XV World Congress of Arrhythmias, Beijing, China - 17-20 September, 2015

Asymptomatic AF after cryptogenetic stroke: Incidence, clinical significance & therapeutic implications

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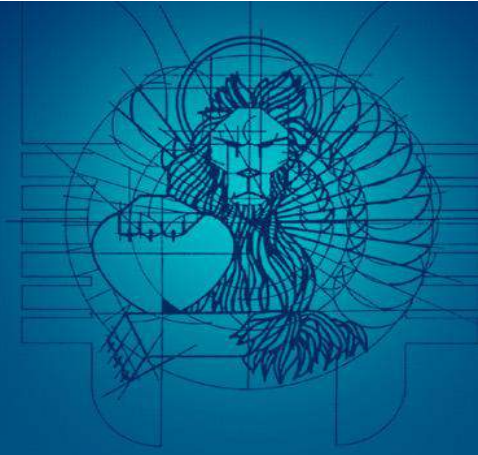
AF & Symptoms



Atrial Fibrillation

Symptomatic

palpitations, dyspnea, fatigue, angina, dizziness, syncope

Asymptomatic or Silent

not perceived at all by the patient

Asymptomatic AF / Detection Methods

Intermittent AF monitoring

- Standard-12 lead ECG
- 24-h / 7-d Holter monitoring
- In-hospital telemetry
- Mobile continuous outpatient telemetry
- Event recorder / Intermittent TTEM

Continuous AF monitoring

- PM - ICD Device memory
- External & Implantable loop recorder

EURObservational Research Programme-AF (EORP-AF) Pilot General Registry

	Total	EHRA I (%)	EHRA II (%)	EHRA III (%)	EHRA IV (%)
N° of Patients	3119	1237 **(39.7%)**	963 **(30.9%)**	746 (23.9%)	173 (5.5%)

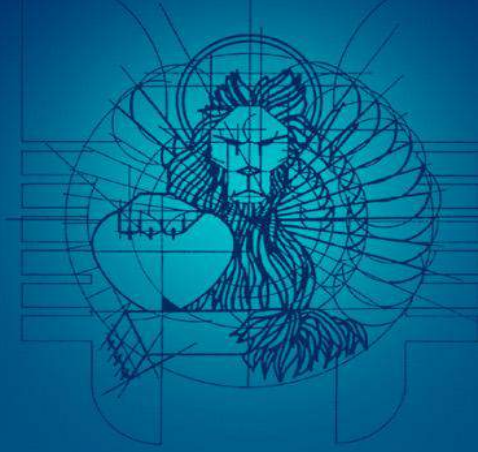
Boriani G et al. Am J Med. 2015 May;128(5):509-18

Prevalence of Asymptomatic AF

Clinical Settings	Percent
Incidental finding at standard ECG ECG	**16-25**
Pts treated with AADs TTEM	**56-70**
PM – ICD recipients Device memory	**51-74**
Pts with criptogenetic ischemic stroke HM - ILR	**0-42**
Pts after AF ablation HM - MCOT - PM/ICD - ILR	**0-31**

