Adavances in Cardiac Arrhythmias and
Great Innovations in Cardiology

Turin 2014

Can rhythm control strategy reduce the risk of clinical and silent cerebral ischemia?

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University of Turin, Italy

Disclosure form

Economic

No conflicts of interest related to this topic to declare

Ideologic

YES

Two reasons to pursue rhythm control strategy

- If we have been created in sinus rhythm there must be a reason

Faith

- For 2 millions years in the evolution of the human species sinus rhythm has always been maintained

Rational

Atrial fibrillation therapy: Aims

Symptoms relief and quality of life

Reduction of related major comorbidities

e.g. clinical (stroke/TIA) and “silent” cerebral ischemia

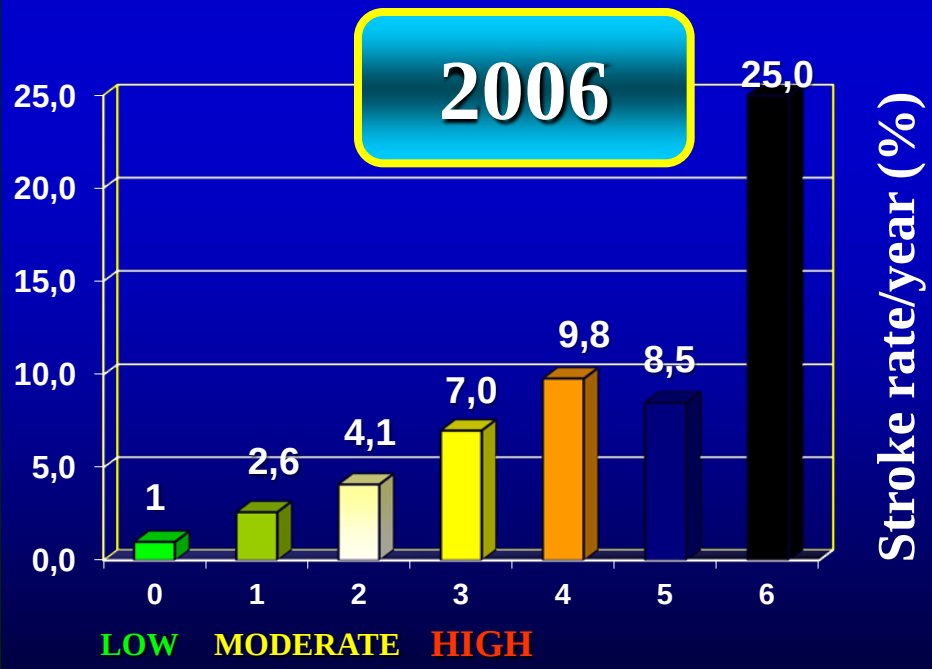
Reduction of mortality

CHADS2 score

Congestive heart failure	1
Hypertension	1
Age > 75 years	1
Diabetes mellitus	1
Prior Stroke or TIA	2

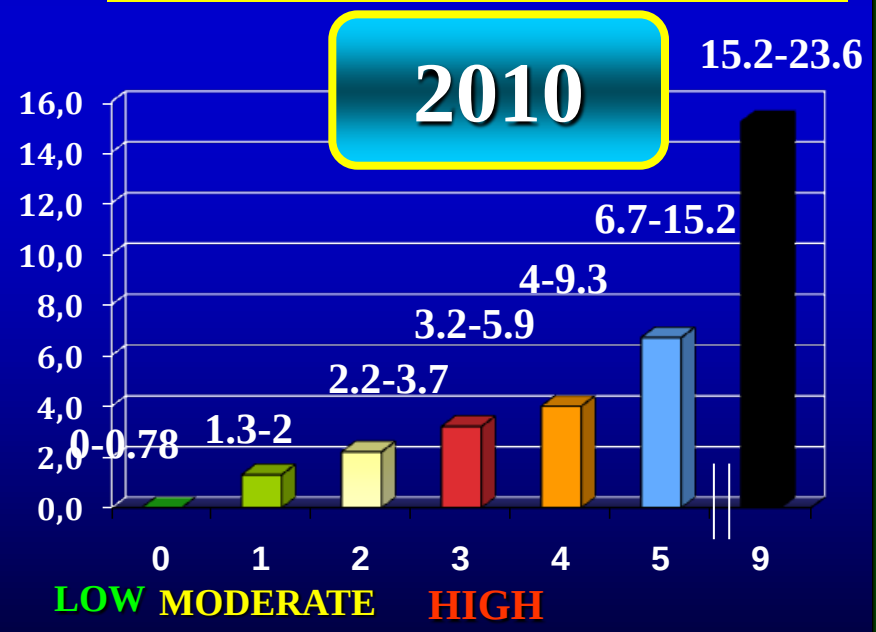
CHA2DS2vasc score

Congestive heart failure	1
Hypertension	1
Age > 75 years	2
Diabetes mellitus	1
Prior Stroke or TIA	2
vasculopathy	1
age>65	1
sex	1



Gage JAMA 2001; Fang Circulation 2005

Stroke rate/year (%)



ESC Guidelines 2010; Olesen JB et al BMJ 2011

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Trial name	RELY	ROCKET AF	ARISTOTLE	ENGAGE AF-TIMI 48
Brand Name	**Pradaxa**	**Xarelto**	**Eliquis**	**Lixiana**
Comparator	Warfarin (INR 2-3)			
N	18.113	14.264	18.201	21.105
Age	71.5 ± 8.7	73 (65-78)	70 (63-76)	72 (64-78)
Age > 75 yrs	7258 (40.1%)	6229 (43.6%)	5678 (31.1%)	8474 (40.2%)
CHADS2	**2.1**	**3.5**	**2.1**	**2.8**
Study Design	Open-label (warfarin) Non inferiority	Double-blind Non inferiority	Double-blind Non inferiority	Double-blind
Dose of Study Drug	110 mg bid or 150 mg bid	20 mg od 15 mg od)	5 mg bid 2.5 mg bid	60 mg od 30 mg od

