puede realizar su actividad física diaria sin estar limitado por cables y sin necesidad de depender de personal médico especializado. Estas características junto con la información de contexto, la actividad física del paciente y su posición/postura, permite el desarrollo de un nuevo rango de soluciones y casos de uso (https://www.nuubo.com/tecnologia).

A diferencia de los métodos utilizados en la actualidad, la tecnología propuesta TWH, sin cables y sin adhesivos, evita irritaciones en la piel facilitando la tolerancia durante 30 días por parte de los usuarios. Estos registros son analizados después para detectar si existe fibrilación auricular.

2. ¿ES UNA PRESTACIÓN DE LA CARTERA DE SERVICIOS DEL SISTEMA NACIONAL DE SALUD?

Esta tecnología podría quedar incluida en el apartado 5.1.7, en este sentido la Cartera de Servicios tiende a ser generalista y no especificar los procedimientos diagnósticos o terapéuticos. Pero hay que considerar dos aspectos diferentes, uno el que corresponde a la monitorización en sí misma, que no hay dudas de su inclusión y otra la herramienta que se utilice para ello.

5. Indicación o prescripción, y la realización, en su caso, de procedimientos diagnósticos y terapéuticos

5.1 Técnicas y procedimientos precisos para el diagnóstico y tratamiento médico y quirúrgico de las siguientes patologías clasificadas según la Clasificación Internacional de Enfermedades:

5.1.7. Enfermedades del sistema circulatorio: Fiebre reumática aguda, enfermedad cardiaca reumática crónica, enfermedad hipertensiva, cardiopatía isquémica, enfermedades de la circulación pulmonar, otras formas de enfermedad cardiaca, enfermedad cerebrovascular, enfermedades de las arterias, arteriolas y capilares y enfermedades de venas y linfáticos y otras enfermedades del aparato circulatorio.

3. ¿ESTÁ CONSIDERADA UNA TECNOLOGÍA SANITARIA (TS) EMERGENTE PROPUESTA PARA SU PRIORIZACIÓN Y EVALUACIÓN DENTRO DE LA COMISIÓN DE PRESTACIONES ASEGURAMIENTO Y FINANCIACIÓN (CPAF) DE LA SUBDIRECCIÓN GENERAL DE CALIDAD Y COHESIÓN DEL MSSSI?

No está considerada una tecnología sanitaria emergente propuesta para evaluación en 2018. Ni tampoco se ha priorizado para que la Red de Agencias de Evaluación de Tecnologías Sanitarias realice un informe de evaluación para el año 2019.

4. ¿HAY INFORME DE EVALUACIÓN REALIZADO POR UNA AGENCIA DE EVALUACIÓN DE TS O REVISIONES SISTEMÁTICAS DE LA LITERATURA?

Se realizaron tres búsquedas en la literatura científica siguiendo la metodología para búsquedas rápidas:

1. NHS Centre for Reviews and Dissemination (CRD) que incluye

a. -DARE (Database of Abstracts of Reviews of Effects): contiene resúmenes de artículos que valoran y sintetizan RS de efectividad.
b. -NHS EED: contiene resúmenes de artículos sobre evaluaciones económicas de intervenciones en atención sanitaria.
c. -HTA (Health Technology Assessment): contiene informes de evaluación de tecnologías sanitarias e información de proyectos en curso realizados por las mismas agencias.
d. -INAHTA: informes de otras agencias o unidades de Evaluación de Tecnologías Sanitarias. Incluye los informes de la Red Española de Agencias de EvTS.
e. -EuroScan International Network: informes de tecnologías nuevas y emergentes.

2. Biblioteca Cochrane Plus
3. PubMed

Palabras clave: cryptogenic stroke, atrial fibrillation, holter, Textile Wearable Holter TWH.

Fechas: enero 2014 a enero 2019

En la primera búsqueda (NHS CRD), se han encontrado 4 estudios, ninguno en relación con monitorización a través de prendas textiles.

Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, Smith CJ. ***Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis*** *Stroke. 2014 Feb;45(2):520-6.* ***(2)***

> Background and Purpose: Atrial fibrillation (AF) confers a high risk of recurrent stroke, although detection methods and definitions of paroxysmal AF during screening vary. We therefore undertook a systematic review and meta-analysis to determine the frequency of newly detected AF using noninvasive or invasive cardiac monitoring after ischemic stroke or transient ischemic attack.
>
> Methods: Prospective observational studies or randomized controlled trials of patients with ischemic stroke, transient ischemic attack, or both, who underwent any cardiac monitoring for a minimum of 12 hours, were included after electronic searches of multiple databases. The primary outcome was detection of any new AF during the monitoring period. We prespecified subgroup analysis of selected (prescreened or cryptogenic) versus unselected patients and according to duration of monitoring.
>
> Results: A total of 32 studies were analyzed. The overall detection rate of any AF was 11.5% (95% confidence interval, 8.9%-14.3%), although the timing, duration, method of monitoring, and reporting of diagnostic criteria used for paroxysmal AF varied. Detection rates were higher in selected (13.4%; 95% confidence interval, 9.0%-18.4%) than in unselected patients (6.2%; 95% confidence interval, 4.4%-8.3%). There was substantial heterogeneity even within specified subgroups.
>
> Conclusions: Detection of AF was highly variable, and the review was limited by small sample sizes and marked heterogeneity. Further studies are required to inform patient selection, optimal timing, methods, and duration of monitoring for detection of AF/paroxysmal AF.