Raviele A. CircArrhythmElectrophysiol 2015; 8: 249-251

Cryptogenetic Stroke



Definition

Stroke without a cause after extensive investigations

Incidence

30-40% of all strokes

Possible explanation

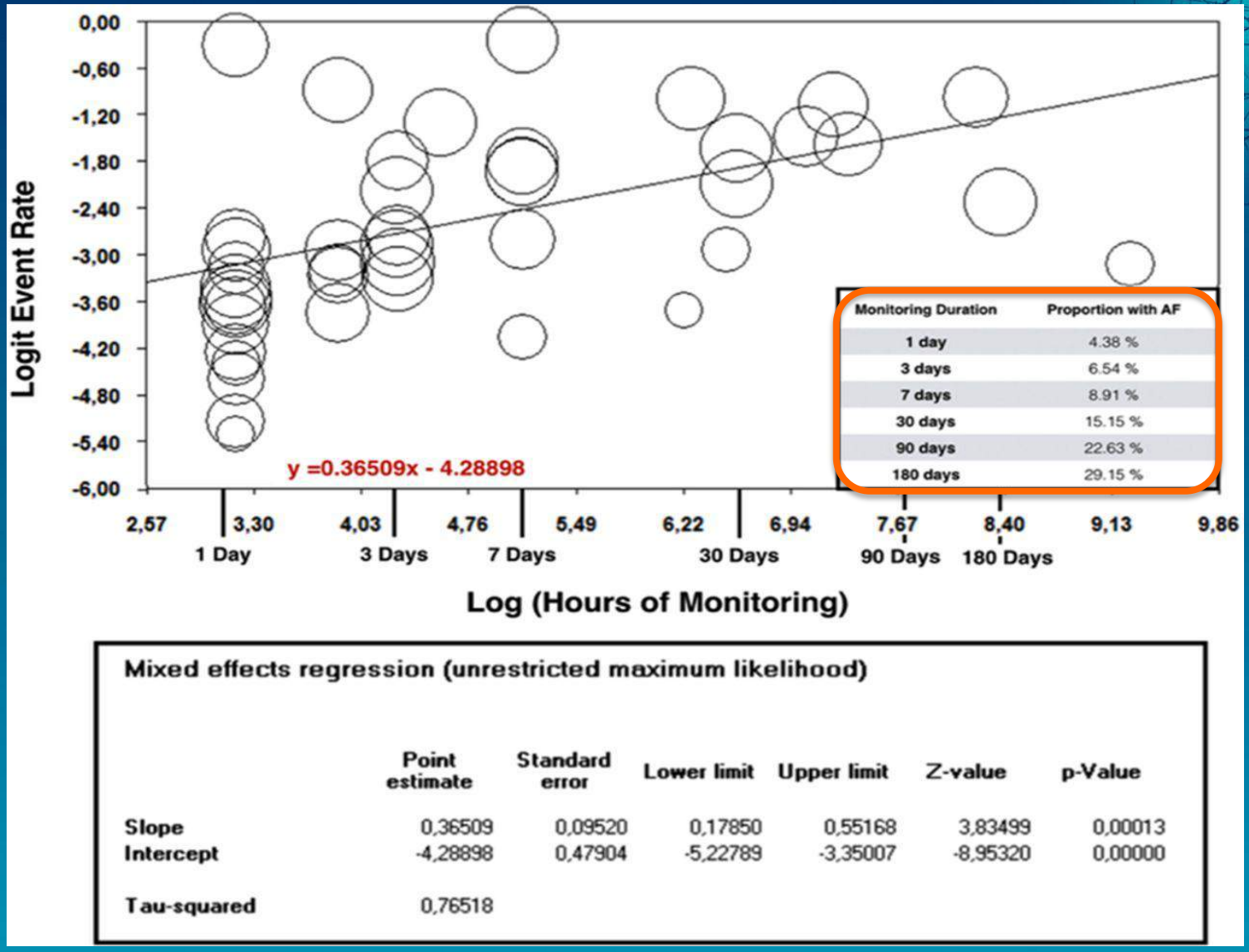
Occult or subclinical AF

Prevalence of Asymptomatic AF

ECG monitoring system	Percent
Standard12-lead ECG	**2-4**
Mobile cardiac outpatient telemetry (MCOT)	**9.0**
Continuous ECG monitoring for 24-72 h	**2.4-18.5**
Event recorder (up to 30 d)	**14.2-16.1**
PM-ICD	**28%**
ILR	**8.9-33.7%**
All systems	**0-42**

Andrade JG, et al. Frontiers in Physiology 2015; 6 Article 100

Metaregression analysis assessing the relationship between duration of atrial fibrillation (AF) monitoring and AF event rate. y axis, Logarithm of the event rate. x axis, Logarithm of the number of hours of monitoring.

