



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA

Centro Congressi
di Confindustria

**Auditorium
della Tecnica**

9ª Edizione

30 Settembre

1 Ottobre

2022



CARDIONEUROLOGIA: STROKE E DINTORNI

Fibrillazione atriale e stroke: stato
dell'arte e percorsi multidisciplinari

Toni Danilo



Disclosures

- Advisory Board, presentazioni a congresso, workshops
 - Abbott
 - Alexion
 - Astra Zeneca
 - Bayer
 - Boehringer Ingelheim
 - Bristol Myers Squibb
 - Daiichi Sankyo
 - Medtronic
 - Pfizer-BMS
- Unrestricted research grant
 - Boehringer Ingelheim



Guideline

European Stroke Organisation (ESO) guideline on screening for subclinical atrial fibrillation after stroke or transient ischaemic attack of undetermined origin

**Marta Rubiera¹ , Ana Aires², Kateryna Antonenko³,
Sabrina Lémeret⁴ , Christian H Nolte^{5,6} , Jukka Putaala⁷,
Renate B Schnabel^{8,9}, Anil M Tuladhar¹⁰, David J Werring¹¹,
Dena Zeraatkar^{12,13} and Maurizio Paciaroni¹⁴**

**EUROPEAN
STROKE JOURNAL**

European Stroke Journal
2022, Vol. 7(3) CVII–CXXXIX
© European Stroke Organisation 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/23969873221099478
journals.sagepub.com/home/eso





PICO 1: In adult patients with ischaemic stroke or TIA of undetermined origin, does a longer duration of cardiac rhythm monitoring compared to a shorter duration of cardiac rhythm monitoring increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

Evidence-based recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin, we recommend a prolonged cardiac monitoring instead of standard 24 h monitoring to increase the detection of subclinical AF.

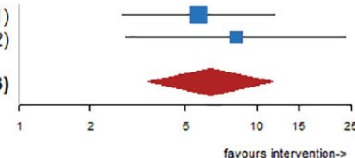
Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Strong for intervention**

Detection rate of AF > 30 sec

Study	n(I)	N(I)	n(C)	N(C)	weight	OR (95%CI)
Gladstone 2014	45	280	9	277	67.6%	5.70 (2.73-11.91)
Sanna 2014	29	221	4	220	32.4%	8.16 (2.82-23.62)
Total (CS or TIA only)	74	501	13	497	100.0%	6.40 (3.50-11.73)

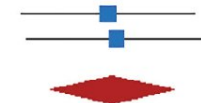
$I^2=0\%$, $p=0.59$



AC increase in case/control studies and RCTs

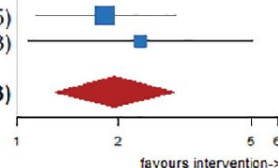
Study	n(I)	N(I)	n(C)	N(C)	weight	OR (95%CI)
Observational studies						
Cuadrado-Godia 2020	59	90	38	101	51.7%	3.16 (1.74-5.71)
Triantafyllou 2020	23	123	24	373	48.3%	3.34 (1.81-6.18)
Total (CS or TIA only)	82	213	62	474	100.0%	3.25 (2.12-4.97)

$I^2=0\%$, $p=0.89$



Controlled trials

	52	280	31	279	72.2%	1.82 (1.13-2.95)
	22	221	10	220	27.8%	2.32 (1.07-5.03)
only	74	501	41	499	100.0%	1.95 (1.30-2.93)



Expert consensus statement

In adult patients with ischaemic stroke or TIA of undetermined origin, we suggest prolonged cardiac rhythm monitoring for AF for more than 48 h.

PICO 2: In adult patients with ischaemic stroke or TIA of undetermined origin, does the addition of out-patient cardiac rhythm monitoring, compared with in-hospital cardiac rhythm monitoring alone increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

Evidence-based recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin, we suggest the use of additional outpatient monitoring compared with in-hospital cardiac rhythm monitoring to increase the detection of subclinical AF.

Quality of evidence: **Very low** ⊕

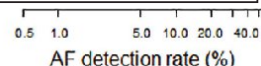
Strength of recommendation: **Weak for intervention** ⊕

