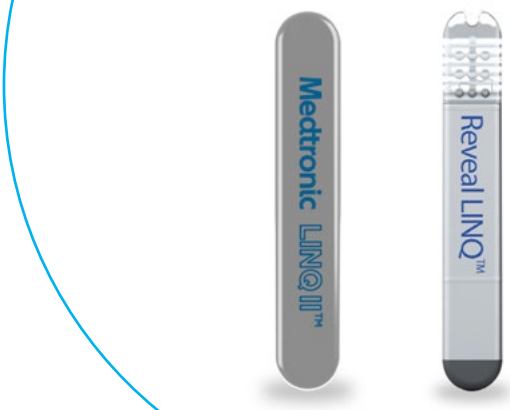
Medtronic

Meta-analysis summary: Prolonged cardiac rhythm monitoring and secondary stroke prevention

In patients with cryptogenic cerebral ischemia[1]



As published in *Stroke*, June 2019[1]

Objective

Evaluate the impact of prolonged cardiac rhythm monitoring (PCM) on secondary stroke prevention using data from available-to-date randomized clinical trials (RCTs) and observational studies.

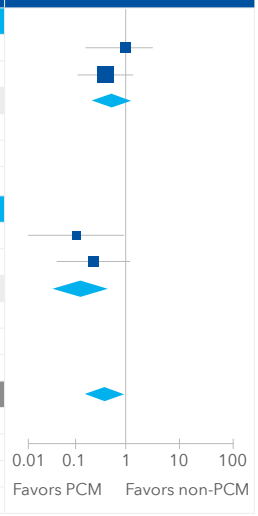
Results

Patients who underwent PCM compared to conventional cardiac monitoring show:

- **2.5x increased incidence of AF detection** (n = 1,102, RR = 2.46, 95% CI :1.61-3.76, and p < 0.0001)
- **2.1x increased incidence of anticoagulant initiation** (n = 956, RR = 2.07, 95% CI: 1.36-3.17, and p = 0.0008)
- **55% decreased risk of recurrent stroke** (n = 1,102, RR = 0.45, 95% CI: 0.21-0.97, and p = 0.04)

Forest plot presenting the differences between prolonged and conventional (non-prolonged) cardiac rhythm monitoring in the risk of recurrent stroke, stratified by the study type.

	PCM		Non-PCM			Risk ratio	Risk ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, random, 95% CI	M-H, random, 95% CI
1.9.1 Randomized clinical trial							
CRYSTAL AF	4	221	4	220	25.9%	1.00 [0.25, 3.93]	
FIND AF	5	220	9	198	38.3%	0.55 [0.19, 1.61]	
Subtotal (95% CI)		**421**		**418**	64.3%	**0.69 [0.30, 1.61]**	
Total events	9		13				
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (p = 0.50); I² = 0%							
Test for overall effect: Z = 0.86 (p = 0.39)							
1.9.2 Observational studies							
Brown ESUS-AF	1	47	12	70	13.3%	0.12 [0.02, 0.92]	
Rodríguez-Campello, et al.	2	65	9	81	22.4%	0.28 [0.06, 1.24]	
Subtotal (95% CI)		**112**		**151**	35.7%	**0.21 [0.06, 0.69]**	
Total events	3		21				
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 1 (p = 0.52); I² = 0%							
Test for overall effect: Z = 2.57 (p = 0.01)							
Total (95% CI)		**533**		**569**	100.0%	**0.45 [0.21, 0.97]**	
Total events	12		34				
Heterogeneity: Tau² = 0.10; Chi² = 3.55, df = 3 (p = 0.31); I² = 16%							
Test for overall effect: Z = 2.04 (p = 0.04)							
Test for subgroup differences: Chi² = 2.56, df = 1 (p = 0.11); I² = 60.9%							



Conclusion

The use of prolonged cardiac monitoring has a potential impact on secondary stroke prevention, as patients with cryptogenic IS (ischemic stroke)/TIA undergoing PCM had higher rates of AF detection, anticoagulant initiation, and lower stroke recurrence.

Stroke definition

The definition of the index events in available studies included cryptogenic stroke (CS) defined according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria in two studies,[2,3] embolic strokes of undetermined source (ESUS) in one study,[4] and select IS patients (with no history of AF and no significant extracranial or intracranial arterial stenosis) in one study.[5]

Method

A comprehensive literature search of MEDLINE, SCOPUS, CENTRAL, and conference proceedings was conducted to identify studies reporting stroke recurrence rates in patients with a history of cryptogenic stroke or TIA receiving PCM as compared to patients receiving conventional (non-PCM) cardiac monitoring. Literature search was performed on October 14, 2018.

