



Advances in Cardiovascular Arrhythmias and Great Innovations in Cardiology
XXIV Giornate Cardiologiche Torinesi

Atrial fibrillation and silent cerebral ischemic lesions: prevalence and clinical impact

Matteo Anselmino, MD PhD

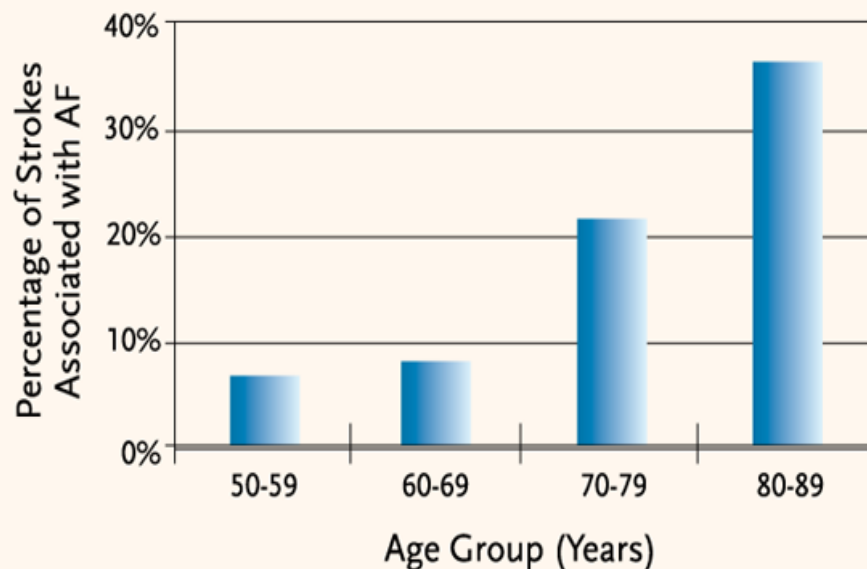
**Division of Cardiology
Department of Medical Sciences**

**Città della Salute e della Scienza Hospital
University of Turin, Italy**

Thromboembolic risk

Atrial fibrillation and thromboembolic risk

Percentage of Strokes
Associated with Atrial Fibrillation



15% of all strokes (33% in the elderly) are associated to AF

every year 4.2% of AF patients will have a stroke

about 1 out of 3 AF patients will have a stroke in their life

AF patients present a 5 times higher risk of stroke or thromboembolic complications compared to non AF controls

Atrial fibrillation and cognitive decline

The Rotterdam Study:

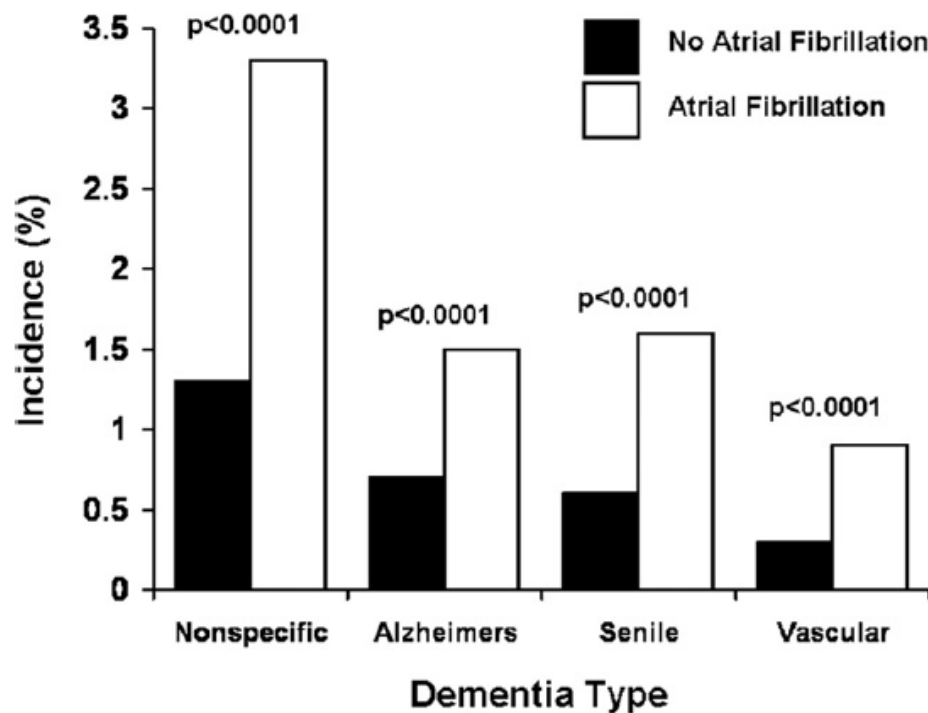
6584 pts, (55-106 years) 195 pts with AF (3%)
635 (9.6%) cognitive impairment, 276 (4%) dementia

Atrial fibrillation reported a positive association with
cognitive impairment (OR 1.7 1.2-2.5) and
dementia (OR 2.3 1.4-3.7)
independently from age, sex and clinical strokes

Atrial fibrillation and cognitive decline

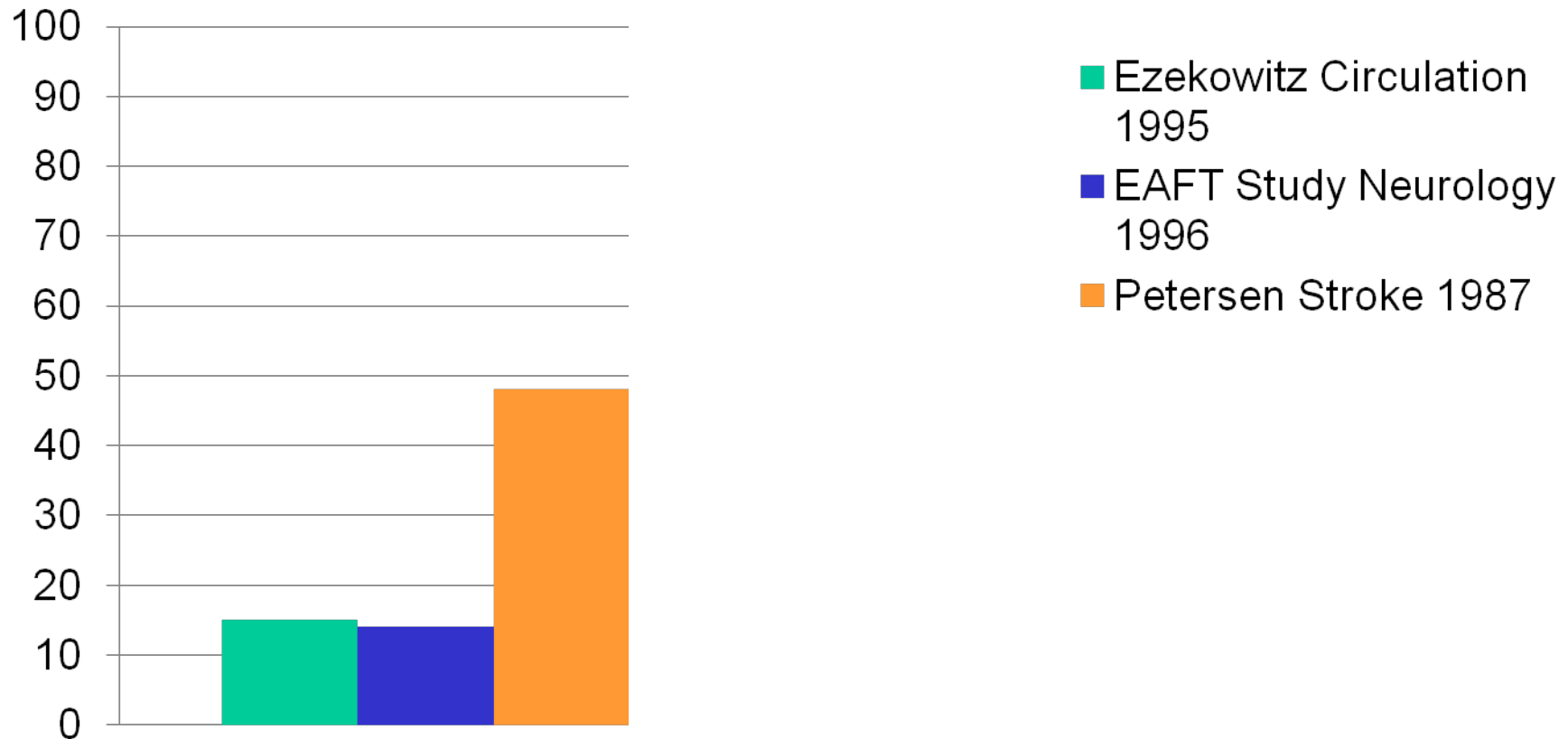
Intermountain Heart Collaborative Study:

age 61 ± 18 , M 60%, Ht 44%, hyperlip 39%, diabetes 16%, cerebral vascular accidents 3.6%, 27% AF and 4.1% dementia)



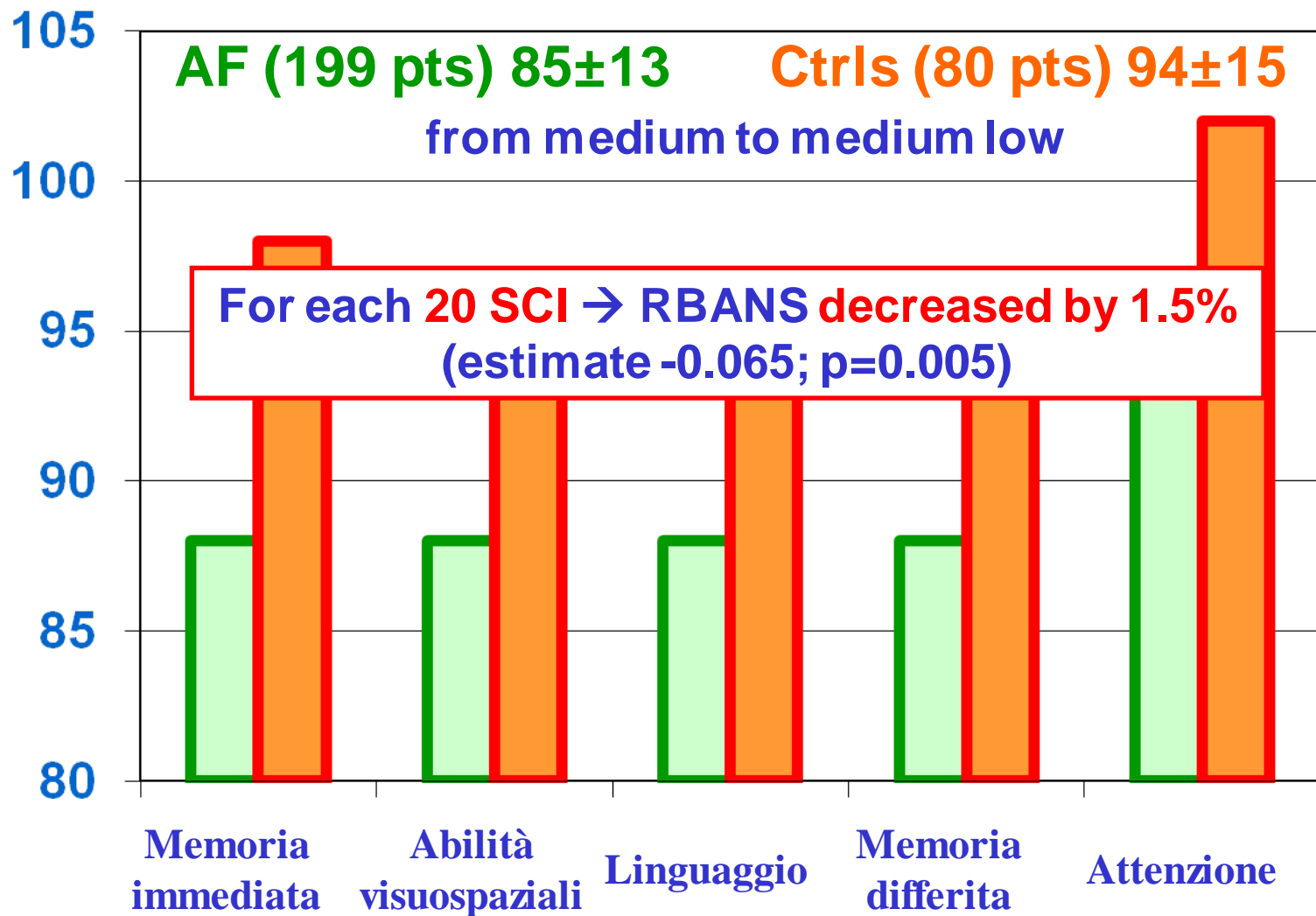
AF was found to be an independent risk factor for the development of cognitive decline and dementia

