



HOT TOPICS IN CARDIOLOGIA 2021

27 e 28 Settembre

Sede della Camera di Commercio di Napoli

II SESSIONE

Moderatori: V. Andreone, F. Greco, F. Paladino

10:30 **Nuovi sistemi di chiusura PFO** A. Gaspardone

10:45 **Chiusura auricola** A. Rapacciolo

11:00 **Ablazione FA** A. Mantovan

11:15 **Il tempo non è solo muscolo... anche cervello** M. Muto

11:30 **Ruolo della cardiologia interventistica strutturale "in urgenza" in una struttura senza cardiocirurgia** D. D'Andrea

11:45 **Experts a confronto:** G. De Rosa, D. Fontana, C. Materazzi, G. Maresca, G. Quaranta

RELATORE:

Prof. Antonio Rapacciolo
Dipartimento di Scienze
Biomediche Avanzate
Università degli Studi di Napoli
Federico II

Ogni giorno in Italia

150 nuovi casi di **ictus** dovuti a fibrillazione atriale

600 nuovi casi di **fibrillazione atriale**

**Quando il ritmo è una
questione di cuore.**



SCREENING GRATUITO

per la diagnosi precoce dei disturbi del ritmo cardiaco



**GIORNATA
MONDIALE
CONTRO LA
FIBRILLAZIONE
ATRIALE**

3 ICTUS su 4
causati dalla **FIBRILLAZIONE ATRIALE**

Controlla la **pressione arteriosa**
e la **FIBRILLAZIONE ATRIALE**
per ridurre il **rischio ICTUS**



A.L.I.Ce. Italia Onlus

Associazione per la **Lotta**
all'**Ictus Cerebrale**

www.aliceitalia.org

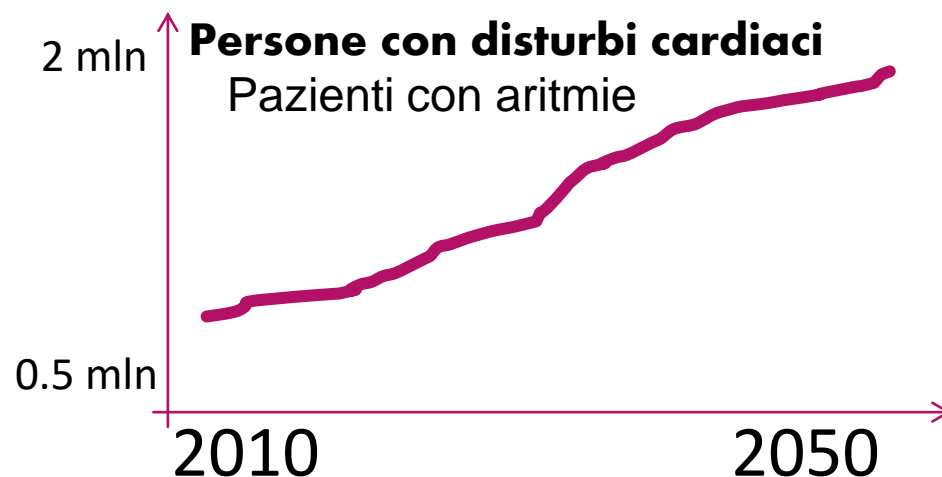
ICTUS = 20.000 €/anno a carico del SSN

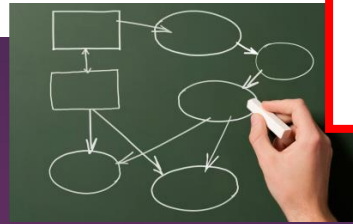


2,5 mld

Fibrillazione atriale = 3.000 €/anno a carico del SSN 1,5 mld

Bisogno sociale 4 mld





2010



```
def add5(x):
    return x+5

def dotwrite(ast):
    nodename = getNodename()
    label=symbol.sym_name.get(int(ast[0]))
    print ' %s [label="%s' % (nodename, label)
    if isinstance(ast[1], str):
        if ast[1].strip():
            print ' %s";' % ast[1]
        else:
            print ''
    else:
        print ''
        children = []
        for n, childenumerate(ast[1:]):
            children.append(dotwrite(child))
        print ' %s -> {' % nodename
        for n, namechildren:
            print '%s' % name,
```