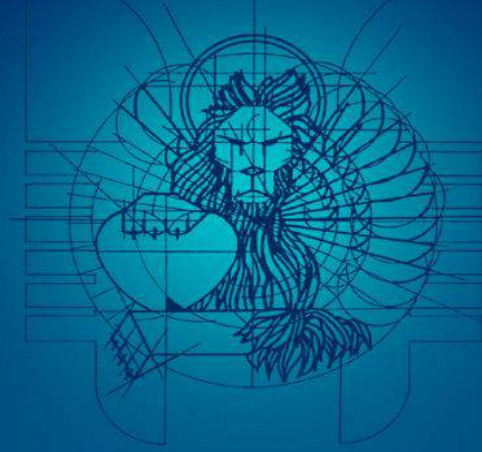


Mixed effects regression (unrestricted maximum likelihood)

	Point estimate	Standard error	Lower limit	Upper limit	Z-value	p-Value
Slope	0,36509	0,09520	0,17850	0,55168	3,83499	0,00013
Intercept	-4,28898	0,47904	-5,22789	-3,35007	-8,95320	0,00000
Tau-squared	0,76518					

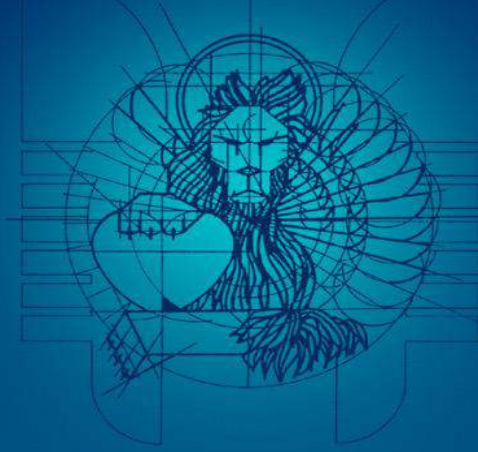
Charles Dussault et al. Circ Arrhythm Electrophysiol. 2015;8:263-269

Incidence of Silent AF



- Asymptomatic AF is a common finding in patients with a stroke of undetermined origin if prolonged ECG monitoring is performed soon after the index event, reaching 30% or more at 3 months if an implantable loop recorder is used

Silent AF / Main Issues



- **Clinical / prognostic significance**
- **Causal relationship with stroke**
- **Therapeutic implications**

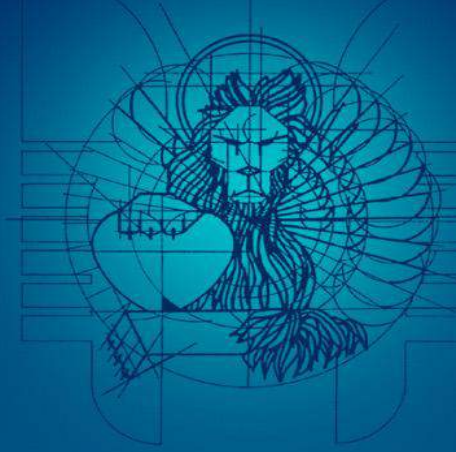
Table 4 Summary of studies on AF detected by dual-chamber cardiac implantable electronic devices and thromboembolic risk