Canadian Agency for Drugs and Technologies in Health (CADTH), ***Loop recorders to detect atrial arrhythmias in patients post-discharge who have had a cryptogenic stroke: a review of clinical and cost-effectiveness****. Ottawa. Rapid Response-Summary with Critical Appraisal. 2014. This is a bibliographic record of a published health technology assessment from a member of INAHTA.(3)*

The clinical evidence base identified for loop recorders includes four comparative studies (novel technology versus usual care) and, with the exception of one feasibility study, the novel technology showed superior rates of AF detection. A single economic analysis found monitoring to be cost-effective due to detection of AF and subsequent use of anticoagulant therapy. A number of larger studies are underway with two involving Canadian sites.

Context**:** Atrial fibrillation (AF) is the most common type of atrial arrhythmia (irregular heartbeat) and a major risk factor for stroke. Strokes caused by AF result in higher morbidity and mortality than those from most other causes. Because AF is often asymptomatic, there is growing interest in monitoring technologies that can detect AF for days, weeks, or even months after hospitalization — especially for the 20% to 30% of patients whose strokes are cryptogenic (cannot be attributed to a specific cause). Once AF is detected, patients can be treated with anticoagulant drugs, which can reduce the annual risk of recurrent stroke by 40% to 60%.

Technology: Longer monitoring periods may allow for higher AF detection rates. Externally worn loop recorders and Holter monitors can record electrocardiograms for weeks. However, implantable loop recorders —which are surgically inserted under the skin of the chest wall— can record electrocardiograms for up to three years.

Issue: A review of the clinical effectiveness, safety, and cost-effectiveness of loop recorders, compared with Holter monitors, for detecting atrial arrhythmias will help inform decisions about their use in cryptogenic stroke patients following discharge from the hospital.

Methods**:** A limited literature search was conducted of key resources, and titles and abstracts of the retrieved publications were reviewed. Full-text publications were evaluated for final article selection according to predetermined selection criteria (population, intervention, comparator, outcomes, and study designs).

Results**:** The literature search identified 369 citations, with 10 additional articles identified from other sources. After screening the abstracts, 36 were deemed potentially relevant, and 5 met the criteria for inclusion in this review: 4 clinical studies and 1 economic analysis.

Key Messages**:** For detection of AF in cryptogenic stroke patients following discharge from the hospital:

- Both external and implantable loop recorders appear to be better than limited or no post-discharge monitoring.
- Loop recorders were found to be cost-effective (based on limited evidence; devices were assumed to be worn externally).
- Loop recorders and Holter monitors were both found to be generally safe (with one report of contact dermatitis from an external loop recorder).

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Levin LA, Husberg M, Sobocinski PD, Kull VF, Friberg L, Rosenqvist M, Davidson T. ***A cost-effectiveness analysis of screening for silent atrial fibrillation after ischaemic stroke.*** *Europace. 2015 Feb;17(2):207-14 (4)*

Aims: The purpose of this study was to estimate the cost-effectiveness of two screening methods for detection of silent AF, intermittent electrocardiogram (ECG) recordings using a handheld recording device, at regular time intervals for 30 days, and short-term 24 h continuous Holter ECG, in comparison with a no-screening alternative in 75-year-old patients with a recent ischaemic stroke.

Methods and results: The long-term (20-year) costs and effects of all alternatives were estimated with a decision analytic model combining the result of a clinical study and epidemiological data from Sweden. The structure of a cost-effectiveness analysis was used in this study. The short-term decision tree model analysed the screening procedure until the onset of anticoagulant treatment. The second part of the decision model followed a Markov design, simulating the patients' health states for 20 years. Continuous 24 h ECG recording was inferior to intermittent ECG in terms of cost-effectiveness, due to both lower sensitivity and higher costs. The base-case analysis compared intermittent ECG screening with no screening of patients with recent stroke. The implementation of the screening programme on 1000 patients resulted over a 20-year period in 11 avoided strokes and the gain of 29 life-years, or 23 quality-adjusted life years, and cost savings of €55 400.

Conclusion: Screening of silent AF by intermittent ECG recordings in patients with a recent ischaemic stroke is a cost-effective use of health care resources saving costs and lives and improving the quality of life.

HAYES, Inc. ***Implantable cardiac loop recorders for detection of atrial fibrillation following cryptogenic stroke****. Lansdale: HAYES, Inc. Healthcare Technology Brief Publication. 2017 (5)*

Los informes de evaluación de TS de la Agencia Hayes Inc son de alta calidad, pero son privados y sus costes muy elevados. En la parte de libre acceso se encuentra una breve descripción de la TS.