2012

cardionica®
Spin-off dell'Istituto Superiore di Sanità

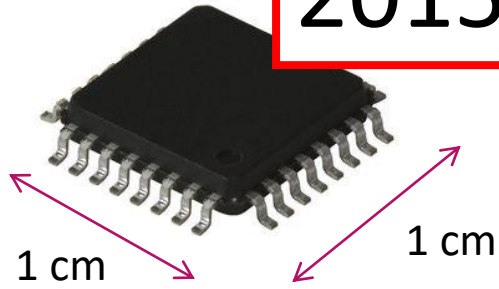
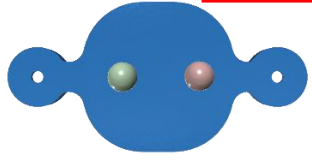
2016



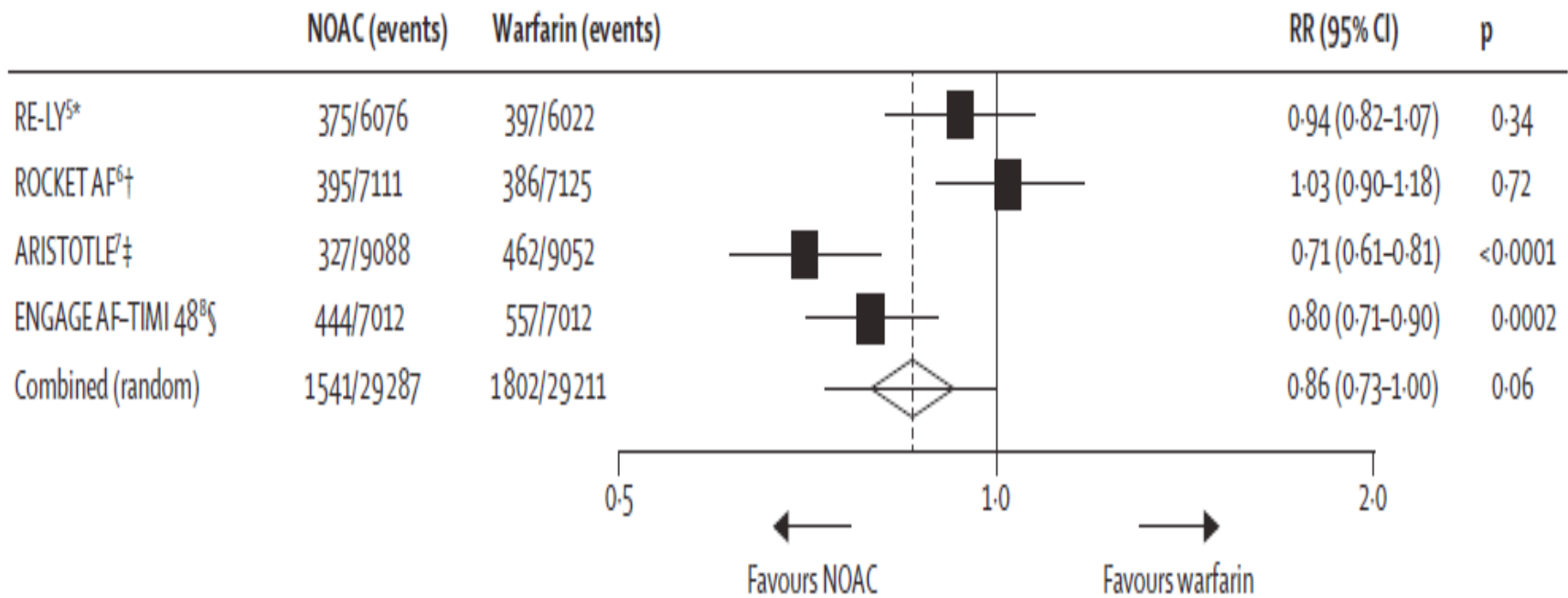
2015



2014



Major bleeding



Dabigatran 150 mg bid

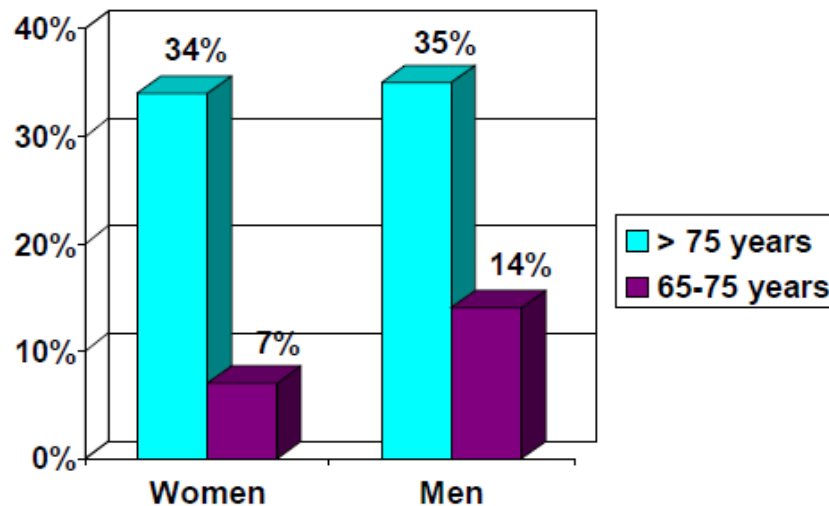
Rivaroxaban 20 mg od

Apixaban 5 mg bid

Edoxaban 60 mg od

Prevalence of irreversible contraindication* to OAC in general AF population depending on age and gender

* SPAF III study: Major bleeding previous 6 months, frequent falls, inability to comply to treatment, excessive alcohol consumption, (uncontrolled hypertension, daily use of NSAIDs)



Higher Incidence of LAA thrombus in patients with AF

Published reports of patients with non-Rheumatic AF found thrombus present in 12.6% of patients