Atrial fibrillation and silent cerebral ischemias



Limits: small samples, retrospective design, dyshomogeneous population without control group, definition, CT vs. MR, lack of AF characterization

Atrial fibrillation, silent ischemias and cognitive decline



Gaita et al. *ongoing*

Summary - 1

Symptomatic cerebral ischemic events
are a small portion of the
thromboembolic risk of AF patients

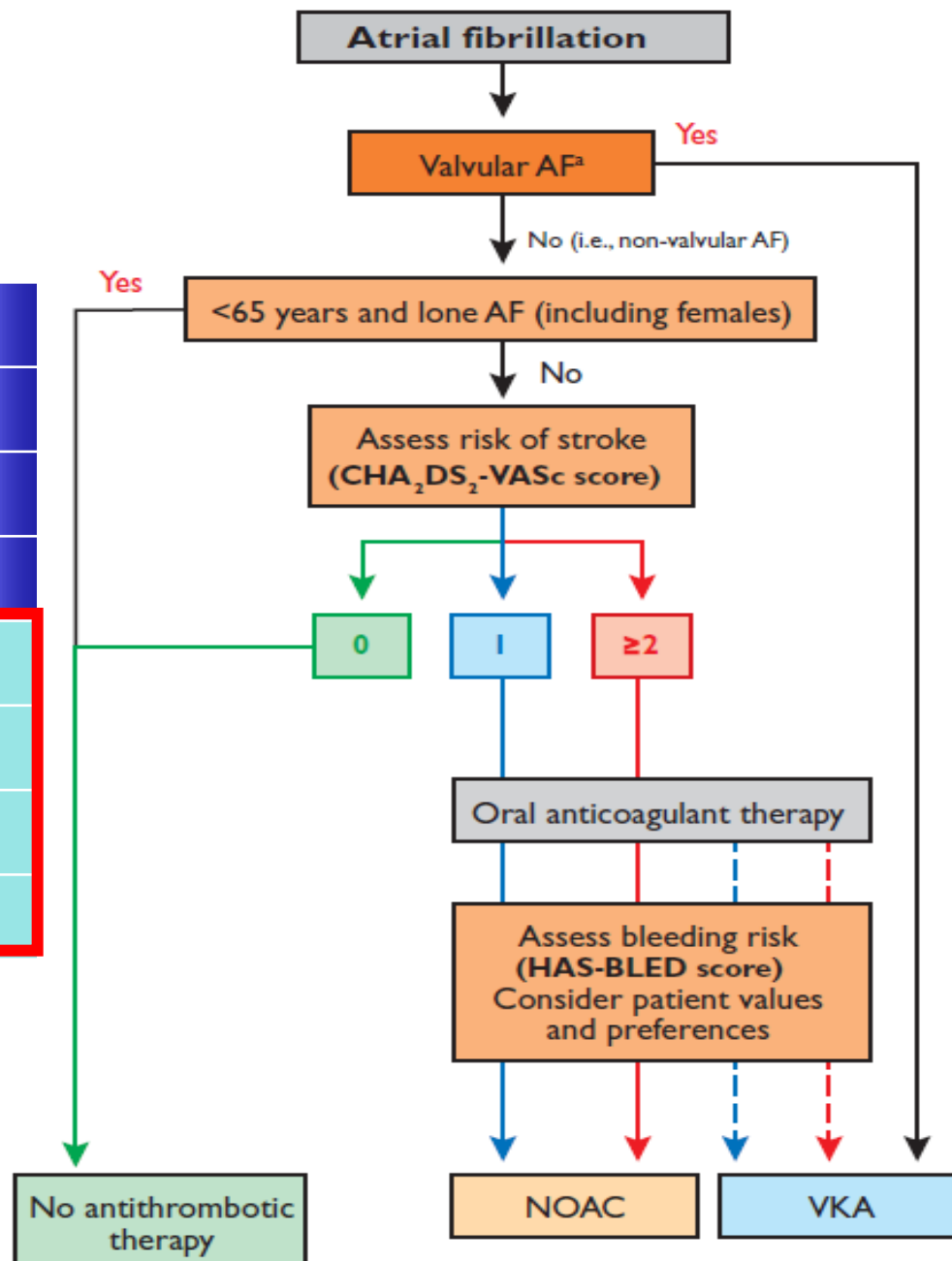
Silent cerebral ischemias are extremely
frequent within AF patients