Authors' conclusions: approximately one-third of strokes are cryptogenic (lack an identifiable and treatable cause). Undetected atrial fibrillation (AF) is one suspected cause of cryptogenic stroke. Inability to detect suspected AF after cryptogenic stroke presents a clinical management dilemma. Description of Technology: Cardiac implantable loop recorders (ILRs) assess arrhythmias in symptomatic and asymptomatic patients. These small, battery-operated, titanium-encased devices are implanted subcutaneously in the left parasternal region with the use of local anesthesia. ILRs are useful when electrocardiography (ECG) abnormalities are suspected but have not been confirmed on traditional ECG or Holter recordings. Patient Population: ILRs are indicated for patients with clinical syndromes or situations at increased risk for cardiac arrhythmias, and those who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain, which may suggest a cardiac arrhythmia. Clinical Alternatives: Alternatives to ILRs for detection of AF in patients who have experienced a cryptogenic stroke include standard ECG or continuous external ECG or Holter monitor recordings, event recorders, external loop recorders, and cardiovascular telemetry devices.

En la segunda búsqueda, biblioteca Cochrane, se encontraron 153 estudios, de los cuales se seleccionaron los 25 ensayos clínicos controlados (ECAs) de la clinical trials database. De ellos, 8 artículos se referían a la monitorización en pacientes con ictus criptogénico y se corresponden a cuatro ECAs – EMBRACR, CRYSTAL AF, Find-AFRANDOMISED y MOBILE AF (solo el registro del diseño del ensayo)- publicados entre 2014 y 2017. Se copian a continuación sus resúmenes.

Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, Vaid H, O'Donnell M, Laupacis A, Côté R, Sharma M, Blakely JA, Shuaib A, Hachinski V, Coutts SB, Sahlas DJ, Teal P, Yip S, Spence JD, Buck B, Verreault S, Casaubon LK, Penn A, Selchen D, Jin A, Howse D, Mehdiratta M, Boyle K, Aviv R, Kapral MK, Mamdani M, EMBRACE Investigators and Coordinator. ***Atrial fibrillation in patients with cryptogenic stroke.*** *New England journal of medicine, 2014, 370(26): 2467-2477 (6)*

Background: Atrial fibrillation is a leading preventable cause of recurrent stroke for which early detection and treatment are critical. However, paroxysmal atrial fibrillation is often asymptomatic and likely to go undetected and untreated in the routine care of patients with ischemic stroke or transient ischemic attack (TIA).

Methods: We randomly assigned 572 patients 55 years of age or older, without known atrial fibrillation, who had had a cryptogenic ischemic stroke or TIA within the previous 6 months (cause undetermined after standard tests, including 24-hour electrocardiography [ECG]), to undergo additional noninvasive ambulatory ECG monitoring with either a 30-day event-triggered recorder (intervention group) or a conventional 24-hour monitor (control group). The primary outcome was newly detected atrial fibrillation lasting 30 seconds or longer within 90 days after randomization. Secondary outcomes included episodes of atrial fibrillation lasting 2.5 minutes or longer and anticoagulation status at 90 days.

Results: Atrial fibrillation lasting 30 seconds or longer was detected in 45 of 280 patients (16.1%) in the intervention group, as compared with 9 of 277 (3.2%) in the control group (absolute difference, 12.9 percentage points; 95% confidence interval [CI], 8.0 to 17.6; P<0.001; number needed to screen, 8). Atrial fibrillation lasting 2.5 minutes or longer was present in 28 of 284 patients (9.9%) in the intervention group, as compared with 7 of 277 (2.5%) in the control group (absolute difference, 7.4 percentage points; 95% CI, 3.4 to 11.3; P<0.001). By 90 days, oral anticoagulant therapy had been prescribed for more patients in the intervention group than in the control group (52 of 280 patients [18.6%] vs. 31 of 279 [11.1%]; absolute difference, 7.5 percentage points; 95% CI, 1.6 to 13.3; P=0.01).

Conclusions: Among patients with a recent cryptogenic stroke or TIA who were 55 years of age or older, paroxysmal atrial fibrillation was common. Noninvasive ambulatory ECG monitoring for a target of 30 days significantly improved the detection of atrial fibrillation by a factor of more than five and nearly doubled the rate of anticoagulant treatment, as compared with the standard practice of short-duration ECG monitoring. (Funded by the Canadian Stroke Network and others; EMBRACE ClinicalTrials.gov number, NCT00846924.).

DJ Gladstone, P Dorian, M Spring, V Panzov, M Mamdani, JS Healey, KE Thorpe AU: Gladstone DJ. ***Atrial premature beats predict atrial fibrillation in cryptogenic stroke: results from the EMBRACE trial****. Stroke; a journal of cerebral circulation, 2015, 46(4): 936-939 (7)*

Background and Purpose: Many ischemic strokes or transient ischemic attacks are labeled cryptogenic but may have undetected atrial fibrillation (AF). We sought to identify those most likely to have subclinical AF.

Methods: We prospectively studied patients with cryptogenic stroke or transient ischemic attack aged ≥55 years in sinus rhythm, without known AF, enrolled in the intervention arm of the 30 Day Event Monitoring Belt for Recording Atrial Fibrillation After a Cerebral Ischemic Event (EMBRACE) trial. Participants underwent baseline 24-hour Holter ECG poststroke; if AF was not detected, they were randomly assigned to 30-day ECG monitoring with an AF auto-detect external loop recorder. Multivariable logistic regression assessed the association between baseline variables (Holter-detected atrial premature beats [APBs], runs of atrial tachycardia, age, and left atrial enlargement) and subsequent AF detection.