90% of the thrombus was found in the LAA

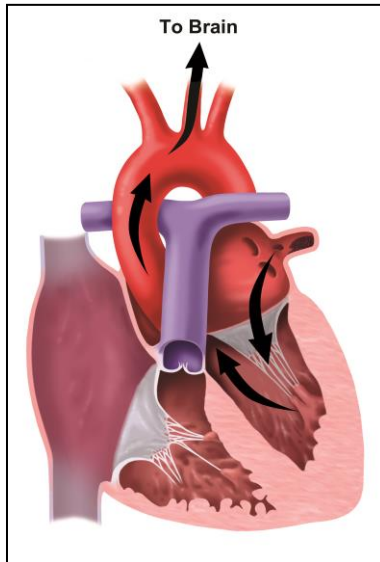
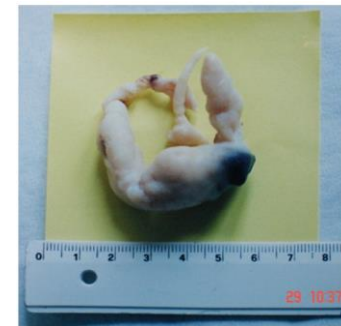


TABLE 1. Review of Published Reports Detailing the Frequency and Site of Thrombus Location in Patients With Nonrheumatic Atrial Fibrillation*

Setting	No. of Patients	Thrombus Location (n, %)		
		LA Appendage	LA Cavity	Total
TEE†	317	66 (20.8)	1 (0.3)	67 (21.1)
TEE	233	34 (14.6)	1 (0.4)	35 (15.0)
Autopsy	506	35 (6.9)	12 (2.4)	47 (9.3)
TEE	52	2 (3.8)	2 (3.8)	4 (7.7)
TEE	48	12 (25.0)	1 (2.1)	13 (27.1)
TEE and operation	171	8 (4.7)	3 (1.8)	11 (6.4)
ACUTE	549	67 (12.2)	9 (1.6)	76 (13.8)
TEE	272	19 (7.0)	0 (0)	19 (7.0)
TEE	60	6 (10.0)	0 (0)	6 (10.0)
Total	2208	249 (11.3)	29 (1.3)	278 (12.6)



PHILIPS

TIS0.2 MI 0.5

X7-2t/Adulti

FR 13Hz
8.2cm

Battiti 3D 1

M4

3D
3D 39%
3D 40dB
Gen.