Meta-Analysis of Efficacy and Safety of New Oral Anticoagulants Versus Warfarin in Patients with Atrial Fibrillation

Stroke, Systemic Embolism

150 mg bid

RRR 22%
ARR 0.7%

Major Bleeding

RRR 12%
ARR 0.7%

	RR (CI)	NOA	W
RE-LY **150 mg bid**	0.94 (0.82, 1.07)	399/6076	421/6022
ROCKET AF	1.03 (0.89, 1.18)	395/7111	386/7125
ARISTOTLE	0.70 (0.61, 0.81)	327/9088	462/9052
Subtotal (I-squared = 87.2%, p = 0.000)	0.88 (0.71, 1.09)	1121/22275	1269/22199

Intracranial Bleeding

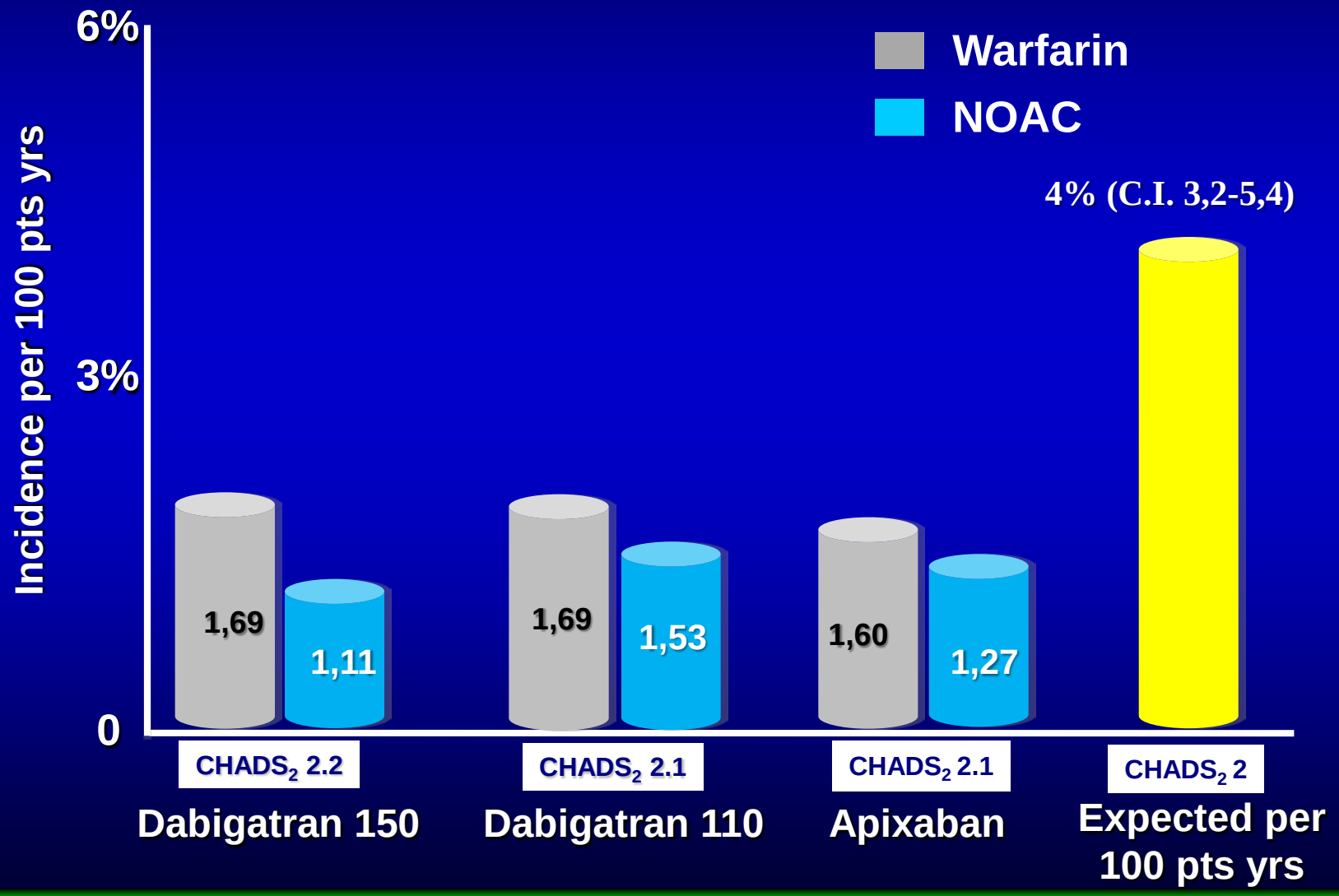
RRR 51%
ARR 0.7%

	RR (CI)	NOA	W
RE-LY **150 mg bid**	0.41 (0.28, 0.60)	36/6076	87/6022
ROCKET AF	0.66 (0.47, 0.92)	55/7111	84/7125
ARISTOTLE	0.42 (0.31, 0.59)	52/9088	122/9052
Subtotal (I-squared = 54.9%, p = 0.109)	0.49 (0.36, 0.66)	143/22275	293/22199