Results: Among 237 participants, the median baseline Holter APB count/24 h was 629 (interquartile range, 142-1973) among those who subsequently had AF detected versus 45 (interquartile range, 14-250) in those without AF (P<0.001). APB count was the only significant predictor of AF detection by 30-day ECG (P<0.0001), and at 90 days (P=0.0017) and 2 years (P=0.0027). Compared with the 16% overall 90-day AF detection rate, the probability of AF increased from <9% among patients with <100 APBs/24 h to 9% to 24% in those with 100 to 499 APBs/24 h, 25% to 37% with 500 to 999 APBs/24 h, 37% to 40% with 1000 to 1499 APBs/24 h, and 40% beyond 1500 APBs/24 h.

Conclusions: Among older cryptogenic stroke or transient ischemic attack patients, the number of APBs on a routine 24-hour Holter ECG was a strong dose-dependent independent predictor of prevalent subclinical AF. Those with frequent APBs have a high probability of AF and represent ideal candidates for prolonged ECG monitoring for AF detection.

H Yong, K Thavorn, JS Hoch, M Mamdani, KE Thorpe, P Dorian, M Sharma, A Laupacis, DJ Gladstone ***Potential Cost-Effectiveness of Ambulatory Cardiac Rhythm Monitoring After Cryptogenic Stroke.*** *Stroke; a journal of cerebral circulation, 2016, 47(9): 2380-2385 (8)*

Background and purpose: Prolonged ambulatory ECG monitoring after cryptogenic stroke improves detection of covert atrial fibrillation, but its long-term cost-effectiveness is uncertain.

Methods: We estimated the cost-effectiveness of noninvasive ECG monitoring in patients aged ≥55 years after a recent cryptogenic stroke and negative 24-hour ECG. A Markov model used observed rates of atrial fibrillation detection and anticoagulation from a randomized controlled trial (EMBRACE) and the published literature to predict lifetime costs and effectiveness (ischemic strokes, hemorrhages, life-years, and quality-adjusted life-years [QALYs]) for 30-day ECG (primary analysis) and 7-day or 14-day ECG (secondary analysis), when compared with a repeat 24-hour ECG.

Results: Prolonged ECG monitoring (7, 14, or 30 days) was predicted to prevent more ischemic strokes, decrease mortality, and improve QALYs. If anticoagulation reduced stroke risk by 50%, 30-day ECG (at a cost of USD $447) would be highly cost-effective ($2000 per QALY gained) for

patients with a 4.5% annual ischemic stroke recurrence risk. Cost-effectiveness was sensitive to stroke recurrence risk and anticoagulant effectiveness, which remain uncertain, especially at higher costs of monitoring. Shorter duration (7 or 14 days) monitoring was cost saving and more effective than an additional 24-hour ECG; its cost-effectiveness was less sensitive to changes in ischemic stroke risk and treatment effect.

Conclusions: After a cryptogenic stroke, 30-day ECG monitoring is likely cost-effective for preventing recurrent strokes; 14-day monitoring is an attractive value alternative, especially for lower risk patients. These results strengthen emerging recommendations for prolonged ECG monitoring in secondary stroke prevention. Cost-effectiveness in practice will depend on careful patient selection.

T Sanna, HC Diener, RS Passman, V Di Lazzaro, RA Bernstein, CA Morillo, MM Rymer, V Thijs, T Rogers, F Beckers, K Lindborg, J Brachmann. ***Cryptogenic stroke and underlying atrial fibrillation.*** *New England journal of medicine, 2014, 370(26): 2478-2486 (9)*

Background: Current guidelines recommend at least 24 hours of electrocardiographic (ECG) monitoring after an ischemic stroke to rule out atrial fibrillation. However, the most effective duration and type of monitoring have not been established, and the cause of ischemic stroke remains uncertain despite a complete diagnostic evaluation in 20 to 40% of cases (cryptogenic stroke). Detection of atrial fibrillation after cryptogenic stroke has therapeutic implications.

Methods: We conducted a randomized, controlled study of 441 patients to assess whether long-term monitoring with an insertable cardiac monitor (ICM) is more effective than conventional follow-up (control) for detecting atrial fibrillation in patients with cryptogenic stroke. Patients 40 years of age or older with no evidence of atrial fibrillation during at least 24 hours of ECG monitoring underwent randomization within 90 days after the index event. The primary end point was the time to first detection of atrial fibrillation (lasting >30 seconds) within 6 months. Among the secondary end points was the time to first detection of atrial fibrillation within 12 months. Data were analyzed according to the intention-to-treat principle.

Results: By 6 months, atrial fibrillation had been detected in 8.9% of patients in the ICM group (19 patients) versus 1.4% of patients in the control group (3 patients) (hazard ratio, 6.4; 95% confidence interval [CI], 1.9 to 21.7; P<0.001). By 12 months, atrial fibrillation had been detected in 12.4% of patients in the ICM group (29 patients) versus 2.0% of patients in the control group (4 patients) (hazard ratio, 7.3; 95% CI, 2.6 to 20.8; P<0.001).

Conclusions: ECG monitoring with an ICM was superior to conventional follow-up for detecting atrial fibrillation after cryptogenic stroke. (Funded by Medtronic; CRYSTAL AF ClinicalTrials.gov number, NCT00924638.).