Silent cerebral ischemias relate to cognitive decline

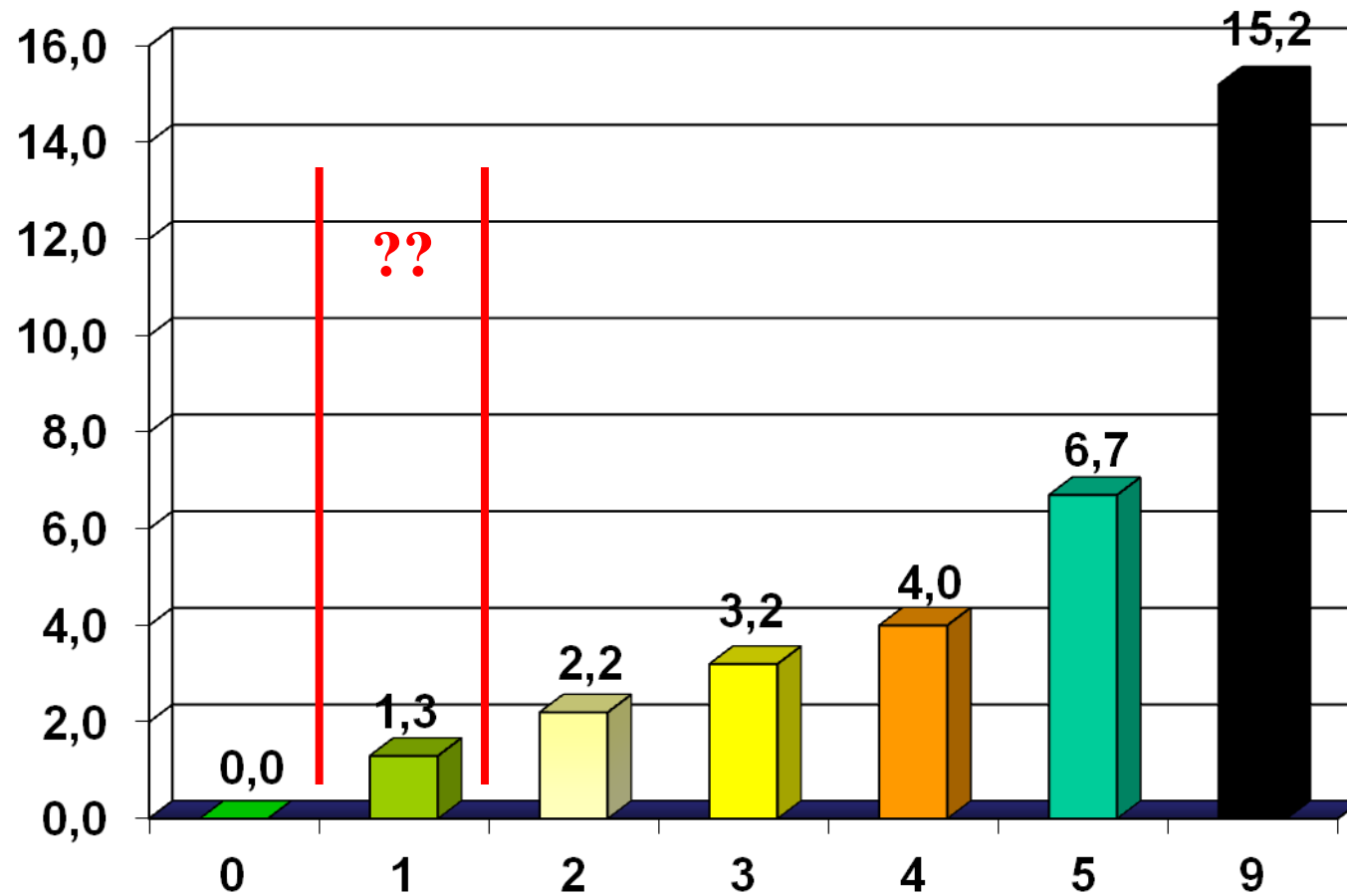
Thromboembolic risk stratification

CHADS₂-Vasc score

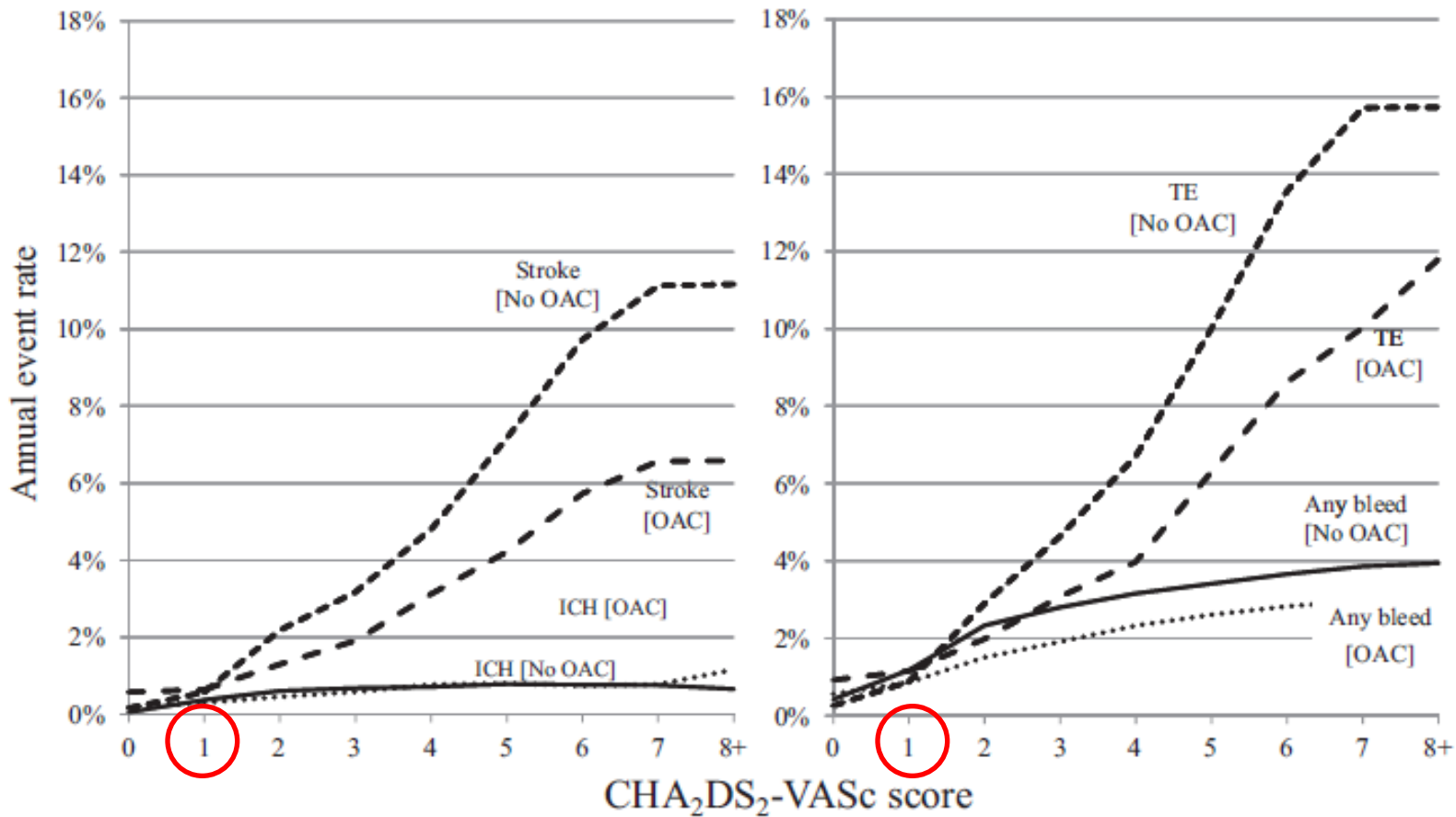
C ongestive HF	1
H ypertension	1
D iabetes mellitus	1
S troke/TIA	2
A ge ≥ 75	2
A ge 65-74	1
V ascular disease	1
S ex category (f)	1



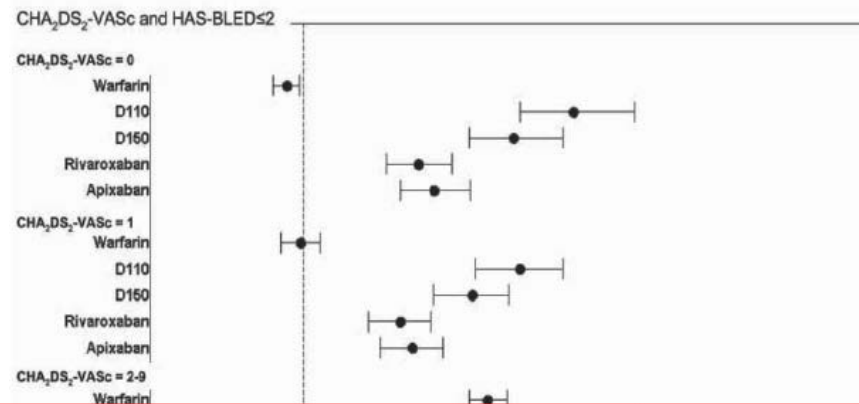
CHADS-Vasc score and thromboembolic risk



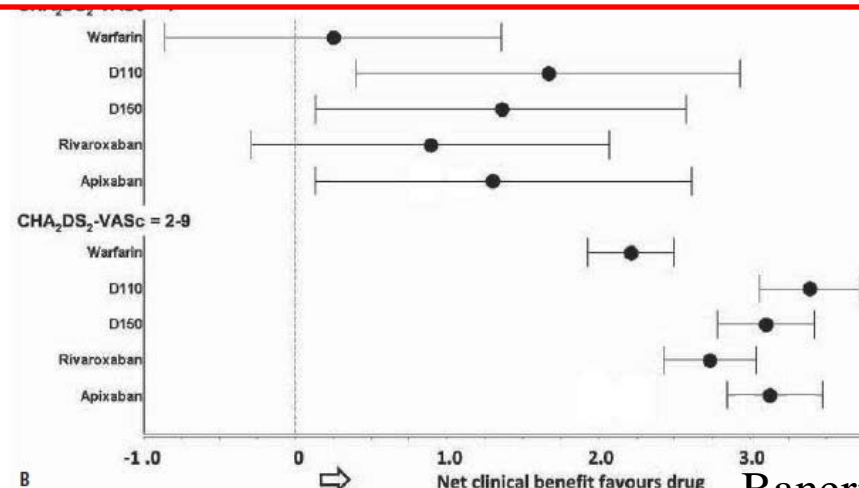
Net clinical benefit on warfarin



Net clinical benefit on NOCs



At **CHADS-Vasc 1** apixaban and both doses of dabigatran (110 mg and 150 mg bid) present positive net clinical benefit
 At **CHADS-Vasc \geq 2** all three new OACs (dabigatran, rivaroxaban and apixaban) appear superior to warfarin



Does the Left Atrial Appendage Morphology Correlate With the Risk of Stroke in Patients With Atrial Fibrillation?

Results From a Multicenter Study

Luigi Di Biase, MD, PhD,*†‡ Pasquale Santangeli, MD,*‡ Matteo Anselmino, MD, PhD,§ Prasant Mohanty, MBBS, MPH,* Ilaria Salvetti, MD,§ Sebastiano Gili, MD,§ Rodney Horton, MD,* Javier E. Sanchez, MD,* Rong Bai, MD,* Sanghamitra Mohanty, MD,* Agnes Pump, MD,* Mauricio Cereceda Brantes, MD,* G. Joseph Gallinhouse, MD,* J. David Burkhardt, MD,* Federico Cesarani, MD,|| Marco Scaglione, MD,¶ Andrea Natale, MD,*† Fiorenzo Gaita, MD§
Austin, Texas; and Foggia, Turin, and Asti, Italy

CT scan N=499

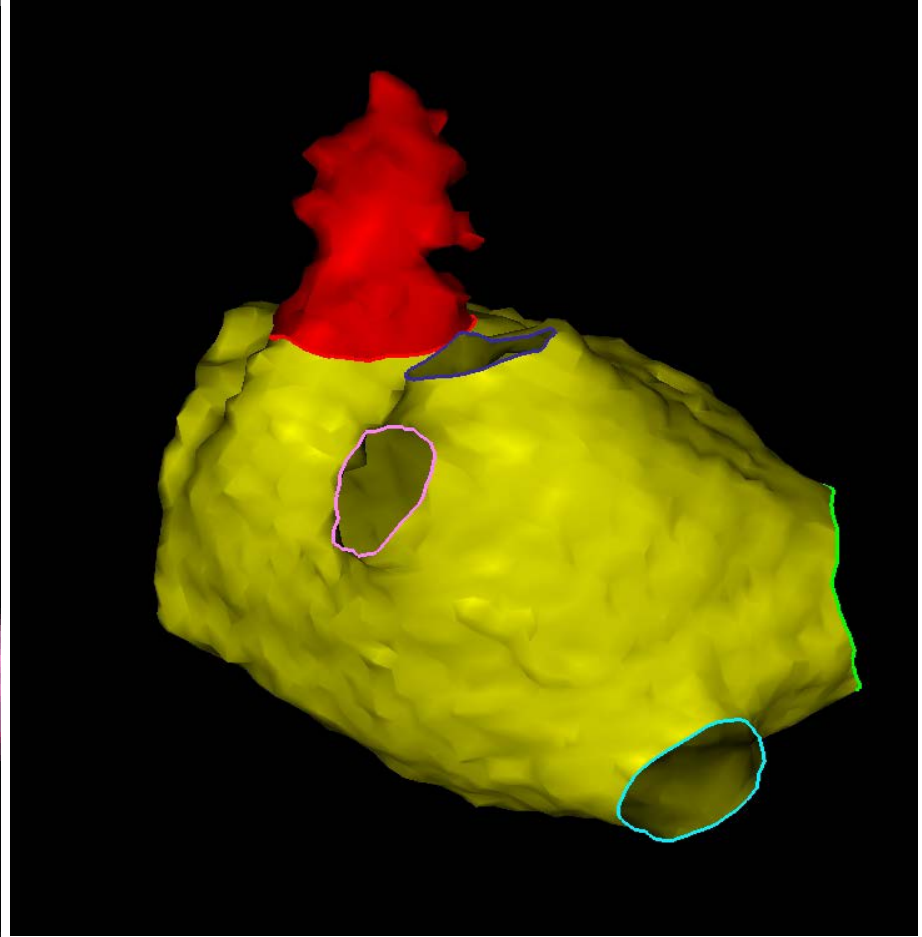
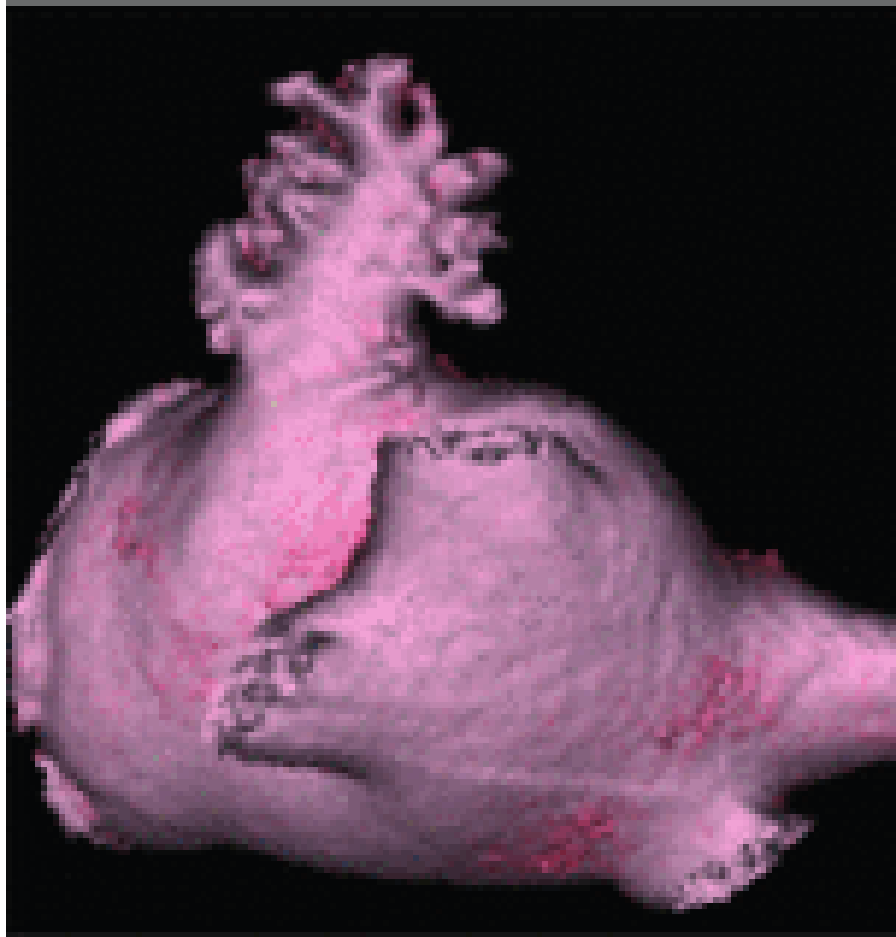
MR scan N=433