Identified records: 885

Studies reporting stroke recurrence rates in patients with history of cryptogenic IS or transient ischemic attack (TIA) receiving PCM compared to patients receiving conventional (non-PCM). This includes:

- Randomized clinical trials (RCTs)
- Prospective/retrospective cohort studies
- Case-control studies

Records excluded: 881

- Duplicates, case reports, and case series
- Studies not reporting stroke recurrence rates during follow-up or not providing data for the reference group receiving non-PCM
- Studies providing data on AF detection rates and/or change in management (anticoagulant initiation) according to PCM results without providing data on stroke recurrence
- Studies not including IS/TIA population, control group, or report on IS/TIA recurrence

Records included: 4

The meta-analysis included two RCTs and two observational studies, for a total of 1,102 patients (mean age: 68 years, 41% women).[2-5]

- Brown ESUS-AF[4]
- CRYSTAL AF[2]
- FIND-AF[5]
- Rodríguez-Campello, et al.[3]

Study limitations

- This analysis provides preliminary evidence for a potential impact of PCM on secondary stroke prevention.
- The data used is based on two RCTs and two observational studies.
- Prolonged cardiac monitoring consisted of insertable cardiac monitors (ICMs) in three of the studies (n = 704) and repeated Holter monitoring (n = 398) in one study (three periods of 10 days). As such, the results don't exclusively pertain to ICMs, although patients with ICMs made up the majority of the cohort.

References

[1] Tsivgoulis G, Katsanos AH, Grory BM, et al. Prolonged Cardiac Rhythm Monitoring and Secondary Stroke Prevention in Patients With Cryptogenic Cerebral Ischemia. *Stroke*. August 2019;50(8):2175-2180.

[2] Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med*. June 26, 2014;370(26):2478-2486.

[3] Rodríguez-Campello A, et al. Atrial fibrillation detection and stroke recurrence in patients with early insertable cardiac monitor. A case-control study. Presented at Europe Stroke Organisation Conference 2018.

[4] Ricci B, Chang AD, Hemendinger M, et al. A Simple Score That Predicts Paroxysmal Atrial Fibrillation on Outpatient Cardiac Monitoring after Embolic Stroke of Unknown Source. *J Stroke Cerebrovasc Dis*. June 2018;27(6):1692-1696.

[5] Wachter R, Gröschel K, Gelbrich G, et al. Holter-electrogram-monitoring in patients with acute ischaemic stroke (Find-AFRANDOMISED): an open-label randomised controlled trial. *Lancet Neurol*. April 2017;16(4):282-290.

Brief Statement

Medtronic LINQ Family Insertable Cardiac Monitor System (ICM) and Remote Monitoring

Indications
The Reveal LINQ ICM is an insertable automatically-activated and patient-activated monitoring system that records subcutaneous ECG and is indicated in the following cases:
- patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
- patients who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain that may suggest a cardiac arrhythmia

This device has not been tested specifically for pediatric use.

The LINQ II ICM is an insertable automatically-activated and patient-activated monitoring system that records subcutaneous ECG and is indicated in adult patients, and in pediatric patients who are at least 2 years old, in the following cases:
- patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
- patients who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain that may suggest a cardiac arrhythmia

Contraindications
There are no known contraindications for the insertion of the LINQ Family ICMs or their accessories. However, the patient's particular medical condition may dictate whether or not a subcutaneous, chronically inserted device can be tolerated.

Warnings and Precautions
Patients with a LINQ Family ICM should avoid sources of diathermy, high sources of radiation, electrosurgical cautery, external defibrillation, lithotripsy, therapeutic ultrasound and radiofrequency ablation to avoid electrical reset of the device, and/or inappropriate sensing as described in the Medical procedure and EMI Warnings, Precautions and Guidance Manual. MRI scans should be performed only in a specified MR environment under specified conditions as described in the LINQ II or Reveal LINQ ICM MRI Technical Manual.

Wireless accessories available for use with a LINQ Family ICM may experience connectivity or performance issues. See product manuals for details and troubleshooting instructions.

Potential Adverse Events
Potential adverse events from the LINQ Family ICM include, but are not limited to, device rejection phenomena (including local tissue reaction), device migration, infection, and erosion through the skin.

There are no known adverse events associated with the use of any LINQ Family ICM wireless accessories.

See the device manuals for detailed information regarding the implant procedure, indications / intended use, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please call Medtronic at (800) 328-2518 (Technical Services), (800) 551-5544 (Patient Services), and/or consult Medtronic's website at www.medtronic.com.

Caution: Federal law (USA) restricts prescription devices to sale by or on the order of a physician.

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