WC Choe, RS Passman, J Brachmann, CA Morillo, T Sanna, RA Bernstein, V Di Lazzaro, HC Diener, MM Rymer, F Beckers, J Koehler, PD Ziegler. : ***A Comparison of Atrial Fibrillation Monitoring Strategies After Cryptogenic Stroke (from the Cryptogenic Stroke and Underlying AF Trial).*** *American journal of cardiology, 2015, 116(6): 889-893 (10)*

Ischemic stroke cause remains undetermined in 30% of cases, leading to a diagnosis of cryptogenic stroke. Paroxysmal atrial fibrillation (AF) is a major cause of ischemic stroke but may go undetected with short periods of ECG monitoring. The Cryptogenic Stroke and Underlying

Atrial Fibrillation trial (CRYSTAL AF) demonstrated that long-term electrocardiographic monitoring with insertable cardiac monitors (ICM) is superior to conventional follow-up in detecting AF in the population with cryptogenic stroke. We evaluated the sensitivity and negative predictive value (NPV) of various external monitoring techniques within a cryptogenic stroke cohort. Simulated intermittent monitoring strategies were compared to continuous rhythm monitoring in 168 ICM patients of the CRYSTAL AF trial. Short-term monitoring included a single 24-hour, 48-hour, and 7-day Holter and 21-day and 30-day event recorders. Periodic monitoring consisted of quarterly monitoring through 24-hour, 48-hour, and 7-day Holters and monthly 24-hour Holters. For a single monitoring period, the sensitivity for AF diagnosis was lowest with a 24-hour Holter (1.3%) and highest with a 30-day event recorder (22.8%). The NPV ranged from 82.3% to 85.6% for all single external monitoring strategies. Quarterly monitoring with 24-hour Holters had a sensitivity of 3.1%, whereas quarterly 7-day monitors increased the sensitivity to 20.8%. The NPVs for repetitive periodic monitoring strategies were similar at 82.6% to 85.3%. Long-term continuous monitoring was superior in detecting AF compared to all intermittent monitoring strategies evaluated (p <0.001). Long-term continuous electrocardiographic monitoring with ICMs is significantly more effective than any of the simulated intermittent monitoring strategies for identifying AF in patients with previous cryptogenic stroke.

J Brachmann, CA Morillo, T Sanna, V Di Lazzaro, HC Diener, RA Bernstein, M Rymer, PD Ziegler, S Liu, RS Passman. ***Uncovering Atrial Fibrillation Beyond Short-Term Monitoring in Cryptogenic Stroke Patients: three-Year Results From the Cryptogenic Stroke and Underlying Atrial Fibrillation Trial.*** *Circulation. Arrhythmia and electrophysiology,* ***2016****, 9(1): e003333 (11)*

Background: Atrial fibrillation (AF) can be a cause of previously diagnosed cryptogenic stroke. However, AF can be paroxysmal and asymptomatic, thereby making detection with routine ECG methods difficult. Oral anticoagulation is highly effective in reducing recurrent stroke in patients with AF, but its initiation is dependent on the detection of AF. Cryptogenic Stroke and Underlying Atrial Fibrillation (CRYSTAL AF) is the first randomized study to report the detection of AF in cryptogenic stroke patients using continuous long-term monitoring via insertable cardiac monitors (ICM).

Methods and results: Patients with prior cryptogenic stroke were randomized to control (n=220) or ICM (n=221) and followed for <36 months. Cumulative AF detection rates in the ICM arm increased progressively during this period (3.7%, 8.9%, 12.4%, and 30.0% at 1, 6, 12, and 36 months, respectively), but remained low in the control arm (3.0% at 36 months). This resulted in oral anticoagulation prescription in 94.7% of ICM patients with AF detected at 6 months, 96.6% at 12 months, and 90.5% at 36 months. Among ICM patients with AF detected, the median time to AF detection was 8.4 months, 81.0% of first AF episodes were asymptomatic, and 94.9% had at least 1 day with >6 minutes of AF.

Conclusions: Three-year monitoring by ICM in cryptogenic stroke patients demonstrated a significantly higher AF detection rate compared with routine care. Given the frequency of asymptomatic first episodes and the long median time to detection, these findings highlight the limitations of using traditional AF detection methods. The majority of patients with AF were prescribed oral anticoagulation therapy.

M Weber-Krüger, G Gelbrich, R Stahrenberg, J Liman, P Kermer, GF Hamann, J Seegers, K Gröschel, R Wacht. ***Finding atrial fibrillation in stroke patients: randomized evaluation of enhanced and prolonged Holter monitoring--Find-AF(RANDOMISED) --rationale and design.*** *American heart journal,* ***2014****, 168(4), 438-445: e1 (12)*

Background: Detecting paroxysmal atrial fibrillation (AF) in patients with ischemic strokes presenting in sinus rhythm is challenging because episodes are often short, occur randomly, and are frequently asymptomatic. If AF is detected, recurrent thromboembolism can be prevented efficiently by oral anticoagulation. Numerous uncontrolled studies using various electrocardiogram (ECG) devices have established that prolonged ECG monitoring increases the yield of AF detection, but most established procedures are time-consuming and costly. The few randomized trials are mostly limited to cryptogenic strokes. The optimal method, duration, and patient selection remain unclear. Repeated prolonged continuous Holter ECG monitoring to detect paroxysmal AF within an unspecific stroke population may prove to be a widely applicable, effective secondary prevention strategy.