Age 59 y, men 79%, BMI 27%, EF 60%

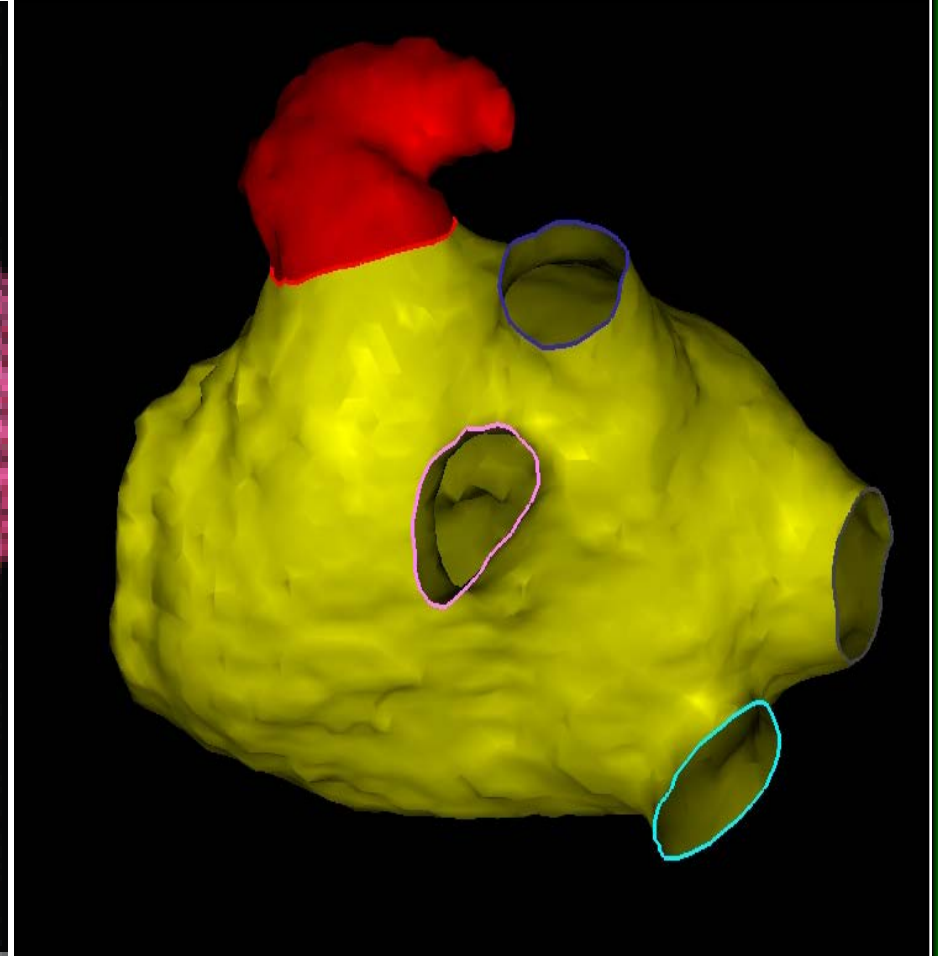
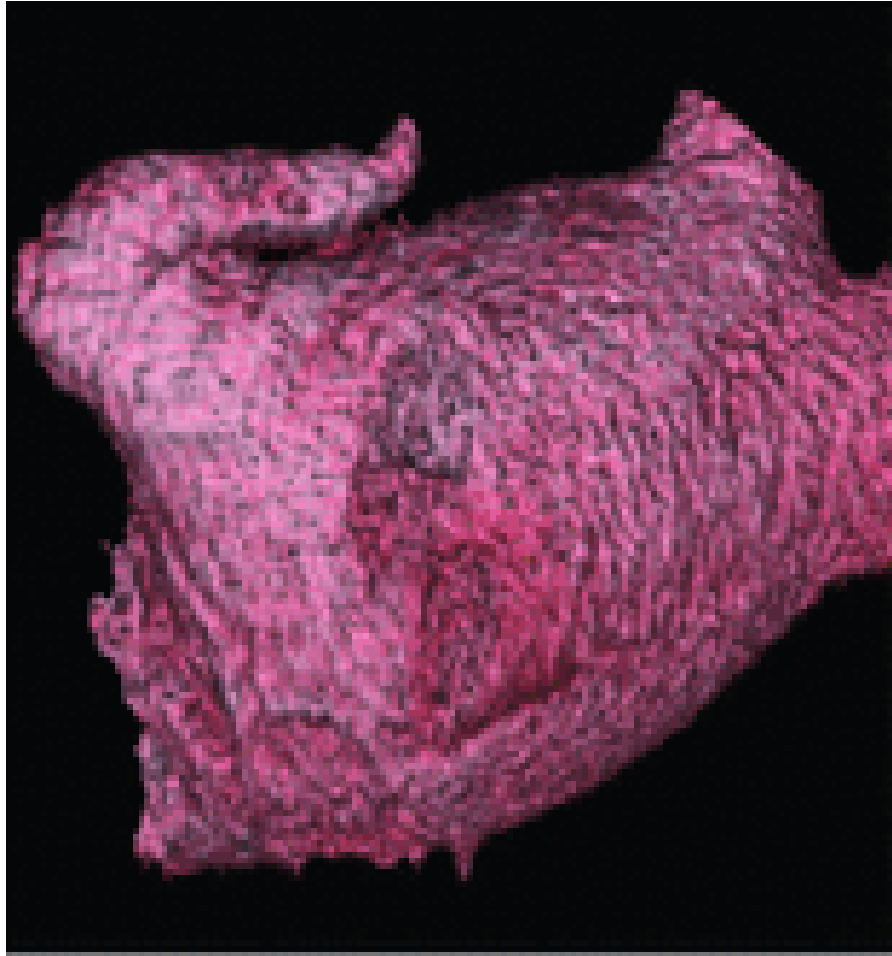
73 (8%) patients had prior history of ischemic stroke
or transient ischemic attack

(drug therapy at time of event unknown)

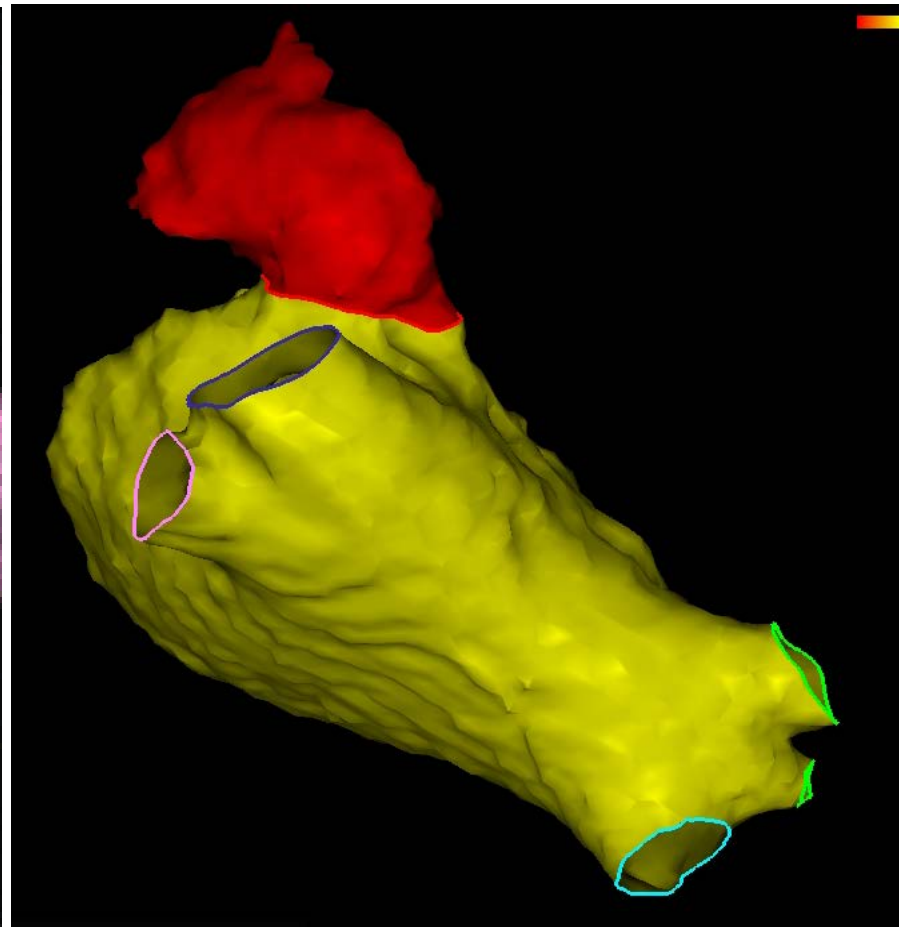
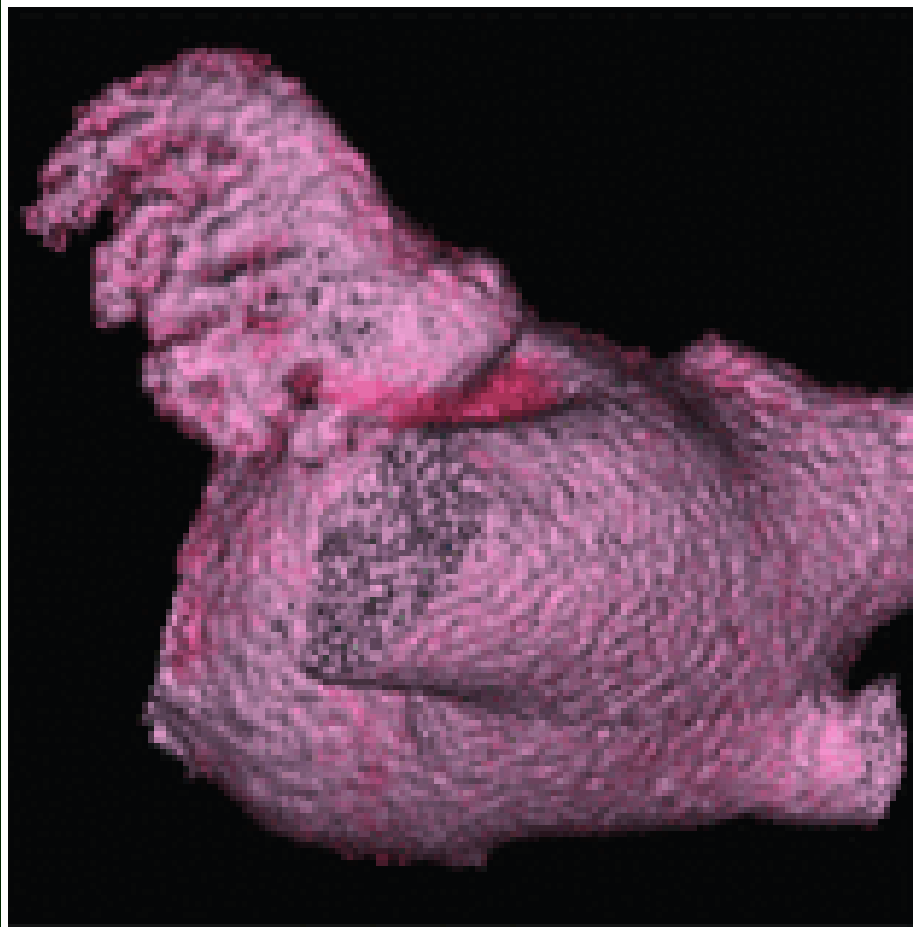
Cactus type LAA, 278 (30%) pts