Miller C. et al. Am J Cardiol 2012

Annual Thromboembolic Risk per 100 pts year

Warfarin vs New Oral Anticoagulants



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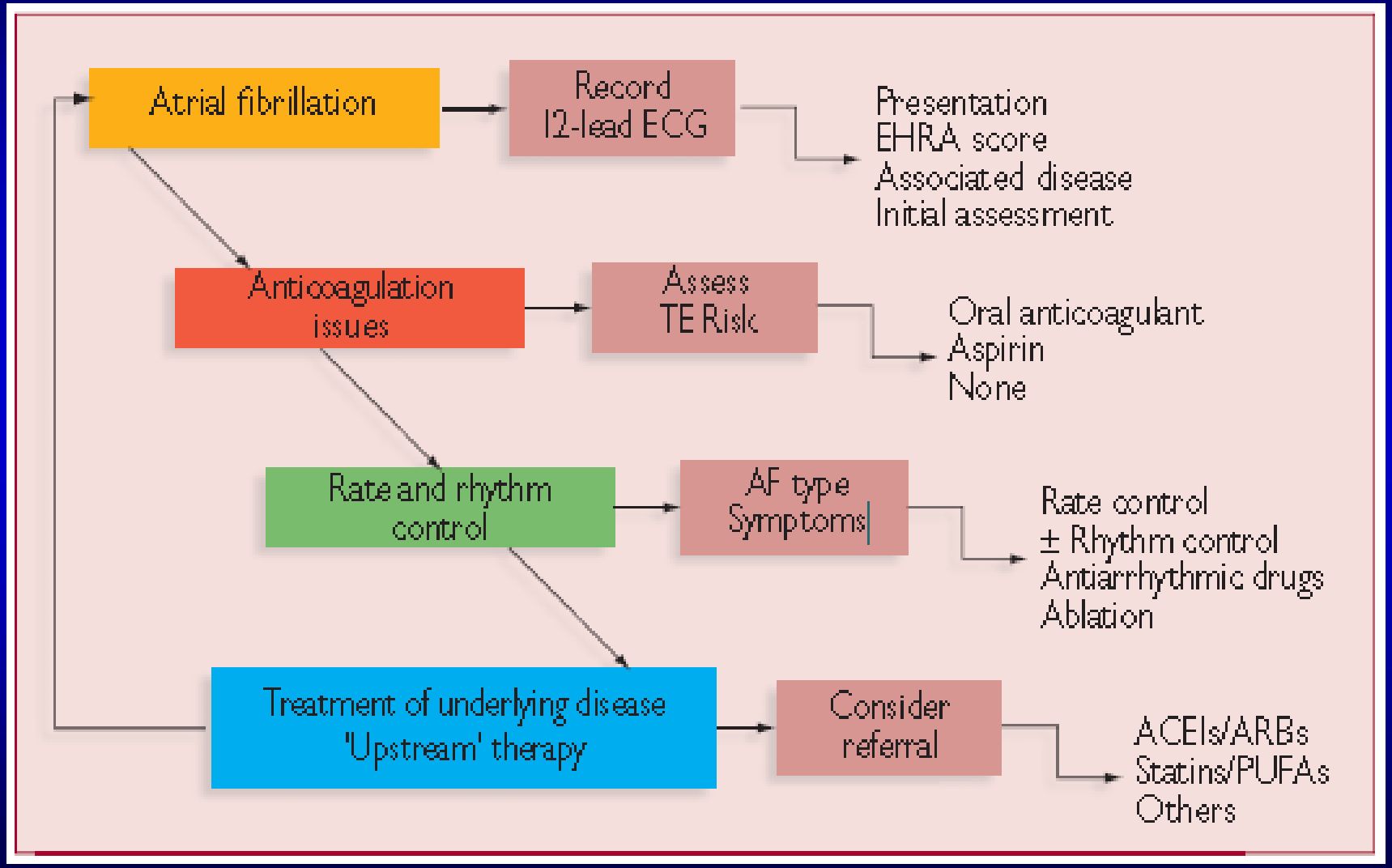
Total patients enrolled 71683 (38.6% ≥75 years)

Less than 2% treated with

<u>rhythm control strategy</u>

Can a rhythm control strategy further reduce thromboembolic risk?