Study Design: Find-AFRANDOMISED is a randomized and controlled prospective multicenter trial. Four hundred patients 60 years or older with manifest (symptoms ≥24 hours or acute computed tomography/magnetic resonance imaging lesion) and acute (symptoms ≤7 days) ischemic strokes will be included at 4 certified stroke centers in Germany. Those with previously diagnosed AF/flutter, indications/contraindications for oral anticoagulation, or obvious causative blood vessel pathologies will be excluded. Patients will be randomized 1:1 to either enhanced and prolonged Holter ECG monitoring (10 days at baseline and after 3 and 6 months) or standard of care (≥24-hour continuous ECG monitoring, according to current stroke guidelines). All patients will be followed up for at least 12 months.

Outcomes: The primary end point is newly detected AF (≥30 seconds) after 6 months, confirmed by an independent adjudication committee. We plan to complete recruitment in autumn 2014. First results can be expected by spring 2016.

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Background: Atrial fibrillation is a major risk factor for recurrent ischaemic stroke, but often remains undiagnosed in patients who have had an acute ischaemic stroke. Enhanced and prolonged Holter-electrocardiogram-monitoring might increase detection of atrial fibrillation. We therefore investigated whether enhanced and prolonged rhythm monitoring was better for detection of atrial fibrillation than standard care procedures in patients with acute ischaemic stroke.

Methods: Find-AFRANDOMISED is an open-label randomised study done at four centres in Germany. We recruited patients with acute ischaemic stroke (symptoms for 7 days or less) aged 60 years or older presenting with sinus rhythm and without history of atrial fibrillation. Patients were included irrespective of the suspected cause of stroke, unless they had a severe ipsilateral

carotid or intracranial artery stenosis, which were the exclusion criteria. We used a computergenerated allocation sequence to randomly assign patients in a 1:1 ratio with permuted block sizes of 2, 4, 6, and 8, stratified by centre, to enhanced and prolonged monitoring (ie, 10-day Holter-electrocardiogram [ECG]-monitoring at baseline, and at 3 months and 6 months of follow-up) or standard care procedures (ie, at least 24 h of rhythm monitoring). Participants and study physicians were not masked to group assignment, but the expert committees that adjudicated endpoints were. The primary endpoint was the occurrence of atrial fibrillation or atrial flutter (30 sec or longer) within 6 months after randomisation and before stroke recurrence. Because Holter ECG is a widely used procedure and not known to harm patients, we chose not to assess safety in detail. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01855035.

Findings: Between May 8, 2013, and Aug 31, 2014, we recruited 398 patients. 200 patients were randomly assigned to the enhanced and prolonged monitoring group and 198 to the standard care group. After 6 months, we detected atrial fibrillation in 14% of 200 patients in the enhanced and prolonged monitoring group (27 patients) versus 5% in the control group (nine of 198 patients, absolute difference 9·0%; 95% CI 3·4–14·5, p=0·002; number needed to screen 11).

Interpretation: Enhanced and prolonged monitoring initiated early in patients with acute ischaemic stroke aged 60 years or older was better than standard care for the detection of atrial fibrillation. These findings support the consideration of all patients aged 60 years or older with stroke for prolonged monitoring if the detection of atrial fibrillation would result in a change in medical management (eg, initiation of anticoagulation).

Corrections: Wachter R, Groschel K, Gelbrich G, et al. ***Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-AFRANDOMISED): an open-label randomised controlled trial*** *(The Lancet Neurology, 2017 16(4):282-290. The lancet neurology, 2017, 16(4): 261 (14)*

In the discussion of this Article, the penultimate sentence of the second paragraph should read "A more thorough diagnostic work-up before randomisation might have led to a selection bias that could have affected the generalisability of the study results because patients with findings suggestive of a specific stroke cause (eg, hypokinetic left ventricular segment or persistent foramen ovale), but no option might have been excluded before the initiation of an intensified ECG monitoring." This correction has been made to the online version as of Feb 16, 2017.

RW Treskes, W Gielen, MJ Wermer, RW Grauss, AP van Alem, RA Dehnavi, CJ Kirchhof, ET van der Velde, AC Maan, R Wolterbeek, OM Overbeek, MJ Schalij, SA Trines ***Mobile phones in cryptogenic stroke patients Bringing sIngle Lead ECGs for Atrial Fibrillation detection (MOBILE-AF): study protocol for a randomised controlled trial.*** *Trials,* ***2017****, 18(1): 402 (15)*

Background: Recently published randomised clinical trials indicate that prolonged electrocardiom (ECG) monitoring might enhance the detection of paroxysmal atrial fibrillation (AF) in cryptogenic stroke or transient ischaemic attack (TIA) patients. A device that might be suitable for prolonged ECG monitoring is a smartphone-compatible ECG device (Kardia Mobile, Alivecor, San Francisco, CA, USA) that allows the patient to record a single-lead ECG without the presence of trained health care staff. The MOBILE-AF trial will investigate the effectiveness of the ECG device for AF

detection in patients with cryptogenic stroke or TIA. In this paper, the rationale and design of the MOBILE-AF trial is presented.

Methods: For this international, multicentre trial, 200 patients with cryptogenic stroke or TIA will be randomised. One hundred patients will receive the ECG device and will be asked to record their ECG twice daily during a period of 1 year. One hundred patients will receive a 7-day Holter monitor.