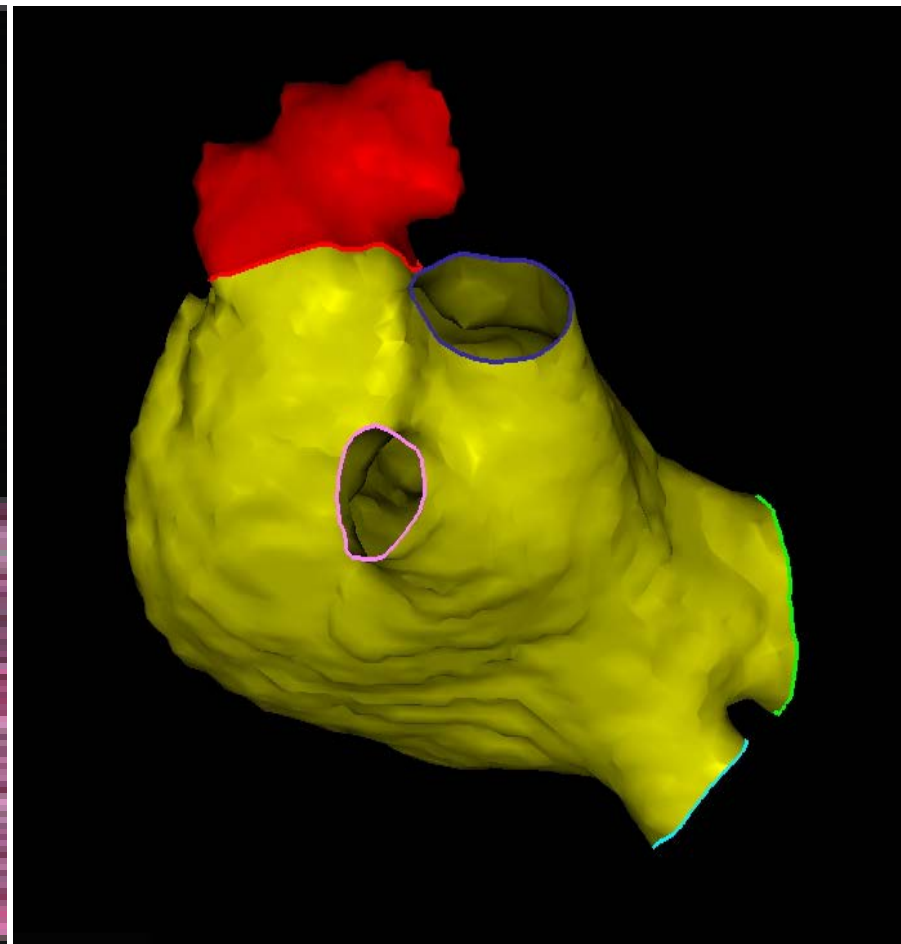
Chickenwing type LAA, 451 (48%) pts



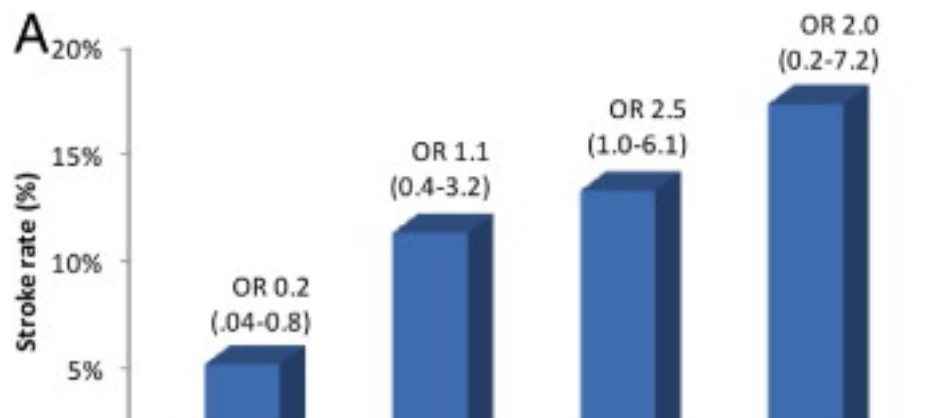
Windsock type LAA, 179 (19%) pts



Cauliflower type LAA, 24 (3%) pts



Left atrial appendage morphology and thromboembolic risk



non-Chicken Wing

OR 2.95 95%CI 1.75-4.99 p=0.041

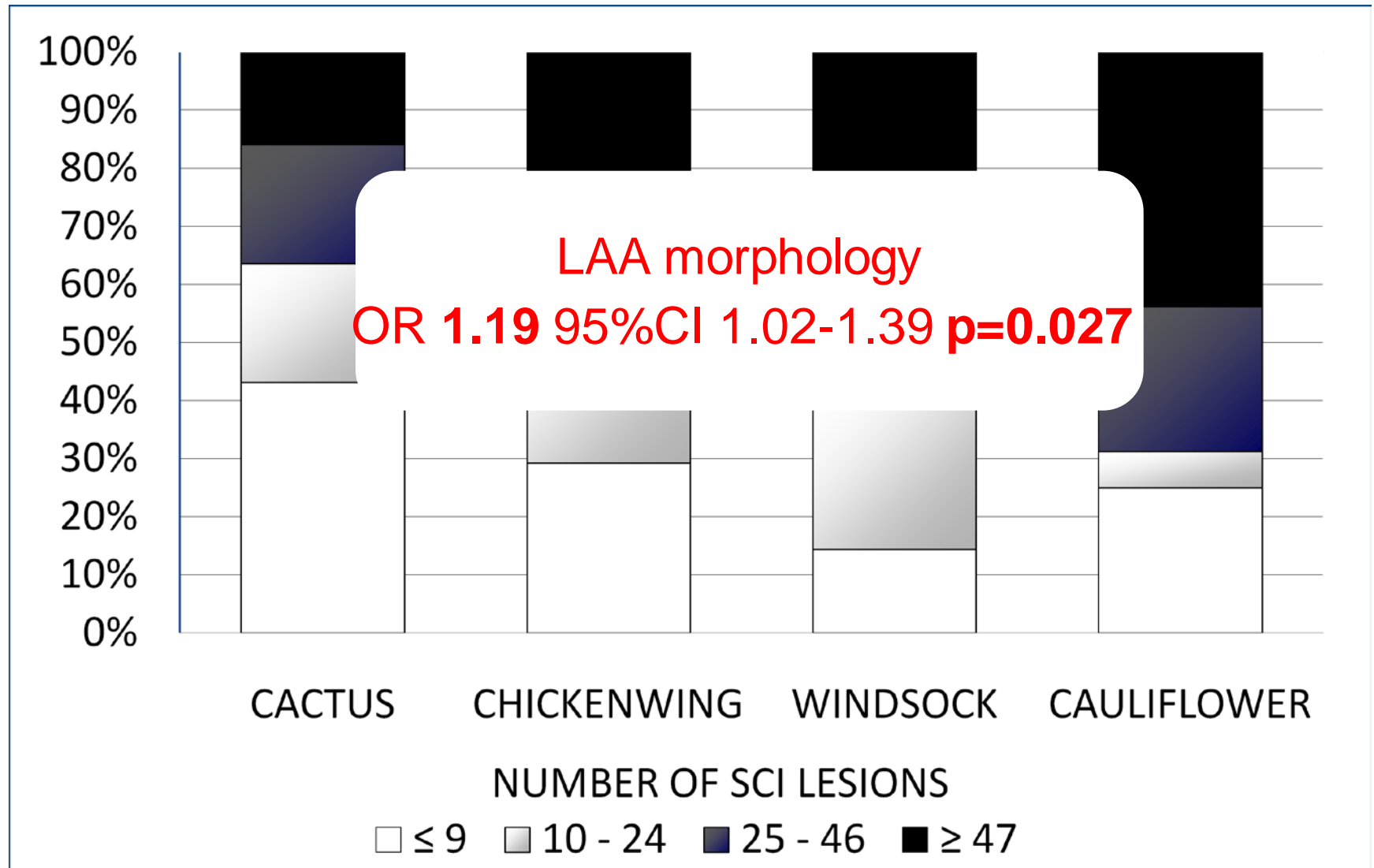
Left atrial appendage morphology and silent cerebral ischemias

MR scan N=311

62.1 paroxysmal, 37.9% persistent AF
age 57, 79% males, CHADS-Vasc <2 70%

SCI were detected in 275 (88.4%) patients,
with a mean number of lesions in each patient
of 34.7 ± 37.2

Left atrial appendage morphology and silent cerebral ischemias



Summary - 2

Thromboembolic risk stratification
is based on symptomatic events

Thromboembolic risk stratification may improve
(left atrial appendage morphology...)