Year	Trial	No. of patients	Duration of follow-up	Atrial rate cutoff	AF burden threshold	Hazard ratio for TE event	TE event rate (below vs above AF burden threshold)
2003	Ancillary MOST[47]	312	27 months (median)	>220 bpm	5 minutes	6.7 ($P = .020$)	3.2% overall (1.3% vs 5%)
2005	Italian AT500 Registry[49]	725	22 months (median)	>174 bpm	24 hours	3.1 ($P = .044$)	1.2% annual rate
2009	Botto et al[50]	568	1 year (mean)	>174 bpm	$CHADS_2$ + AF burden	N/A	2.5% overall (0.8% vs 5%)
2009	TRENDS[51]	2486	1.4 years (mean)	>175 bpm	5.5 hours	2.2 ($P = .060$)	1.2% overall (1.1% vs 2.4%)
2012	Home Monitor CRT[52]	560	370 days (median)	>180 bpm	3.8 hours	9.4 ($P = .006$)	2.0% overall
2012	ASSERT[31]	2580	2.5 years (mean)	>190 bpm	6 minutes	2.5 ($P = .007$)	(0.69% vs 1.69%)

AF = atrial fibrillation; TE = thromboembolic event.

Glotzer TV et al. Heart Rhythm 2014; Epub before Print

Silent AF / Significance



- It is not yet known what is the length of asymptomatic AF episodes or the amount of asymptomatic AF burden that convey a substantial risk.

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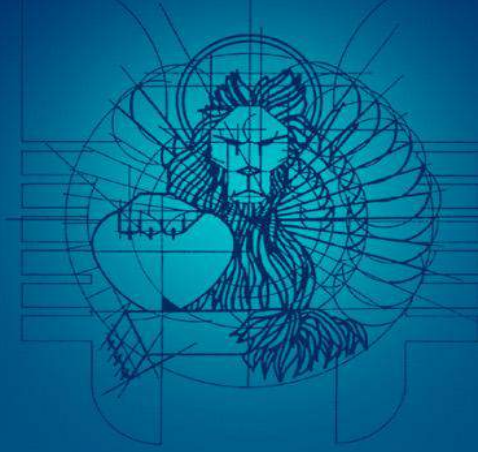
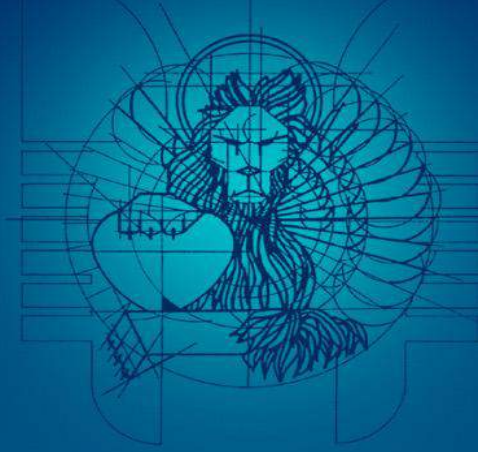


- The episode duration and burden of asymptomatic AF that best predict subsequent stroke are still matters of debate and need to be addressed by future studies

Silent AF / Main Issues



- **Clinical / prognostic significance**
- **Causal relationship with stroke**
- **Therapeutic implications**

Silent AF & Stroke

- Direct cause of stroke ?
- Marker of an increased risk ?

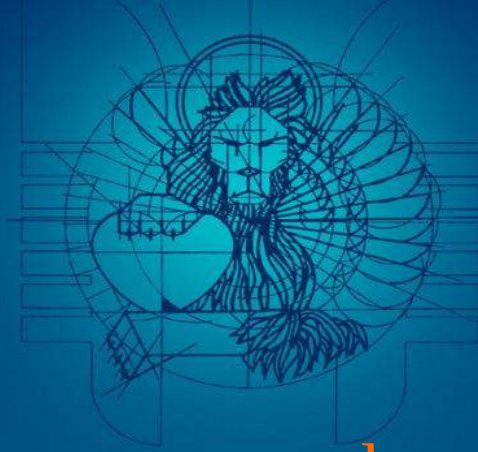
Table 5 Temporal relationship of device-detected AF to thromboembolic events

Year	Trial	No. of patients with TE event	Definition of AF episode	Any AF detected before TE event	AF detected only after TE event	No AF in 30 days before TE event	Any AF in 30 days before TE event
2011	TRENDS[53]	40	5 minutes	20/40 (50%)	6/40 (15%)	29/40 (73%)	11/40 (27%)
2014	ASSERT[54]	51	6 minutes	18/51 (35%)	8/51 (16%)	47/51 (92%)	4/51 (8%)
2014	IMPACT[55]	69	36/48 atrial beats ≥200 bpm	20/69 (29%)	9/69 (13%)	65/69 (94%)	4/69 (6%)

AF = atrial fibrillation; TE = thromboembolic event.