Discussion: The primary outcome of this study is the percentage of patients in which AF is detected in the first year after the index ischaemic stroke or TIA. Secondary outcomes include markers for AF prediction, orally administered anticoagulation therapy changes, as well as the incidence of recurrent stroke and major bleeds. First results can be expected in mid-2019.

5. ¿SE HAN ENCONTRADO OTROS ESTUDIOS QUE PUEDAN APORTAR INFORMACIÓN RELEVANTE?

Se encontraron una revisión sistemática y meta-análisis sobre la monitorización de la AF y dos estudios sobre la monitorización con Textile Wearable Holter (TWH). El primero un estudio piloto multicéntrico español y el otro es el diseño de un ensayo clínico polaco, que aún no ha comenzado a reclutar pacientes.

Dahal K , Chapagain B , Maharjan R , Farah HW , Nazeer A , Lootens RJ , Rosenfeld A. ***Prolonged Cardiac Monitoring to Detect Atrial Fibrillation after Cryptogenic Stroke or Transient Ischemic Attack: A Meta-Analysis of Randomized Controlled Trials****. Ann Noninvasive Electrocardiol. 2016 Jul;21(4):382-8. (16)*

Background: The cause of ischemic stroke or transient ischemic attack (TIA) remains unclear after initial cardiac monitoring in approximately one-third of patients. Randomized controlled trials (RCTs) showed that the prolonged cardiac monitoring of patients with cryptogenic stroke or TIA increased detection of atrial fibrillation (AF). We aimed to perform a meta-analysis of all RCTs that evaluated the prolonged monitoring ≥7 days in patients with cryptogenic stroke or TIA.

Methods: We searched PubMed, EMBASE, Cochrane CENTRAL, and relevant references for RCTs without language restriction (inception through December 2014) and performed meta-analysis using random effects model. Detection of AF, use of anticoagulation at follow-up, recurrent stroke or TIA, and mortality were major outcomes.

Results: Four RCTs with 1149 total patients were included in the meta-analysis. Prolonged cardiac monitoring ≥7 days compared to shorter cardiac monitoring of ≤48 hours duration increased the detection of AF (≥30 seconds duration) in patients after cryptogenic stroke or TIA (13.8% vs. 2.5%;odds ratio [OR], 6.4; 95% confidence interval [CI], 3.50-11.73; P < 0.00001; I(2) , 0%]. It also increased he odds of AF detection of any duration (22.6% vs. 5.2%; 5.68[3.3-9.77]; P < 0.00001; I(2) , 0%). The patients who underwent prolonged monitoring were more likely to be on anticoagulation at follow-up (2.21[1.52-3.21]; P < 0.0001; I (2), 0%). No differences in recurrent stroke or TIA (0.78[0.40-1.55]; P =0.48; I (2), 0%) and mortality (1.33[0.29-6.00]; P = 0.71; I(2) , 0%] were observed between two strategies.

Conclusion: Prolonged cardiac monitoring improves detection of atrial fibrillation and anticoagulation use after cryptogenic stroke or TIA and therefore should be considered instead of shorter duration of cardiac monitoring.

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Background: We describe the feasibility of monitoring with a Textile Wearable Holter (TWH) in patients included in Crypto AF registry.

Methods: We monitored cryptogenic stroke patients from stroke onset (b3 days) continuously during 28 days. We employed a TWH composed by a garment and a recorder. We compared two garments (Lead and Vest) to assess rate of undiagnosed Atrial Fibrillation (AF) detection, monitoring compliance, comfortability (1 to 5 points), skin lesions, and time analyzed. We describe the timing of AF detection in three periods (0–3, 4–15 and 16–28 days).

Results: The rate of undiagnosed AF detection with TWH was 21.9% (32 out of 146 patients who completed the monitoring). Global time compliance was 90% of the time expected (583/644 h). The level of comfortability was 4 points (IQR 3–5). We detected reversible skin lesions in 5.47% (8/146). The comfortability was similar but time compliance (in hours) was longer in Vest group 591 (IQR [521–639]) vs. Lead 566 (IQR [397–620]) (p = 0.025). Also, time analyzed was more prolonged in Vest group 497 (IQR [419–557]) vs. Lead (336 h (IQR [140–520]) (p = 0.001)). The incidence of AF increases from 5.6% (at 3 days) to 17.5% (at 15th day) and up to20.9% (at 28th day). The percentage of AF episodes detected only in each period was 12.5% (0–3 days); 21.7% (4–15 days) and 19% (16–28 days).

Conclusions: 28 days Holter monitoring from the acute phase of the stroke was feasible with TWH. Following our protocol, only five patients were needed to screen to detected one case of AF.

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Background: Today, the main challenge for researchers is to develop new technologies which may help to improve the diagnoses of cardiovascular disease (CVD), thereby reducing healthcare costs and improving the quality of life for patients. This study aims to show the utility of biomedical shirt-based electrocardiography (ECG) monitoring of patients with CVD in different clinical situations using the Nuubo® ECG (nECG) system.