Study	n	N	weight	rate (95%CI)
Desai 2021	22	125	3.5%	17.60% (10.92-24.28)
Toyoda 2021	13	206	3.6%	6.31% (2.99-9.63)
Ungar 2021	92	334	3.7%	27.54% (22.75-32.33)
De Angelis 2020	24	58	3.1%	41.38% (28.70-54.05)
Milstein 2020	67	328	3.7%	20.43% (16.06-24.79)
Pagola 2020	61	264	3.7%	23.11% (18.02-28.19)
Riordan 2020	74	293	3.7%	25.26% (20.28-30.23)
Triantafyllou 2020 (ICM)	26	123	3.5%	21.14% (13.92-28.35)
Triantafyllou 2020 (24h Holter)	28	373	3.7%	7.51% (4.83-10.18)
Exposito 2019 (ILR)	17	80	3.3%	21.25% (12.29-30.21)
Exposito 2019 (external loop)	21	112	3.4%	18.75% (11.52-25.98)
Liantinioti 2019 (1*24h Holter)	20	254	3.7%	7.87% (4.56-11.19)
Liantinioti 2019 (2*24h Holter)	12	85	3.3%	14.11% (6.71-21.52)
Liantinioti 2019 (>=3*24h Holter)	7	34	2.7%	20.59% (7.00-34.18)
Carrazco 2018	31	100	3.4%	31.00% (21.93-40.06)
Seow 2018	11	71	3.2%	15.49% (7.08-23.91)
Kaura 2017	7	43	2.9%	16.28% (5.24-27.31)
Favilla 2015	18	227	3.6%	7.93% (4.41-11.44)
Christensen 2014	14	85	3.3%	16.47% (8.58-24.36)
Cotter 2013	13	51	3.0%	24.49% (13.53-37.45)
Ehren 2013	6	22	2.3%	27.27% (8.66-45.88)
	16	239	3.7%	6.69% (3.52-9.86)
	15	51	3.0%	29.41% (16.91-41.92)
Total	616	3568	77.0%	18.42% (14.58-22.60)
	51	123	3.5%	41.46% (32.76-50.17)
	20	136	3.5%	14.71% (8.75-20.66)

Expert consensus statement

In adult patients with ischaemic stroke or TIA of undetermined origin we suggest initiating ECG monitoring as early as possible during the in-hospital stay, to increase the rate of AF detection.

on rate with outpatient devices



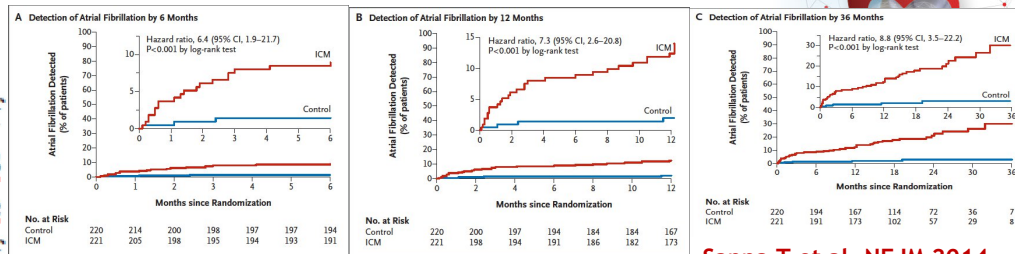
PICO 3: In adult patients with ischaemic stroke or TIA of undetermined origin, do implantable monitoring devices compared to any non-implantable external monitoring device increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

Evidence-based recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin, we suggest the use of implantable devices for cardiac monitoring instead of non-implantable devices to increase the detection of subclinical AF.

Quality of evidence: **Low** ⊕⊕

Strength of recommendation: **Strong for intervention** ↑↑



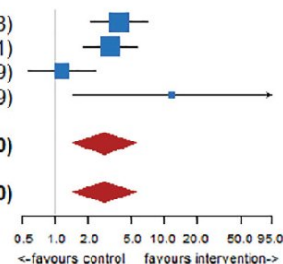
Sanna T et al, NEJM 2014

AF detection in case/control studies

Study	n(I)	N(I)	n(C)	N(C)	weight	OR(95%CI)
Cuadrado-Godia 2020	63	90	38	101	31.3%	3.87 (2.11-7.08)
Triantafyllou 2020	26	123	28	373	31.9%	3.20 (1.80-5.71)
Exposito 2019	17	80	21	112	28.4%	1.17 (0.57-2.39)
Ritter 2013	10	60	1	60	8.4%	11.80 (1.46-95.39)

16 356 88 646 100.0% 2.85 (1.45-5.60)

16 356 88 646 100.0% 2.85 (1.45-5.60)

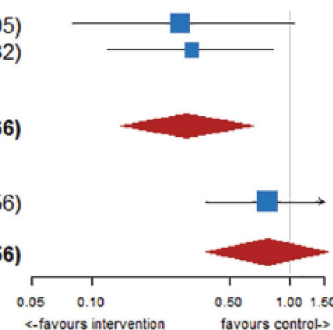


n(I)	N(I)	n(C)	N(C)	weight	OR (95%CI)
3	90	11	101	34.4%	0.28 (0.08-1.05)
5	123	44	373	65.6%	0.32 (0.12-0.82)
0	80	0	112	0.0%	

8 293 55 586 100.0% 0.30 (0.14-0.66)

d trial
 15 221 19 220 100.0% 0.77 (0.38-1.56)

15 221 19 220 100.0% 0.77 (0.38-1.56)



Reduction stroke/TIA recurrence

PICO 4: In adult patients with ischaemic stroke or TIA of undetermined origin, does the presence of potential blood, echocardiographic, ECG or heart and brain imaging biomarkers, compared to their absence, increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

Evidence-based recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin there is continued uncertainty over the advantages of the use of blood, echocardiographic, ECG or heart or brain imaging biomarkers to increase the detection of subclinical AF.