Management cascade for patients with AF

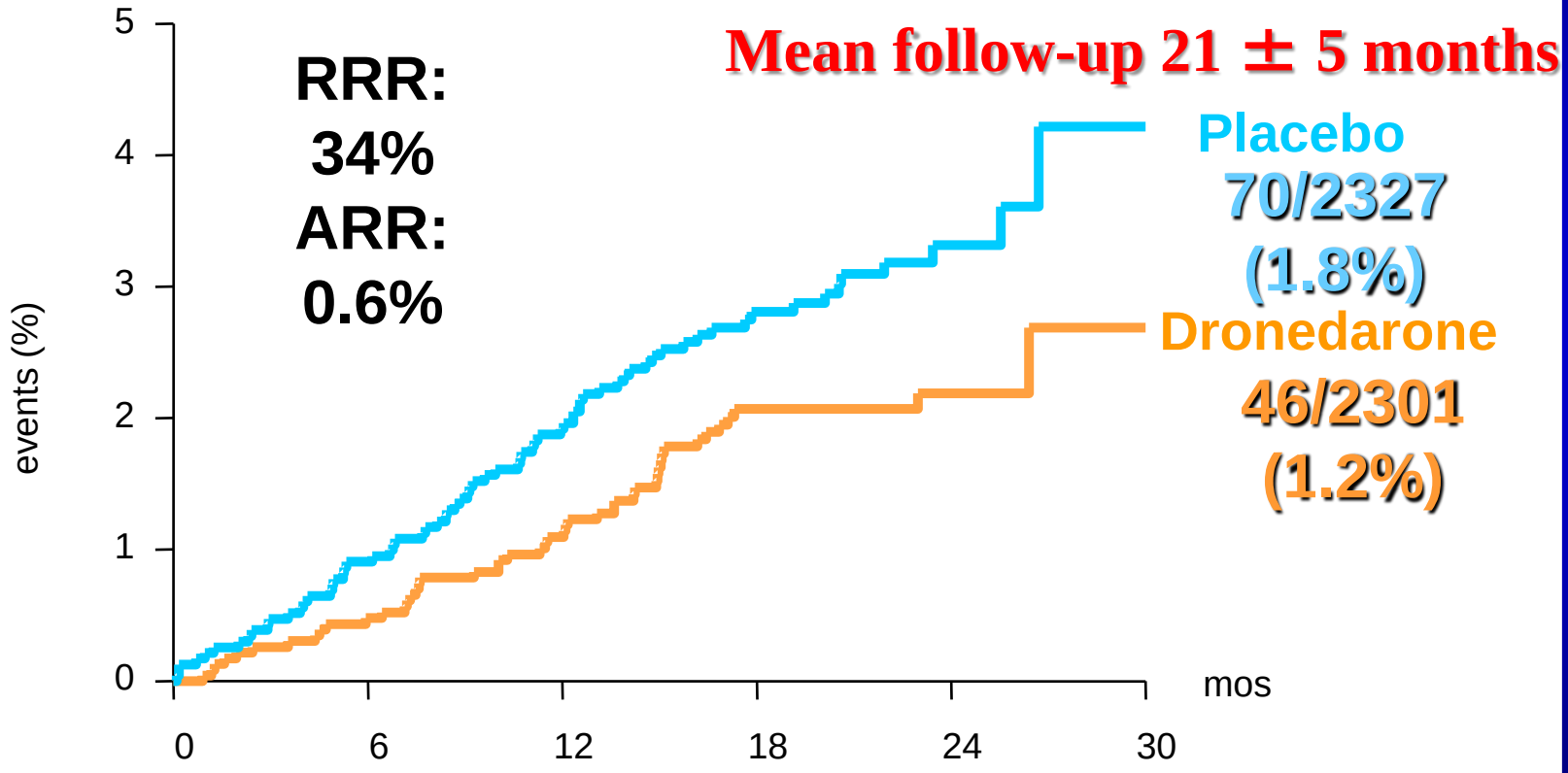


ESC 2010 AF guidelines

ATHENA Substudy Stroke Reduction

4500 AF pts (Paroxysmal 75%) treated with

Dronedarone 400 mg bid (OAT 1403, 61%) vs Placebo (OAT 1384, 59%)



Pz a rischio						
Placebo	2327	2275	2220	1598	618	6
Dronedarone	2301	2266	2223	1572	608	4

ATHENA. Circulation 2009;120:1174-1180

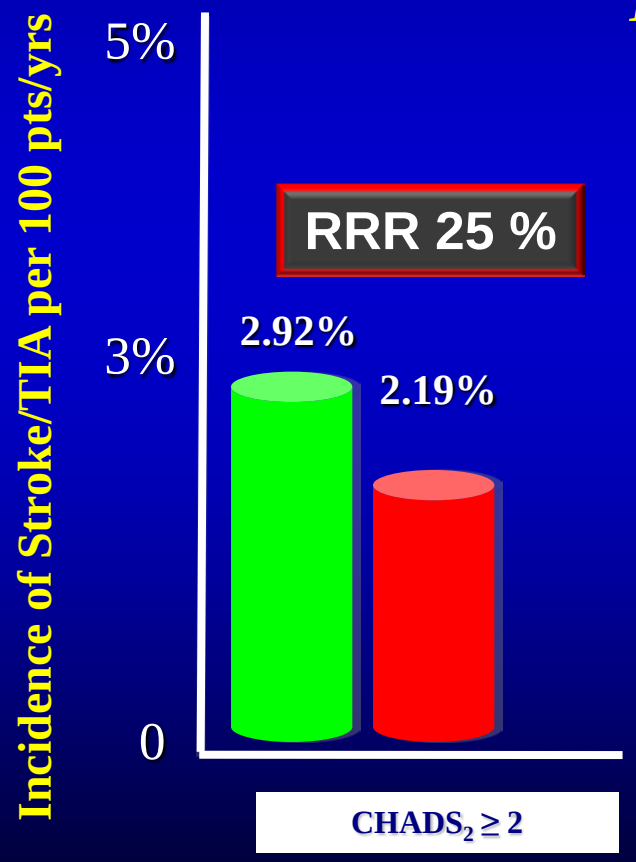
Rhythm Versus Rate Control Therapy and Subsequent Stroke or Transient Ischemic Attack in Patients With Atrial Fibrillation

Meytal Avgil Tsadok, Cynthia A. Jackevicius, Vidal Essebag, Mark J. Eisenberg, Elham Rahme, Karin H. Humphries, Jack V. Tu, Hassan Behlouli and Louise Pilote

Circulation 2012;126:2680-87

57518 AF Quebec pts, aged > 65 y (1999-2007)

Equally treated with OAT (59% in both groups)



Rate control tx
41193 pts

Rhythm control tx.
16325 pts Only AADs

What about rhythm control using TC ablation and long-term thromboembolic risk?

Incidence of cerebral thromboembolic events during long-term follow-up in patients treated with transcatheter ablation for atrial fibrillation

Fiorenzo Gaita[1*], Davide Sardi[1], Alberto Battaglia[1], Cristina Gallo[1], Elisabetta Toso[1], Arianna Michielon[1], Domenico Caponi[2], Lucia Garberoglio[2], Davide Castagno[1], and Marco Scaglione[2]

Europace (2014) 16, 980–986

766 pts mean CHADS 2,0, undergoing AF ablation

CHADS ≤ 1
Off OAT

CHADS2 ≥ 2
On OAT

Mean follow up 60 months

Incidence of cerebral thromboembolic events during long-term follow-up in patients treated with transcatheter ablation for atrial fibrillation

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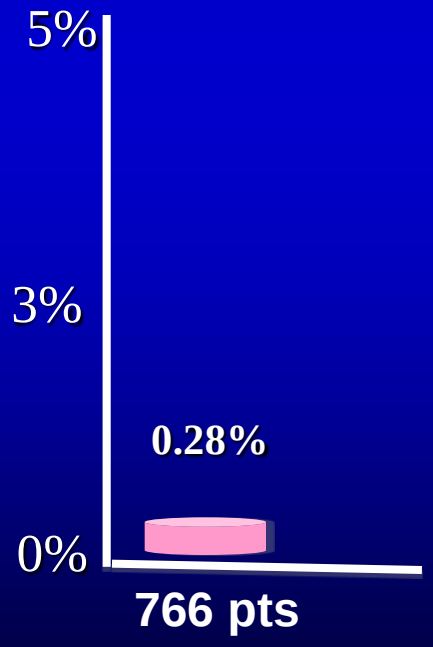
Europace (2014) 16, 980–986