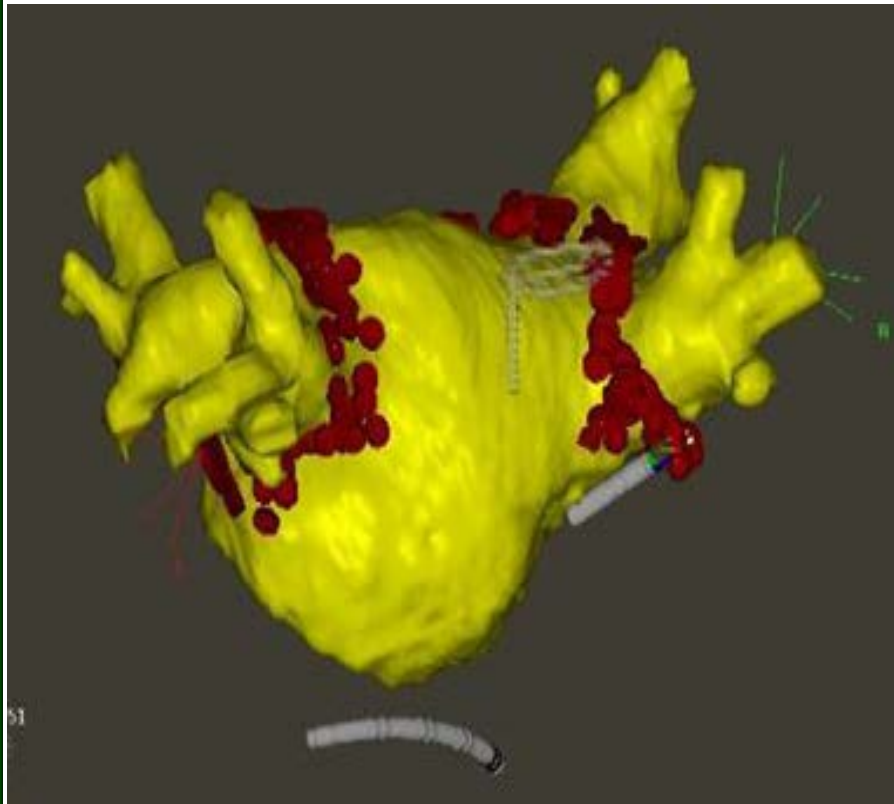
No data is available on the prevention of silent
cerebral ischemias by anticoagulant therapy

Atrial fibrillation ablation

Transcatheter ablation of atrial fibrillation

Pulmonary veins isolation

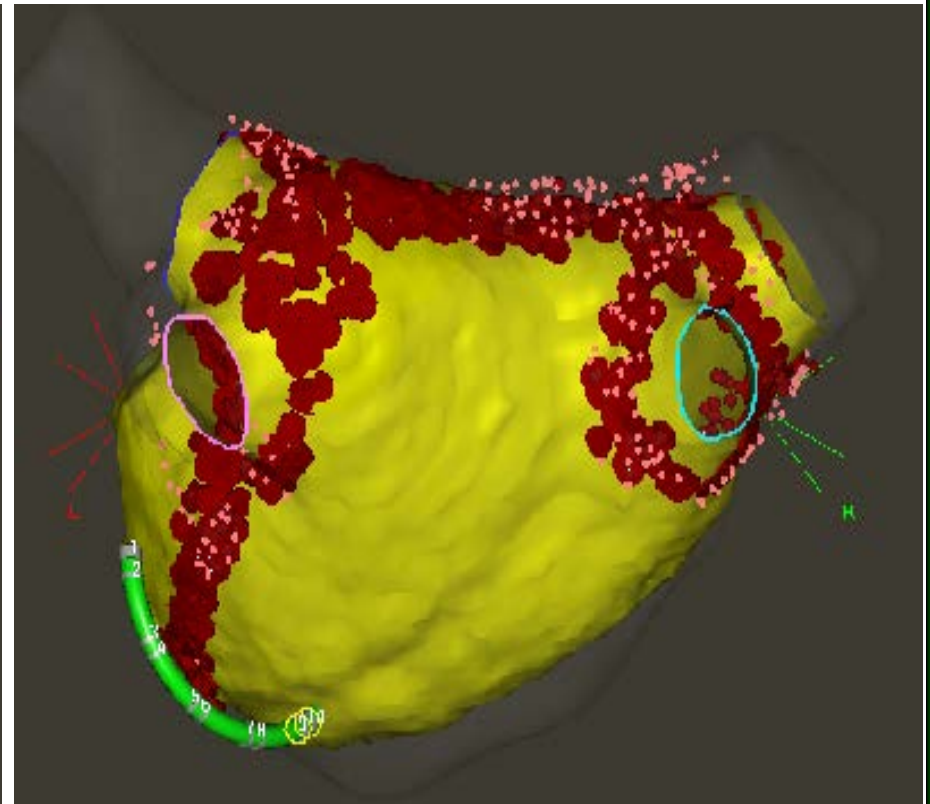
Paroxysmal AF



Haissaguerre N Engl J Med 1998

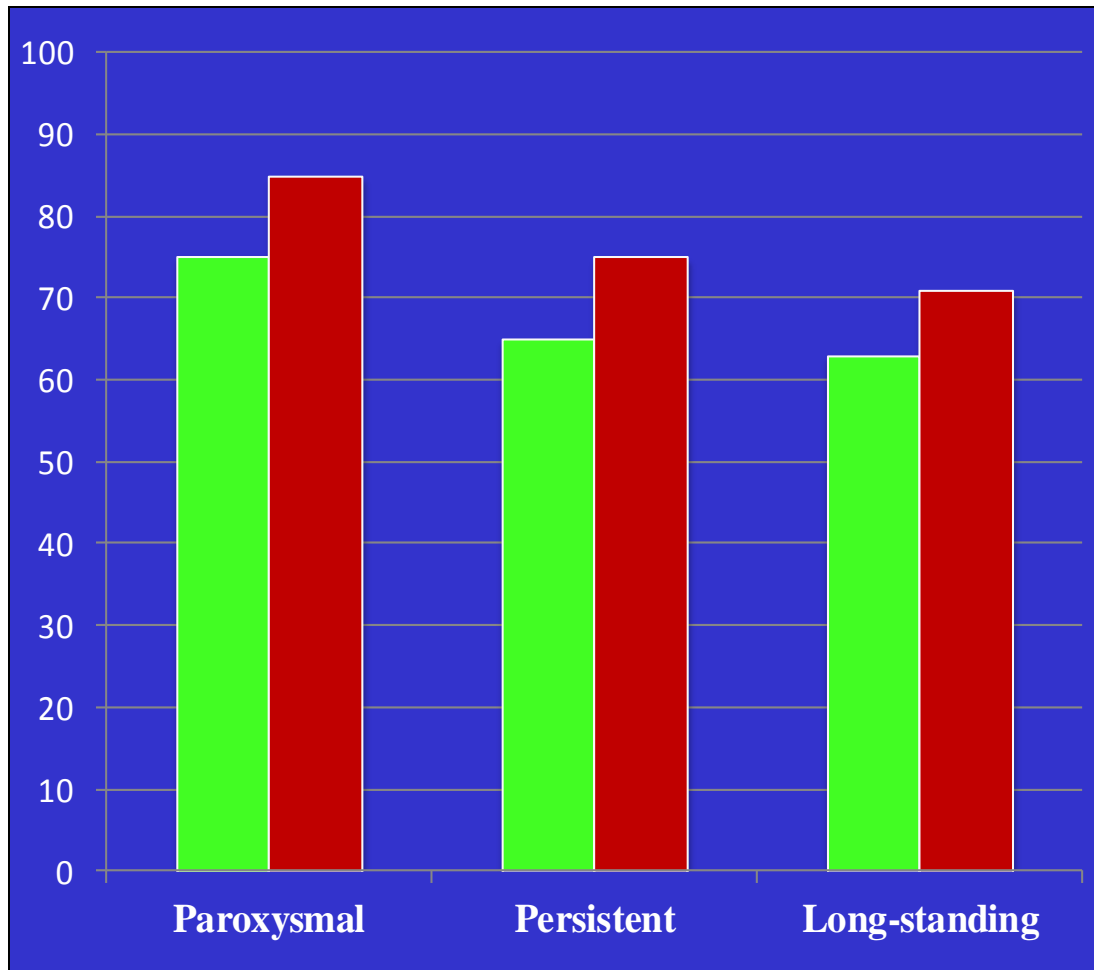
Linear lesions: “7 scheme”

Persistent and long-standing AF



Gaita Circulation 2005

Atrial fibrillation transcatheter ablation: one-year efficacy



16,309 patients

85 centres worldwide

1.3 procedures per patient

4.5% major complications

 Without antiarrhythmic drugs

 With antiarrhythmic drugs

Transcatheter AF ablation complications

From 1% to 3.6%

1033 pts	2249 pts	16309 pts
Experienced centers	Our experience	Worldwide survey

Complications	Pts	1.6%	Pts	1%	Pts	3.6%
Deaths	0	0	0	0	25	0.15
Stroke	1	0.1	4	0.2	37	0.23
TIA	4	0.4	7	0.3	115	0.71
Severe PV stenosis	3	0.3	2	0.09	48	0.29
Tamponade/Perf	5	0.5	6	0.3	213	1.31
Vascular complic	3	0.3	2	0.09	152	0.93

Verma Circulation 2005

Gaita 2010

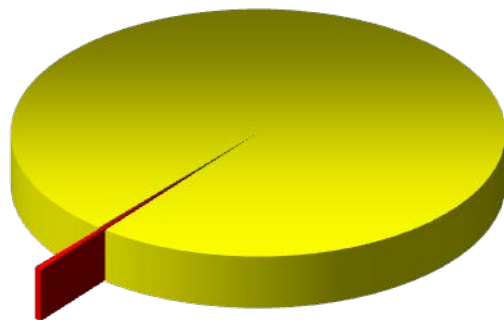
Cappato Circ Arr 2010

Radiofrequency Catheter Ablation of Atrial Fibrillation: A Cause of Silent Thromboembolism? Magnetic Resonance Imaging Assessment of Cerebral Thromboembolism in Patients Undergoing Ablation of Atrial Fibrillation

Fiorenzo Gaita, Domenico Caponi, Martina Pianelli, Marco Scaglione, Elisabetta Toso, Federico Cesarani, Carlo Boffano, Giovanni Gandini, Maria Consuelo Valentini, Roberto De Ponti, Franck Halimi and Jean Francois Leclercq

Symptomatic lesions

0.4% (1/232)
symptomatic for TIA



Predictors of silent cerebral ischemic events

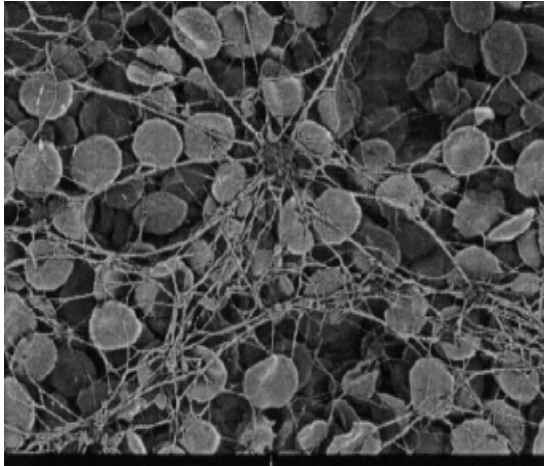
CV OR 2.75

ACT OR 0.98

Mechanisms involved in SCI following AF ablation

- conventional clotting**
- thermal thrombus formation**
- air/gas embolisms**

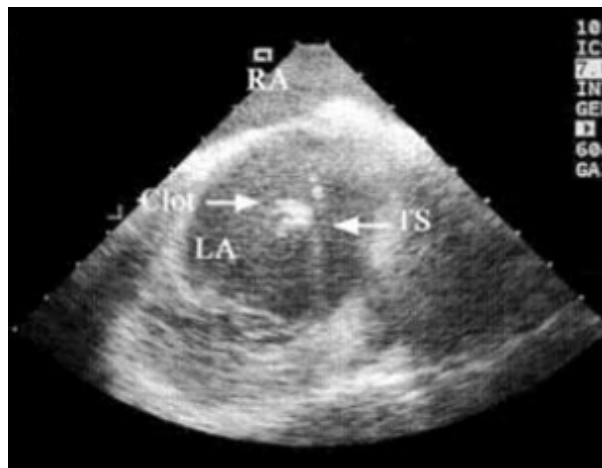
Conventional clotting: introduction of foreign bodies into blood pool