Methods: An investigator-initiated, multicenter, prospective observational study was carried out in a cardiology (adult and pediatric) and cardiac rehabilitation wards. ECG monitoring was used with the biomedical shirt in the following four independent groups of patients: 1) 30 patients after pulmonary vein isolation (PVI), 2) 30 cardiac resynchronization therapy (CRT) recipients, 3) 120 patients during cardiac rehabilitation after myocardial infarction, and 4) 40 pediatric patients with supraventricular tachycardia (SVT) before electrophysiology study. Approval for all study groups was obtained from the institutional review board. The biomedical shirt captures the electrocardiographic signal via textile electrodes integrated into a garment. The software allows the visualization and analysis of data such as ECG, heart rate, arrhythmia detecting algorithm and relative position of the body is captured by an electronic device.

Discussion: The major advantages of the nECG system are continuous ECG monitoring during daily activities, high quality of ECG recordings, as well as assurance of a proper adherence due to adequate comfort while wearing the shirt. There are only a few studies that have examined wearable systems, especially in pediatric populations.

Trial registration: This study is registered in ClinicalTrials.gov: Identifier NCT03068169. (Cardiol J 2018; 25, 1: 52–59)

Key words: remote electrocardiography, atrial fibrillation, cardiac rehabilitation, cardiac resynchronization therapy, electrophysiological study, myocardial infarction, mobile health, pulmonary veins isolation, supraventricular tachycardia, telehealth, telemedicine.

6. PRINCIPALES CONCLUSIONES Y RECOMENDACIONES DE LA BIBLIOGRAFÍA RECOGIDA

La revisión bibliográfica parece indicar que la monitorización prolongada de estos pacientes, tras un ictus catalogado como criptogénico, tiene evidencia de un mayor diagnóstico de fibrilación auricular.
La monitorización prolongada mejora la tasa de diagnóstico de fibrilación auricular, aunque la tasa de detección de FA fue altamente variable en los diferentes estudios por varias causas. Bien por lo exhaustiva que haya sido la búsqueda de la etiopatogenia del ictus (antes de catalogarlo como criptogénico) y también por la marcada heterogeneidad de las muestras: edad de los pacientes, métodos y duración de la monitorización electrocardiográfica (2).

Dentro de lo minuciosa que haya sido la búsqueda previa de la etiopatogenia del ictus, llama la atención los diferentes criterios establecidos en los ensayos CRYSTAL o EMBRACE, siendo mucho más exhaustivos en el primero para catalogar el ictus como criptogénico.

Revisando la selección de los pacientes en las diferentes muestras de pacientes con ictus criptogénico, los pacientes ancianos y con mayor puntuación en la escala para predicción de riesgo tromboembólico (CHA2DS2VASc) es en los que más se detectan episodios de FA y se puede explicar por la propia etiopatogenia de la FA.

Respecto a otras cuestiones, como cuál es el coste efectividad de los distintos métodos de monitorización, así como cuál es la significación clínica, dentro de los informes de evaluación encontrados (3), (4): la monitorización prolongada mostró tasas superiores de detección de FA y ser rentable debido a la detección de FA y al uso posterior de la terapia anticoagulante. Los

resultados refuerzan las recomendaciones para monitorización prolongada del ECG en la prevención secundaria del accidente cerebrovascular y la rentabilidad en la práctica dependerá de la selección cuidadosa del paciente. Así el seguimiento de 14 días es una alternativa de valor atractivo, especialmente para pacientes de menor riesgo con puntuaciones CHA2DS2VASc (10) y en el caso del Holter subcutáneo implantable su utilización sea más rentable en los pacientes con mayor puntuación en la escala de riesgo tromboembólico.

También existe la posibilidad de que parte de la FA detectada no sea causante del evento isquémico. Sin embargo, la presencia de FA incluso en estos pacientes, daría lugar a la terapia de anticoagulación.

La utilización del tejido elástico inteligente (TWH) para el monitoreo cardíaco prolongado desde la fase aguda del ictus es un nuevo concepto de monitorización no invasiva basada en sensores adaptados a la superficie del cuerpo. La tasa de detección de FA fue alta, como bien explican los autores, que lo relacionan con varios factores: monitorización temprana, pacientes con alto riesgo (CHA2DS2VASc) y por el perfil del infarto cerebral similar.

Los resultados del estudio piloto muestran que puede ser una herramienta útil en la fase subaguda, para estos pacientes. En el caso de modelos insertables existe ya evidencia en cuanto a su uso y eficacia. Pero en el caso de TWH**,** aún no ha sido estudiada de forma extendida y sistemática, faltan datos prospectivos aleatorizados multicéntricos y su utilización en clínica es aún baja.

Estos hallazgos resaltan una brecha evidencia-práctica que probablemente contribuye a un diagnóstico excesivo de accidentes cerebrovasculares como criptogénico, un diagnóstico insuficiente de fibrilación auricular y oportunidades de tratamiento anticoagulante perdidas para la prevención secundaria del accidente cerebrovascular

7. CONSIDERACIONES PARA NUESTRA COMUNIDAD

Aunque la monitorización de más larga duración indudablemente mejora la tasa de diagnóstico de fibrilación auricular, se debería evaluar el coste-efectividad de los distintos métodos de monitorización y el impacto del tratamiento de la fibrilación auricular silente en la población con ictus criptogénico.

La elección de la herramienta para la monitorización prolongada es una decisión compleja, ya que debe tenerse en cuenta no solo la efectividad y el coste de la misma, sino también los cambios organizativos y cargas de trabajo que requerirían.

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