TE event rate observed per 100 pts/yr

Total event rate
5 years
1,4%



Incidence of cerebral thromboembolic events during long-term follow-up in patients treated with transcatheter ablation for atrial fibrillation

Fiorenzo Gaita[1*],
Elisabetta Toso[1],
Davide Castagno[1],

Maintenance of sinus rhythm with an ablation strategy in patients with atrial fibrillation is associated with a lower risk of stroke and death

Ross J Hunter,[1] James McCready,[2] Ihab Diab,[1] Stephen P Page,[1] Malcolm Finlay,[2]
Sporton,[1,4] Michael Jones,[5]
[3] Andrew Staniforth,[6]
[2] Richard J Schilling[1,4]

The Risk of Thromboembolism and Need for Oral Anticoagulation After Successful Atrial Fibrillation Ablation

Sakis Themistoclakis, MD,* Andrea Corrado, MD,* Francis E. Marchlinski, MD,† Pierre Jais, MD,‡
Erica Za
Walid I.
David J.
Michel

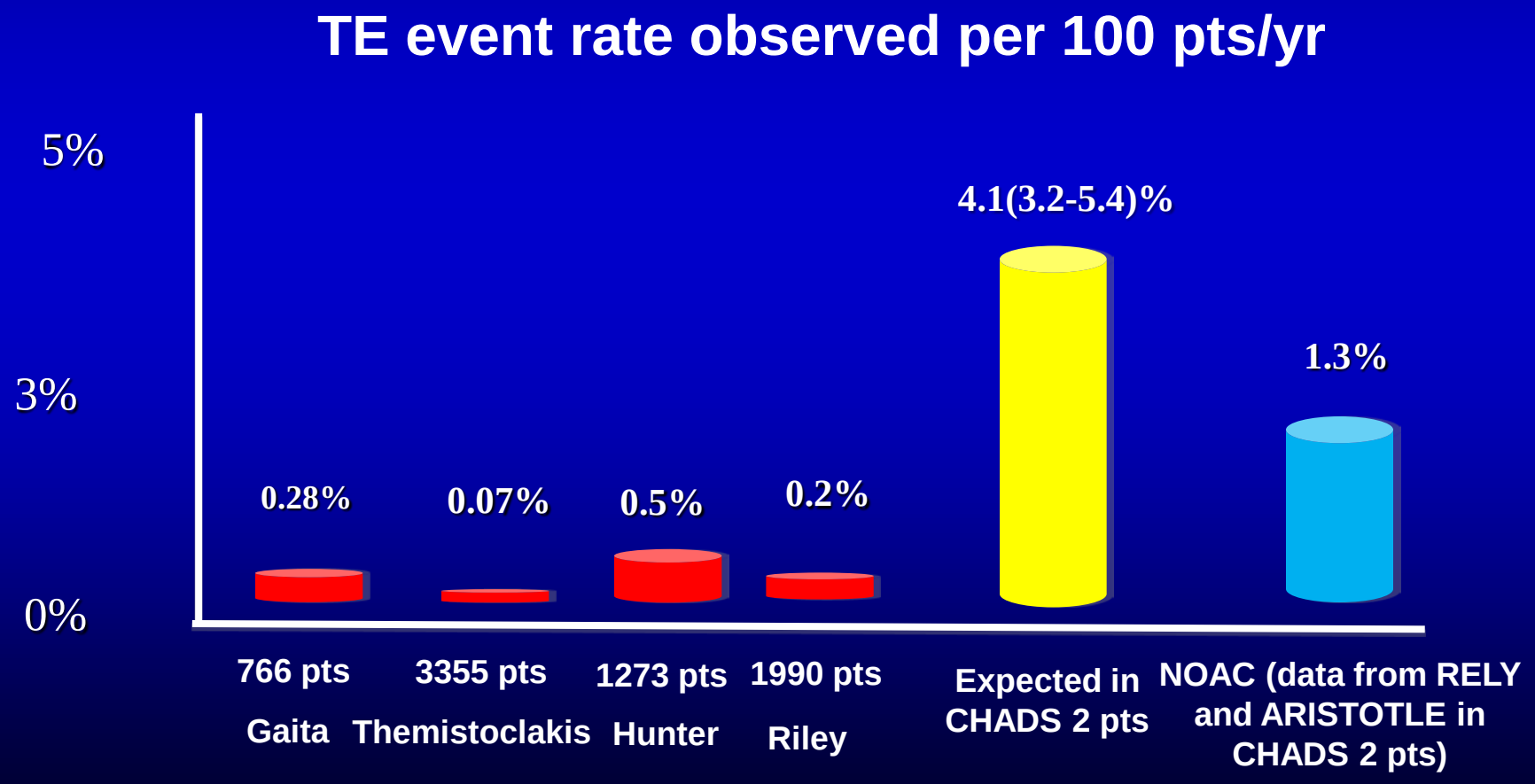
Risk of Stroke or Transient Ischemic Attack After Atrial Fibrillation Ablation with Oral Anticoagulant Use Guided by ECG Monitoring and Pulse Assessment

MICHAEL P. RILEY, M.D., PH.D., ERICA ZADO, PA-C, MATHEW D. HUTCHINSON, M.D., DAVID LIN, M.D., RUPA BALA, M.D., FERMIN C. GARCIA, M.D., DAVID J. CALLANS, M.D., JOSHUA M. COOPER, M.D., RALPH J. VERDINO, M.D., SANJAY DIXIT, M.D., and FRANCIS E. MARCHLINSKI, M.D.

