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.

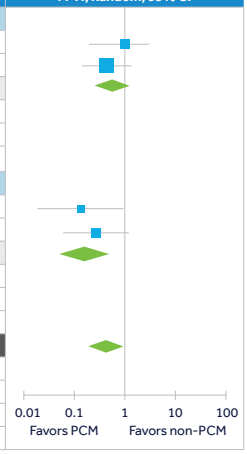
RESULTS:

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: $Tau^2 = 0.00$; $Chi^2 = 0.44$, df = 1 (P = 0.50); $I^2 = 0\%$							
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: $Tau^2 = 0.00$; $Chi^2 = 0.41$, df = 1 (P = 0.52); $I^2 = 0\%$							
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: $Tau^2 = 0.10$; $Chi^2 = 3.55$, df = 3 (P = 0.31); $I^2 = 16\%$							
Test for overall effect: Z = 2.04 (P = 0.04)							
Test for subgroup differences: $Chi^2 = 2.56$, df = 1 (P = 0.11); $I^2 = 60.9\%$							



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 2 RCTs and 2 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.

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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*. Published online June 20, 2019.

[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. *Eur Stroke J*. 2018;3:459. Available at: https://www.morressier.com/article/atrial-fibrillation-detection-stroke-recurrence-patients-early-insertable-cardiac-monitor-casecontrol-study/5ab8f55cd462b8029238c875. Accessed June 11, 2019.

[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.

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