Glotzer TV et al. Heart Rhythm 2014; Epub before Print

Silent AF & Stroke



- These results indicate that a proximate temporal relationship between asymptomatic AF and stroke occurrence does not exist and suggest that AF is not the direct cause of stroke in the majority of patients.
- They also call into question our current understanding of how AF causes embolic events.

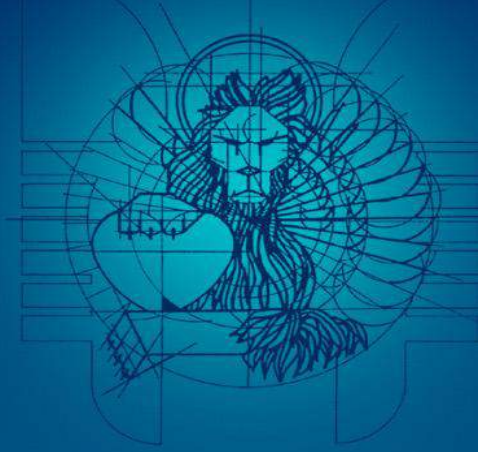
Silent AF & Stroke

- It is likely that multiple mechanisms contribute to stroke in patients with asymptomatic AF.
- In some cases, stroke may be due to stasis from an actual AF episode, in others to chronic atrial and endothelial changes caused by multiple prior AF episodes; and in other cases again, to non-AF mechanisms.

Silent AF & Stroke

- In these latter cases, it may be that the AF is simply a marker of increased stroke from any cause because of its relationship to other comorbidities, such as heart failure, hypertension, diabetes mellitus, occult atrial myopathy, endothelial dysfunction, or other vascular disease risk factors summarized by the CHA2DS2-VASc score system.

Silent AF / Main Issues

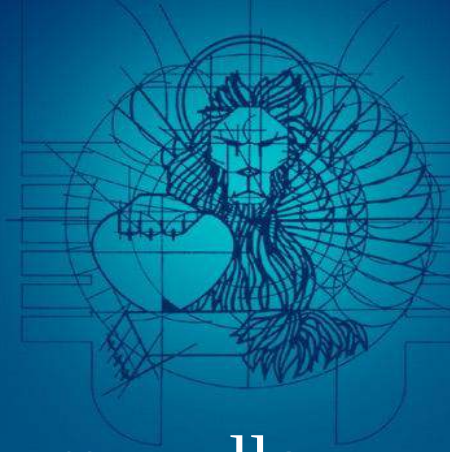


- **Clinical / prognostic significance**
- **Causal relationship with stroke**
- **Therapeutic implications**

Asymptomatic AF / Therapy

- Need for Oral Anticoagulation

Asymptomatic AF / Need for OAC



- Detection of asymptomatic AF theoretically may allow early initiation of anticoagulation, instead of the usual care with antiplatelet therapy, and may lead to a reduction in the risk of recurrent stroke.
- However, whether pts with subclinical AF have to be anticoagulated currently remains an unanswered question.