TE event rate following AF ablation

Total patients evaluated 7384

Mean CHADS 2

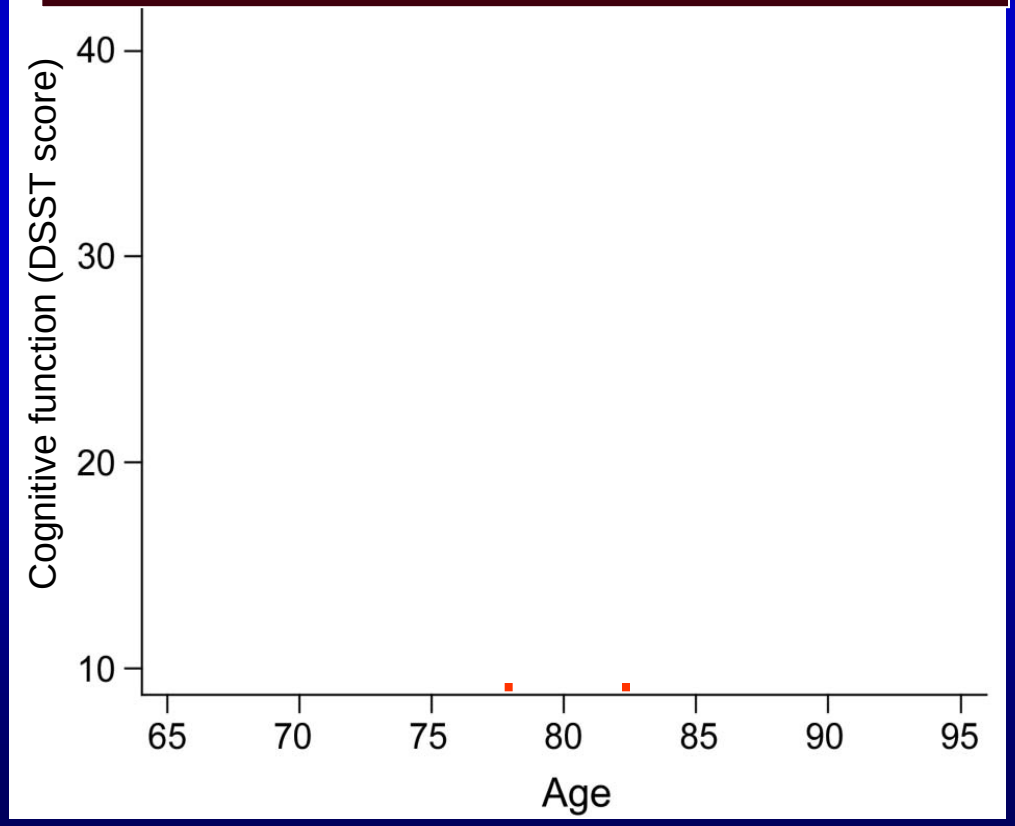


What about
silent cerebral ischemia and
cognitive decline?

Atrial fibrillation and incident dementia

5.150 pts, mean age 73 yrs, Male 41%, Hypertension 57%
Not having atrial fibrillation or a history of stroke at baseline

Conclusion:
Patients with AF have a cognitive performance comparable to that of those with at least five years older



Mean follow-up 7 yrs

Cognitive test performed annually

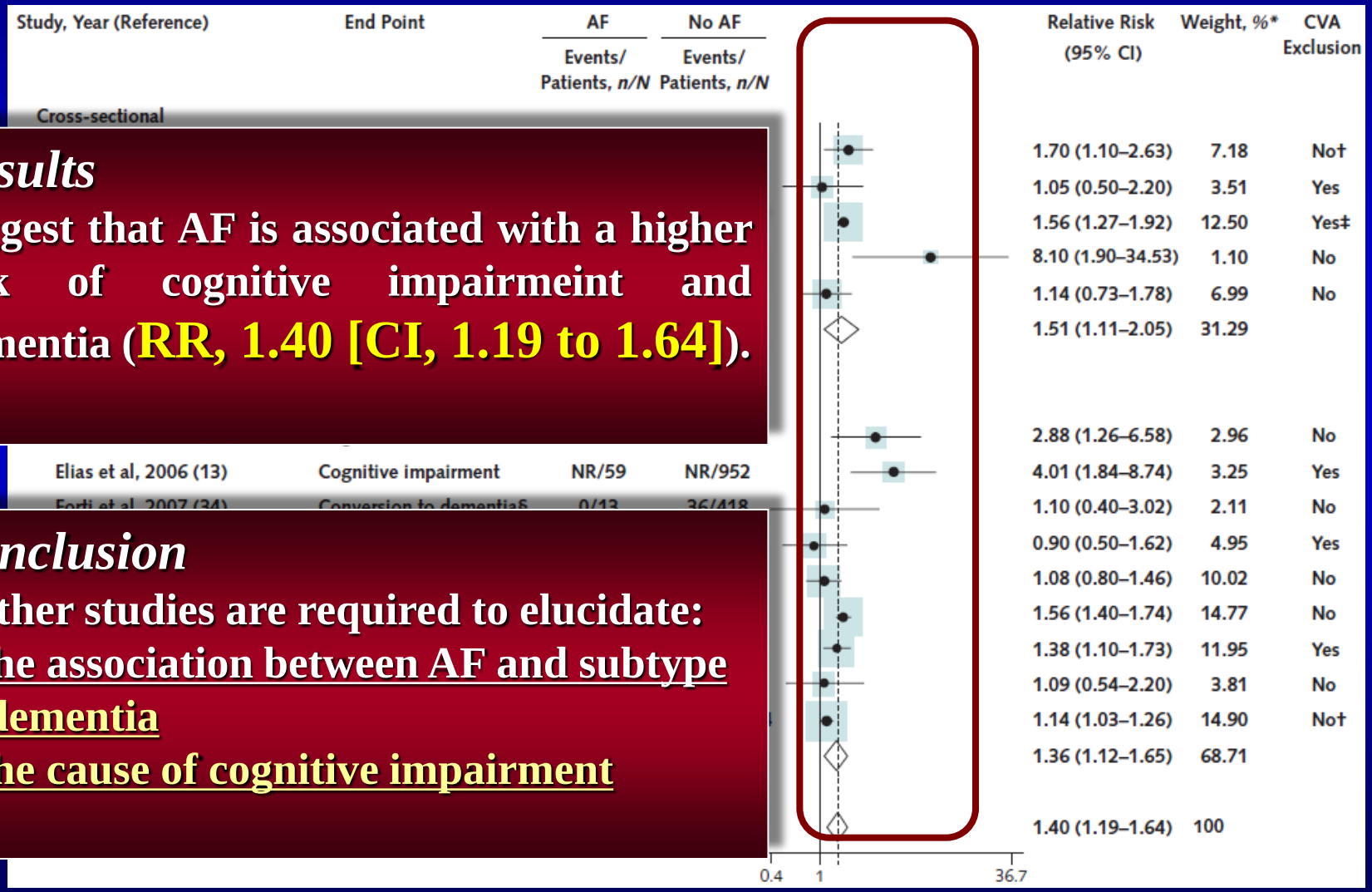
Above 70 yrs of age cognitive performance physiologically declines