Quality of evidence: –

Strength of recommendation: –

LA dilation

Study	n(I)	n(I)	n(C)	N(C)	weight	OR/HR (95%CI)
Riordan 2020	28	94	46	199	11.0%	1.41 (0.81-2.45)*
Todo 2020	N.A	N.A	N.A	N.A	1.8%	0.78 (0.13-4.65)
Triantafyllou 2020	N.A	N.A	N.A	N.A	13.3%	1.49 (0.94-2.35)
Liantinoti 2019	8	22	14	196	5.5%	5.70 (2.22-14.61)
Olsen 2019	N.A	N.A	N.A	N.A	3.2%	1.76 (0.47-6.54)
Özaydin Göksu 2019	16	49	14	84	6.5%	2.4 (1.05-5.54)
Poli 2016	13	18	12	57	6.9%	4.8 (2.1-10.7)
Sudacevski 2016	7	28	19	143	5.1%	2.17 (0.81-5.81)*
Fonseca 2014	10	31	7	49	4.3%	2.86 (0.95-8.57)*
Total (CS or TIA)	82	242	112	728	57.6%	2.23 (1.53-3.26)
I ² =44%, p=0.08						
Melis 2020	32	52	31	86	12.1%	1.61 (0.98-2.66)
Ntaios 2020	N.A	N.A	N.A	N.A	12.5%	2.59 (1.59-4.2)
Rubio-Campal 2020	N.A	N.A	N.A	N.A	3.8%	4.05 (1.2-13.1)
Miyazaki 2018	10	82	4	124	3.3%	3.19 (0.89-11.50)
Ricci 2018	10	27	28	271	5.3%	4.73 (1.82-12.30)
Victor 2018	N.A	N.A	N.A	N.A	5.4%	2.29 (0.89-5.91)

brain infarcts

n(I)	N(I)	n(C)	N(C)	weight	OR/HR (95%CI)
25	95	59	174	33.4%	0.76 (0.47-1.23)

Expert consensus statement

In adult patients with ischaemic stroke or TIA of undetermined origin the presence of potential blood, echocardiographic, ECG or brain imaging biomarkers might increase the probability of AF detection but given the limited current evidence we suggest avoiding their use for excluding patients from long-term ECG monitoring.

PICO 5: In adult patients with ischaemic stroke or TIA of undetermined origin and patent foramen ovale (PFO), do implantable monitoring devices compared to any non-implantable external monitoring device increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

Evidence-based recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin and PFO, there is continued uncertainty over the risks and benefits of the use of implantable monitor devices over any non-implantable external monitor devices to increase the detection of subclinical AF.

Quality of evidence: –

Strength of recommendation: –

AF det

Study

Scacciatella
Kral 2015

Total (CS c
F=0%, p=0.65

Kistiou 202
Israel 2017

Total (ESU
P=37%, p=0.21

TOTAL
P=71%, p=0.01

Expert consensus statement

In adult patients with ischaemic stroke or TIA of undetermined origin and PFO, we suggest prolonged cardiac rhythm monitoring for AF for more than 48h in patients older than 55years to increase the detection of subclinical AF.

Expert consensus statement

We suggest prolonged cardiac rhythm monitoring for AF to increase the rate of anticoagulation or reduce unnecessary PFO occluder implantations in patients with cryptogenic stroke and PFO older than 55years.

Expert consensus statement

The MWG suggests using implantable monitoring devices, compared to any non-implantable external monitoring device to detect paroxysmal AF in patients with cryptogenic stroke and PFO older than 55years.

Expert consensus statement

In patients younger than 55years with undetermined stroke and PFO, we suggest that a basic cardiac monitoring during 24h by telemetry or Holter-ECG could be enough to rule-out subclinical AF, but clinical, stroke and PFO characteristics should be taken into account.



Some questions

ATTICUS: in ESUS pts. at high risk of AF (i.e. at least one of the following criteria: LA size >45 mm, spontaneous echo contrast in LA appendage, LA appendage flow velocity ≤ 0.2 cm/s, atrial high-rate episodes, CHA2DS2-VASc score ≥ 4 , PFO), one-year AF 23%, one-year stroke recurrence 6.8%¹

CRYSTAL-AF pts with clinical profile of NAVIGATE or RE-SPECT trials, 3-year AF in 35.8% and 33.6% of cases, respectively²

Progressive monitoring strategies, starting with non-invasive longer monitoring through external loop-recorders, followed by implantable devices in patients without AF detection. Is it cost-effective?