Asymptomatic AF / Need for OAC

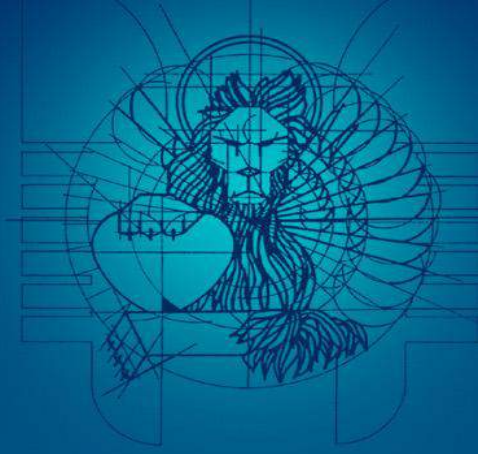
- Indeed, no prospective randomized trials using OAC have been performed in this field to date.
- Furthermore, the lack of proximate temporal relationship between asymptomatic AF and stroke observed in the majority of patients in the ASSERT, TRENDS, and IMPACT trials suggests that oral OAC may not be systematically required for stroke prevention in asymptomatic patients

Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices

David T. Martin[1], Malcolm M. Bersohn[2], Albert L. Waldo[3], Mark S. Wathen[4], Wassim K. Choucair[5], Gregory Y.H. Lip[6], John Ip[7], Richard Holcomb[8], Joseph G. Akar[9], and Jonathan L. Halperin[10]*, on behalf of the IMPACT Investigators