AF onset accelerates cognitive decline

Tacker EL et al Neurology 2013;81:119–125

Cognitive Impairment Associated With Atrial Fibrillation

14 studies. Tot pts 85118 AF patients 14147 No AF patients 70971



Results

suggest that AF is associated with a higher risk of cognitive impairmeint and dementia (RR, 1.40 [CI, 1.19 to 1.64]).

Conclusion

further studies are required to elucidate:

- The association between AF and subtype of dementia

- The cause of cognitive impairment

Ann Intern Med. 2013;158:338-346

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Heart Rhythm Disorders

CME

Prevalence of Silent Cerebral Ischemia in Paroxysmal and Persistent Atrial Fibrillation and Correlation With Cognitive Function

Fiorenzo Gaita, MD,* Laura Corsinovi, MD, PhD,* Matteo Anselmino, MD, PhD,*
Cristina Raimondo, MD,* Martina Pianelli, MD,* Elisabetta Toso, MD,* Laura Bergamasco, Prof,†
Carlo Boffano, MD,‡ Maria Consuelo Valentini, MD,§ Federico Cesarani, MD,‖
Marco Scaglione, MD¶

Turin, Milan, and Asti, Italy

Controls

Paroxysmal AF

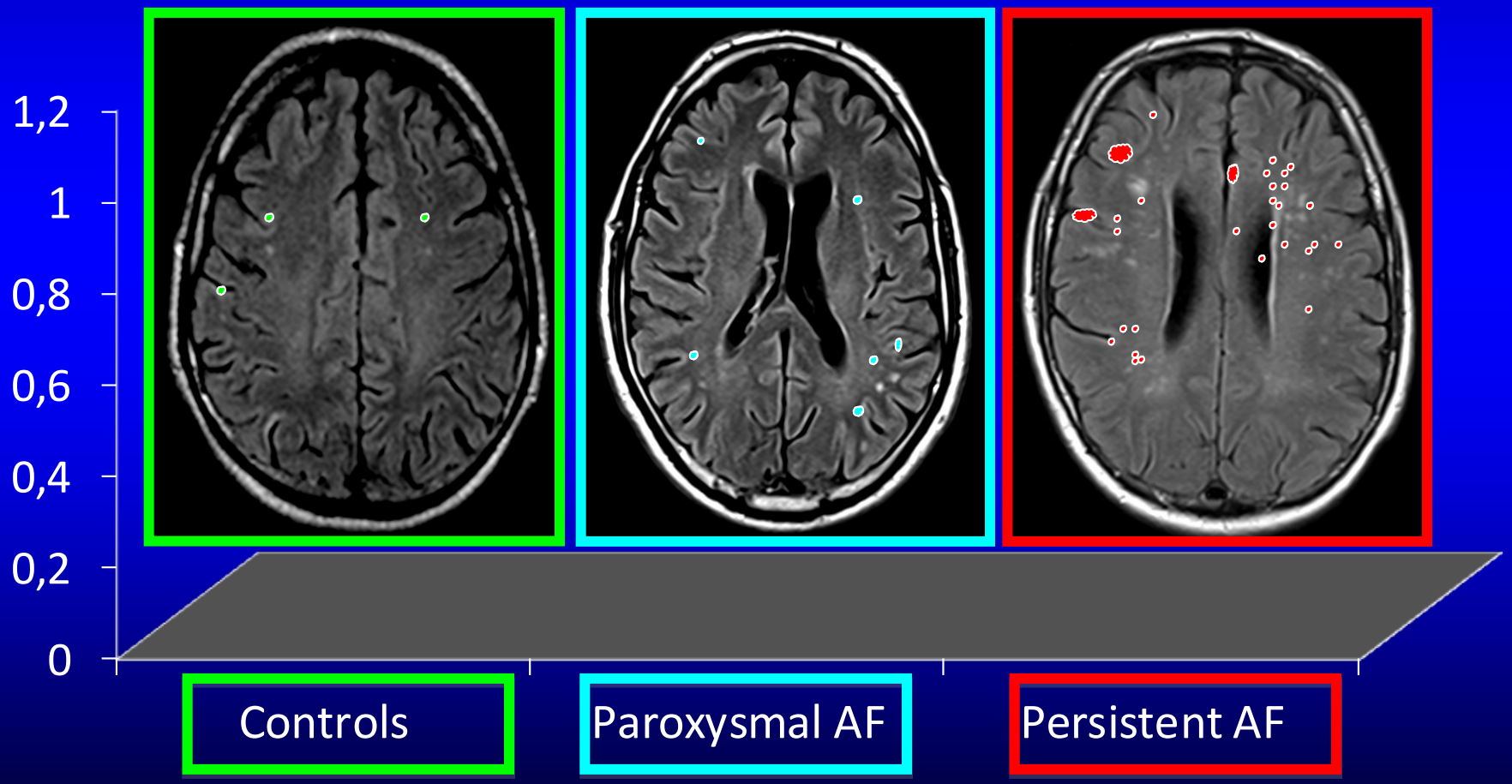
Persistent AF

Undergone to cerebral MRI → SCI

Cognitive test → Cognitive decline

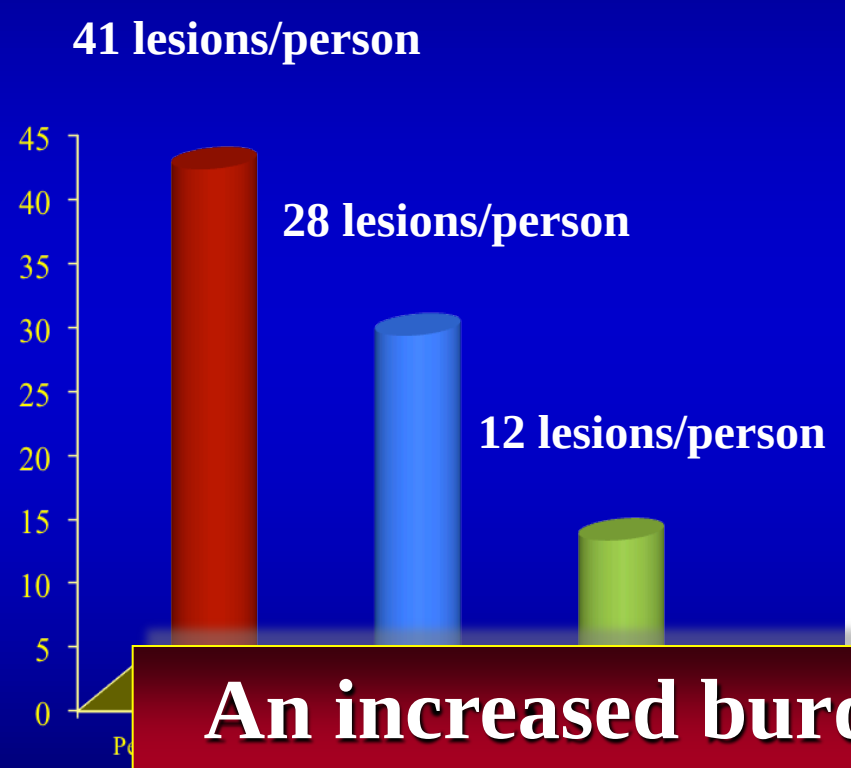
The number of SCI varies according to AF type

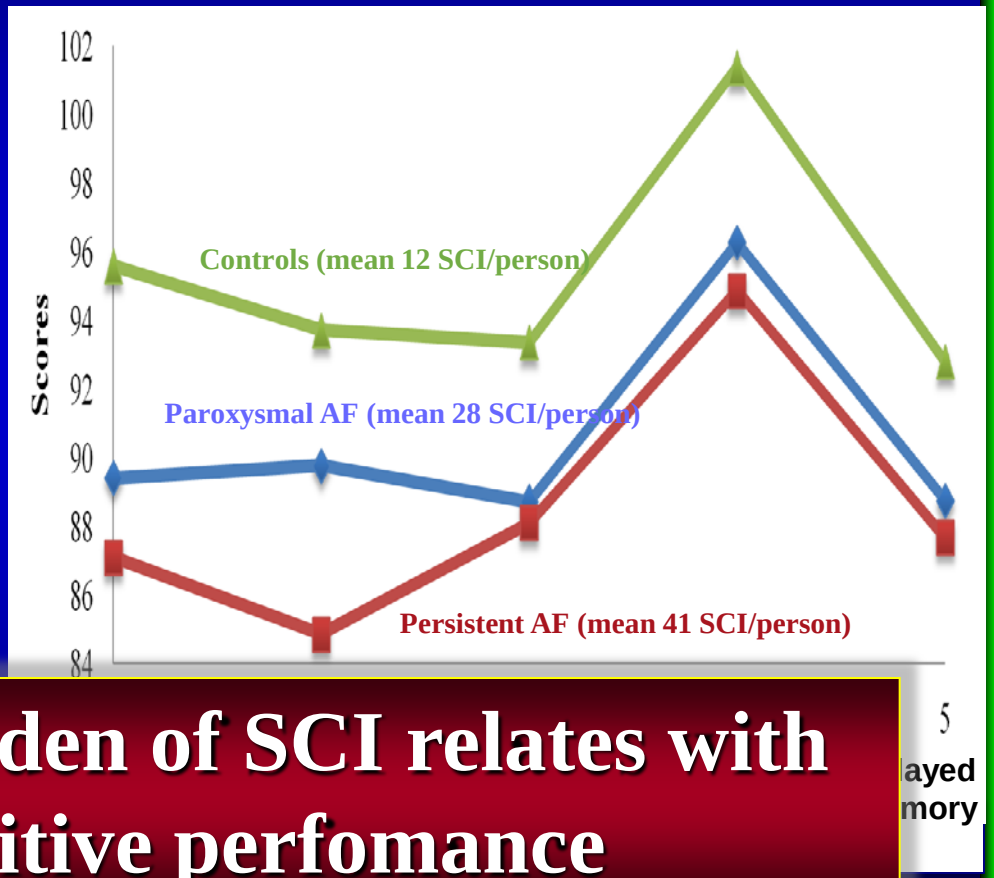
AF showed a higher risk for SCI compared with subjects in sinus rhythm **(Odd ratio 11.2, p value < 0,001)**



Gaita F et al JACC 2013;62(21):1990-7

Correlation between AF type, SCI number and cognitive function





An increased burden of SCI relates with worse cognitive perfomance

Gaita F et al JACC 2013;62(21):1990-7

Conclusion

Thank you for your attention!

Rhythm control strategy associated with well-managed OAT can further reduce thromboembolic events in patients with AF

Further clinical studies focusing on oral anticoagulation and rhythm control strategy are warranted to evaluate their impact on silent ischemia and cognitive decline