**Deposit formed on the catheter
after 30 m blood exposure
despite high heparinization.**

← **Typical thrombus:**
fibrin network, entrapped red blood cells,
no aggregation of denaturized proteins

Demolin JM et al. PACE 2002;25:1219-22



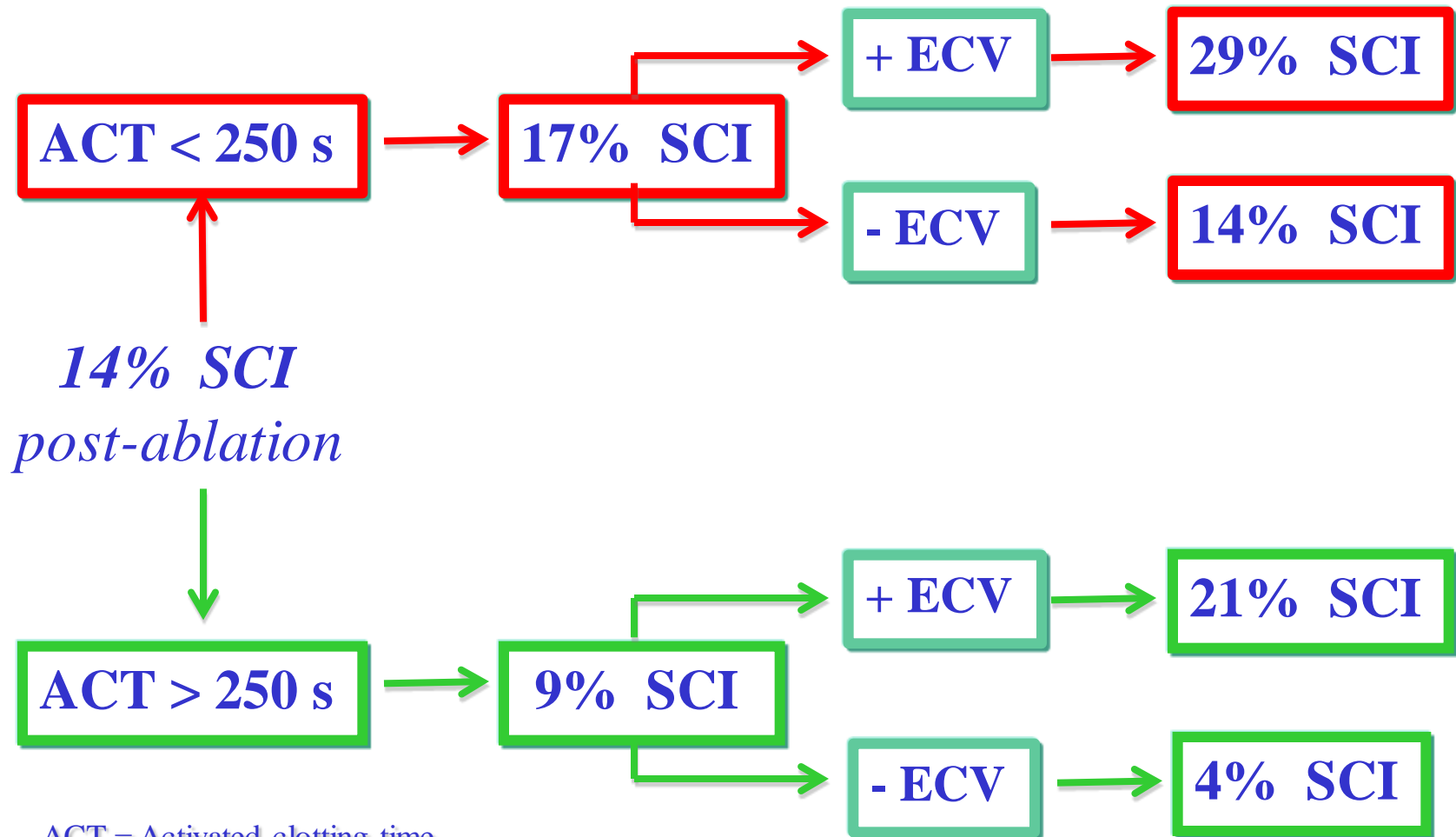
**Thrombus on transseptal sheath was
observed in 9% of the patients within 5-15
m from entering the LA.**

ACT > 250 seconds

Heparin sheath flush: 2 IU/ml

Maleki K et al. JCE 2005;16:561-565

The risk of SCI correlates with anticoagulation levels



ACT = Activated clotting time

Delaying cardioversion following 4-week anticoagulation in case of persistent atrial fibrillation after a transcatheter ablation procedure to reduce silent cerebral thromboembolism: a single-center pilot study

Martina Pianelli^a, Marco Scaglione^b, Matteo Anselmino^a, Domenico Caponi^b, Paloma Garcia^c, Federico Cesarani^c, Elisabetta Toso^a, Cristina Raimondo^b, Franck Halimi^d, Jean François Leclercq^d and Fiorenzo Gaita^a

Procedure start

SR n= 55

AF n=40

Procedure end

SR n=80

AF n=15

SR throughout
the procedure
n=55

SR restoration
by catheters
n=25

Spontaneous
SR restoration
n=11

CV postponed
after 4 weeks
anticoagulation
n=4

Silent ischemia

3/55
5%

1/25
4%

2/11
18%

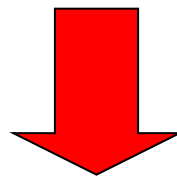
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J Cardiovasc Med 2011

Silent cerebral ischemias and intraprocedural therapeutic INR

51 pts with AF undergoing RF ablation
with

therapeutic INR before and during the procedure
Heparin bolus i.v. 10.000 U prior to transeptal puncture
ACT above 300 s



1 pts (2%) was positive for new silent cerebral lesion
at post procedure brain MRI

Asymptomatic cerebral lesions in AF ablation under therapeutic anticoagulation

100 patients, 50% paroxysmal AF , CFAE vs CFAE+PVI
on Warfarin + Heparin (mean ACT 274 s)

1 TIA (1%), 6 (6%) Silent Cerebral lesions

Multivariate Analysis

	Odds ratio	95% CI	P
CHADS2 score	1.70	0.72–4.02	0.23
LA volume	1.01	0.98–1.05	0.47
LVEF	0.92	0.84–0.99	<0.05
Concomitant CAG	18.82	1.77–200.00	<0.05

CAG = coronary angiography; LVEF = left ventricular ejection fraction.

Asymptomatic cerebral lesions in AF ablation under therapeutic anticoagulation

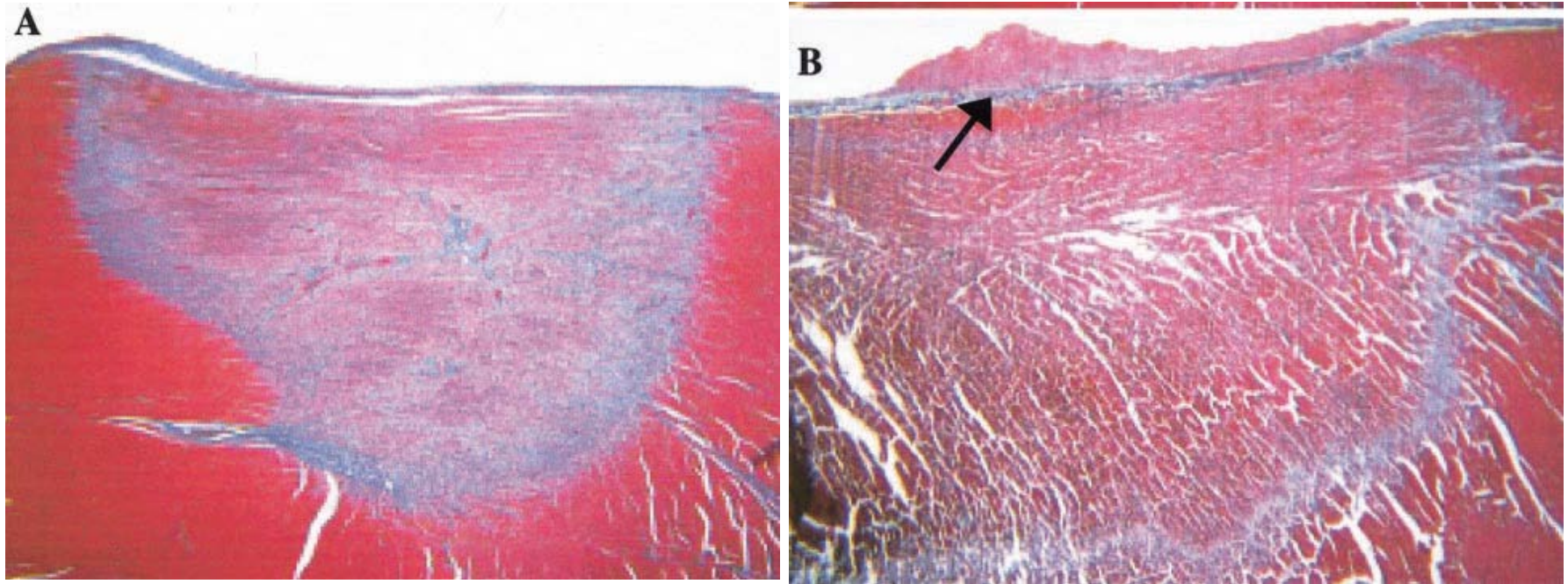
Martinek M, Sigmund E, Lemes CH, Derndorfer M, Aichinger J,
Winter S, Nesser HJ, Puererfellner H

101 pts (62%, paroxysmal AF)

**14 pts (12.6%) were positive for new silent cerebral lesion
at post procedure brain MRI**

*Smoke in transesophageal echo ($p=0.012$),
intraprocedural ECV ($p=0.026$) and CFAE lesions ($p=0.016$)
were the only parameters related to positive post procedure brain MRI*