Eur Heart J 2015; 36: 1660-1668

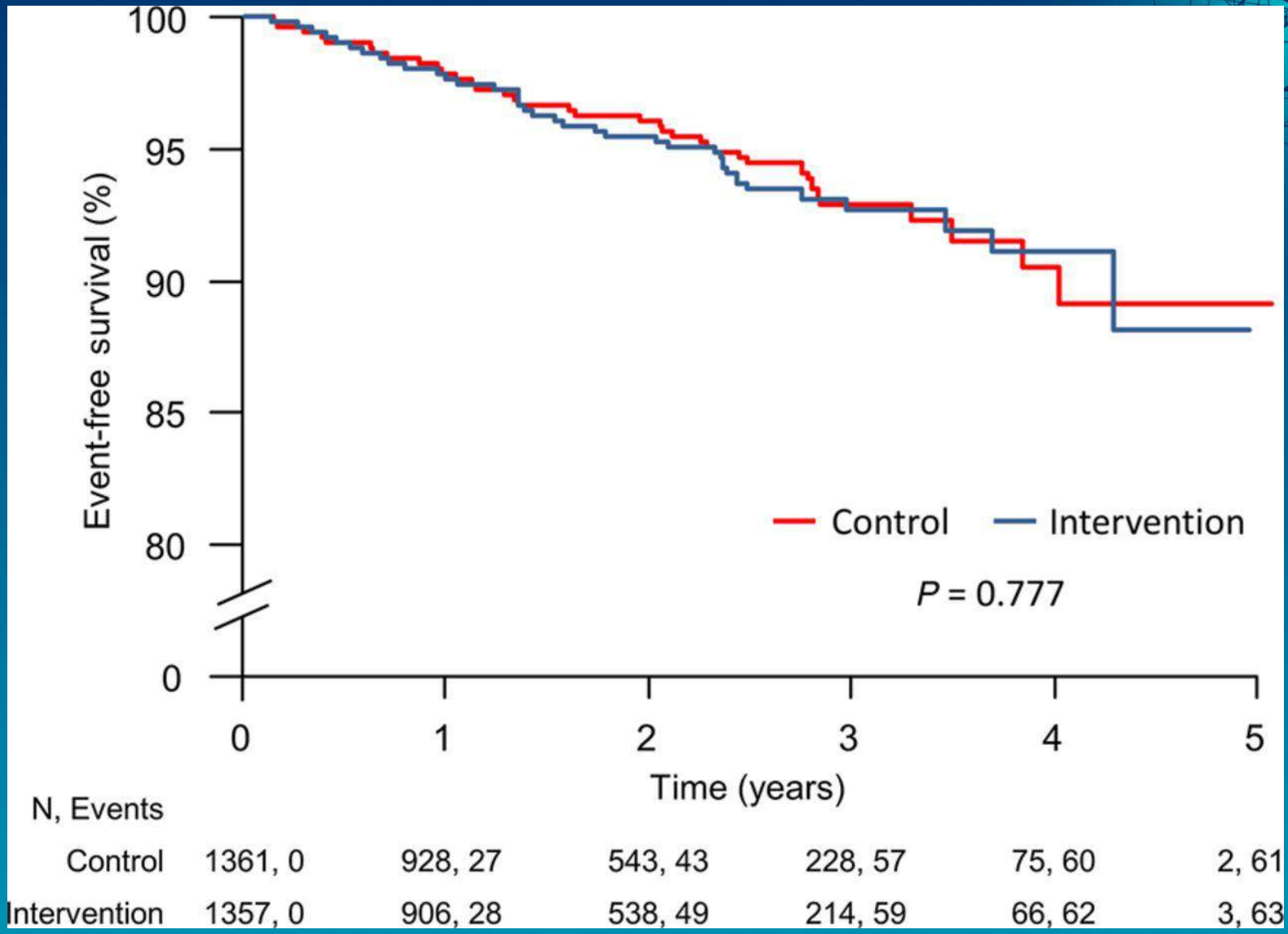
IMPACT / Study Hypothesis



- The trial was designed to test the hypothesis that initiation and withdrawal of OAC guided by continuous ambulatory monitoring of subclinical AF would reduce the rate of stroke and major bleeding compared to conventional clinical management.

Primary Outcome Events

(Stroke, systemic embolism or major bleed)



Martin DT, et al. Eur Heart J 2015; 36: 1660-1668

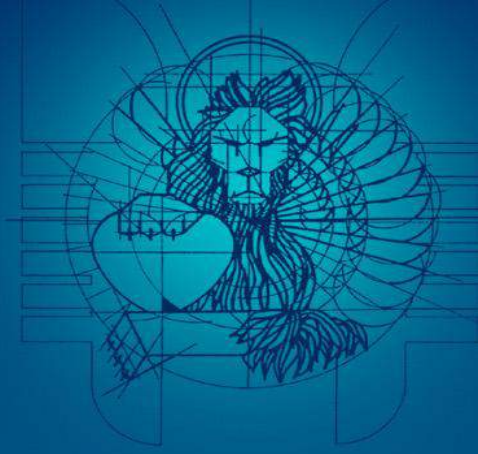
Conclusions (1)

- Asymptomatic or silent AF is a common finding after a cryptogenetic stroke when prolonged ECG monitoring is performed.

Conclusions (2)

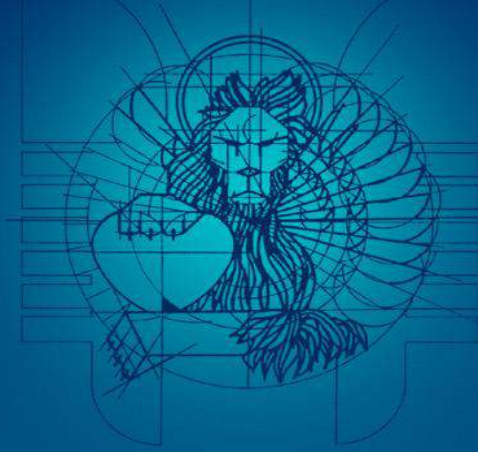
- Patients with asymptomatic AF seem to have the same prognosis than patients with symptomatic AF.
- However, the length of silent AF episodes and the burden of the arrhythmia that convey a greater risk of stroke are still uncertain and need to be clarified by further large prospective studies

Conclusions (3)



- In the majority of patients, there is no proximate temporal relationship between asymptomatic AF and stroke occurrence. This suggests that silent AF is not the direct cause of stroke, but rather represents only a marker of increased thromboembolism

Conclusions (4)



- Future studies have to establish if and when patients with asymptomatic AF really benefit from oral anticoagulant therapy.