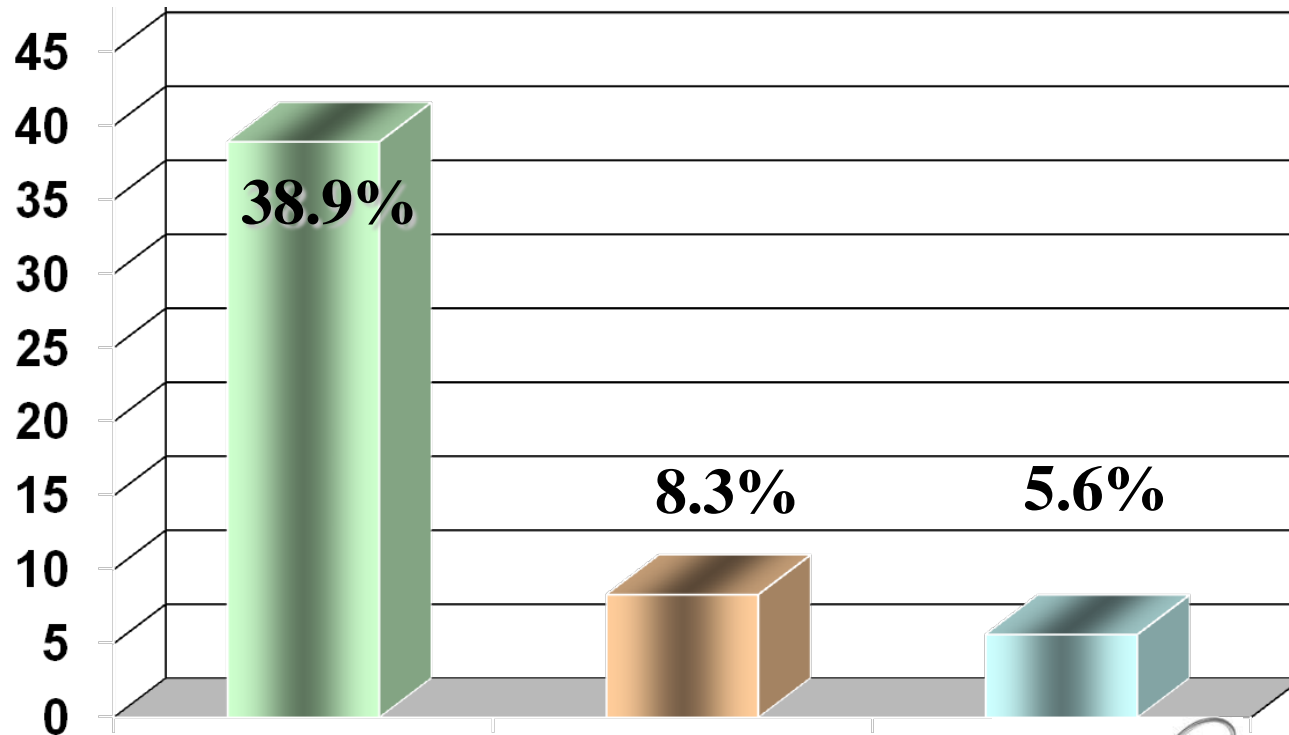
Silent cerebral ischemias and **energy sources**



Cryoablation by preserving the endothelial cell layer reduces by 5.6-fold the risk of endocardium thrombus formation compared to irrigated RF ablation

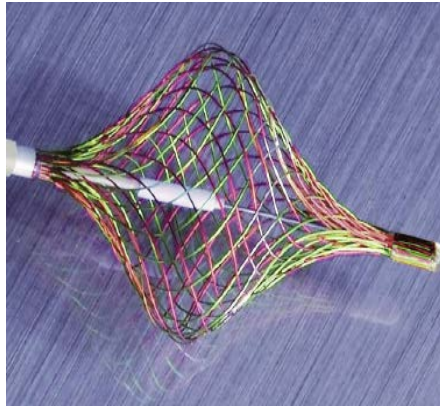
Incidence of Silent Cerebral Thromboembolic Lesions After Atrial Fibrillation Ablation May Change According To Technology Used: Comparison of Irrigated Radiofrequency, Multipolar Nonirrigated Catheter and Cryoballoon

FIORENZA GAITA, M.D.,*,† JEAN FRANÇOIS LECLERCQ, M.D.,‡
BURGHARD SCHUMACHER, M.D.,§ MARCO SCAGLIONE, M.D.,†
ELISABETTA TOSO, M.D.,*,† FRANCK HALIMI, M.D.,‡ ANJA SCHADE, M.D.,§
STEFFEN FROEHNER, M.D.,¶ VOLKER ZIEGLER, M.D.,# DOMENICO SERGI, M.D.,†
FEDERICO CESARANI, M.D.,** and ALESSANDRO BLANDINO, M.D.,*,†



MACPAF trial

15 pts



vs

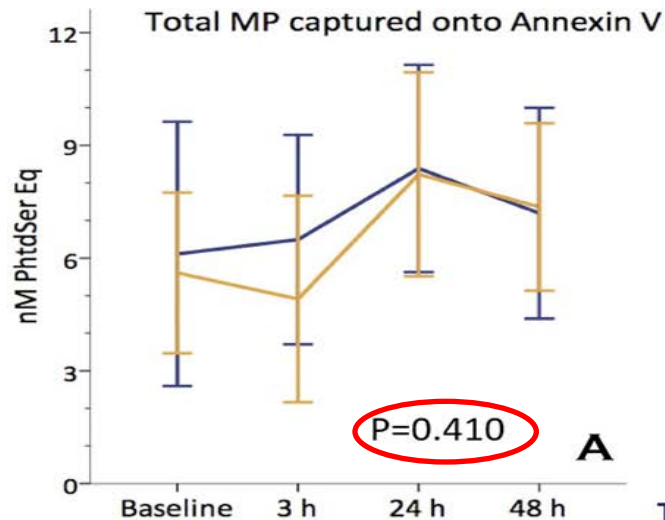


22 pts

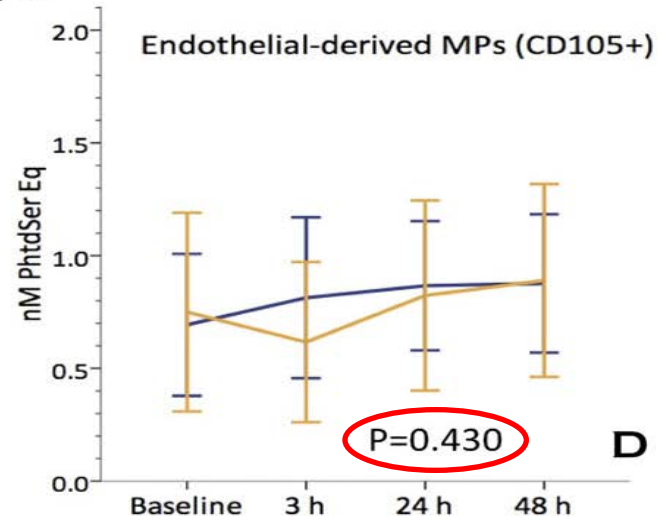
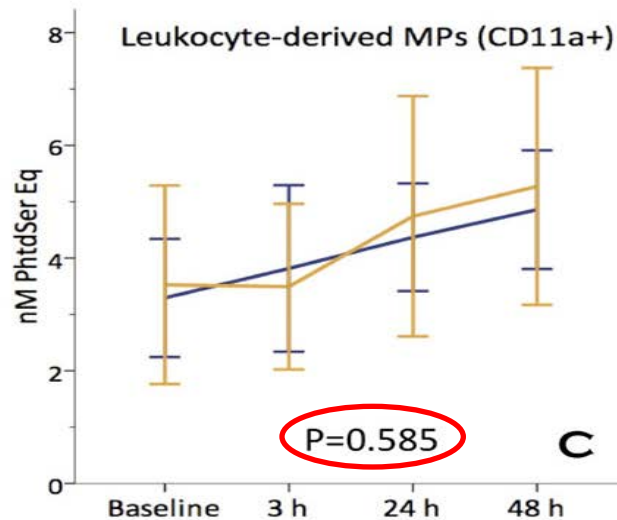
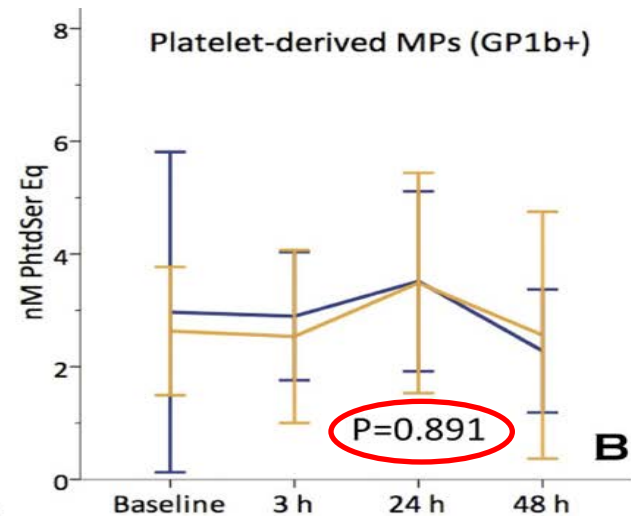
4 (27%) vs. 11 (50%) reported new silent cerebral lesions after ablation.

**Lesion volumes varied from 5 to 150 mm³ and
1 to 5 lesions were detected per patient
(3 Tesla brain MRI)**

Cellular damage, platelet activation, and inflammatory response after PVI



■ Cryoballoon
■ Irrigated-tip RF



Laser energy for PVI

	RFC n=33	LB n=33	CB n=33	p-value
LA-TIME [min]	83 ± 31	132 ± 33	110 ± 32	< 0.05
Procedure- Duration [min]	103 ± 33	149 ± 34	129 ± 29	< 0.05

SCI **8/33 (24%)** **8/33 (24%)** **6/33 (18%)** **p=0.80**

Variables playing a potential role for SCI following AF ablation

Patient's baseline characteristics

(e.g. previous stroke, arrhythmia's duration, pro-thrombotic state)

Inadequate preoperative left atrial clot/smoke evaluation

Perioperative anticoagulation protocol:

heparin bolus after transseptal puncture

anticoagulation discontinuation

low intensity heparinization during the procedure (ACT < 250s)

LWMH bridging following the procedure

Management of foreign bodies inserted into the blood

(e.g. sheath and ablator flushing)

Number, size, type and material of catheters inserted

(e.g. multipolar mapping catheters)

Energy sources

(radiofrequency, cryotherapy, laser)

Procedure duration and total number of lesions

(endothelium damage and microthrombi formation)

Sinus restoration during the procedure

(by catheters, drugs or electrical cardioversion)

Summary - 3

Rhythm control should not cause more thromboembolic events than AF itself
(chronic vs. acute risk)

A list of factors hold the potential to reduce incidence of symptomatic and silent cerebral events

Energy sources and ablation tools should be carefully tested to minimize silent cerebral events

Take home messages

Silent cerebral ischemias relate
to cognitive decline

Left atrial appendage morphology may improve
thromboembolic risk stratification

All efforts should be addressed
to reduce silent cerebral ischemias

*On behalf of all Prof.
Gaita's research group...
thanks for your attention!*