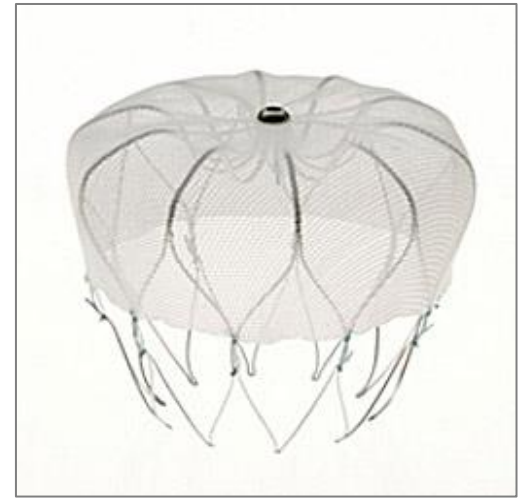
JPEG

Temp. PAZ.: 37.0C
Temp. TEE: 39.8C

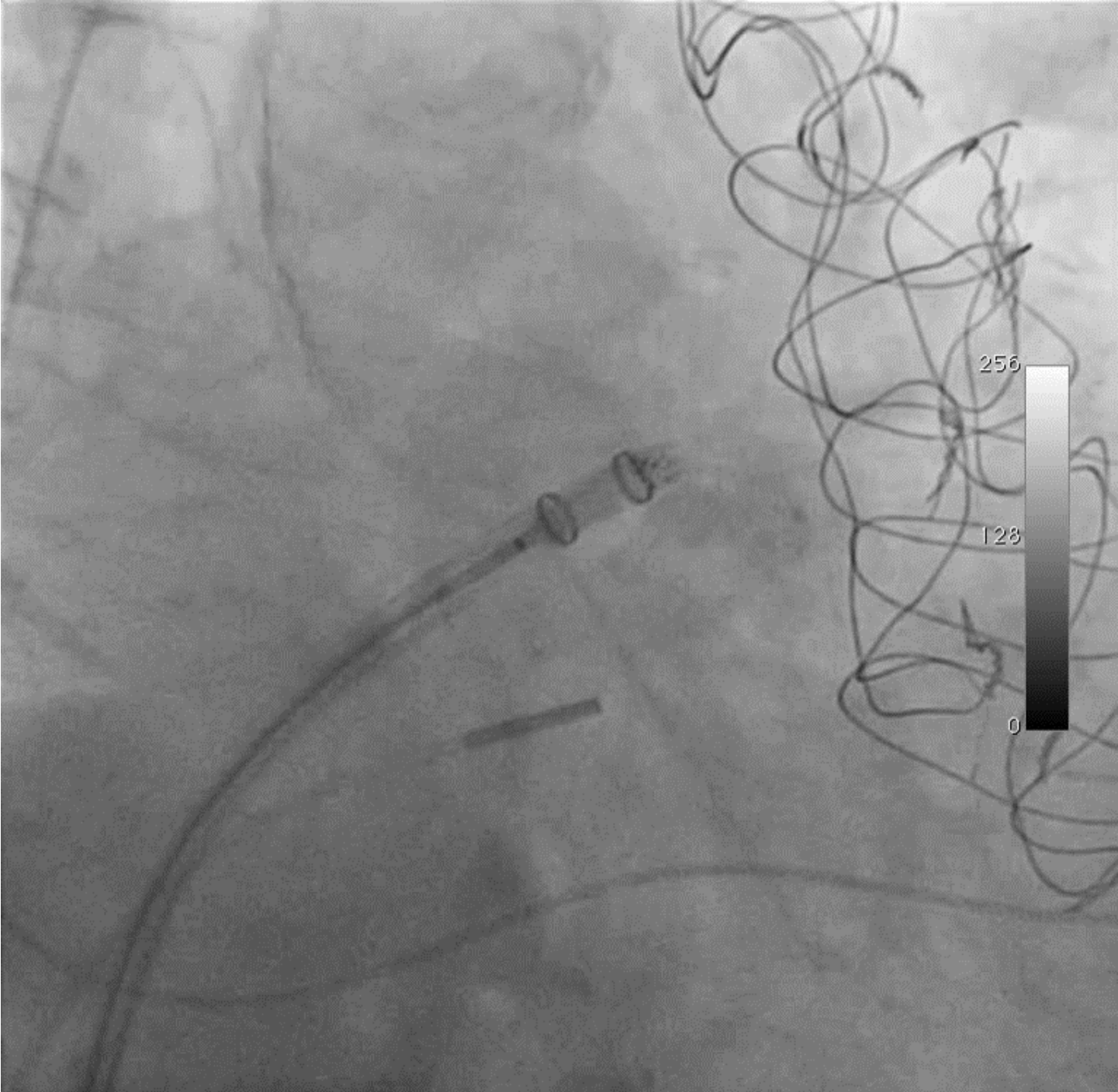
59 bpm

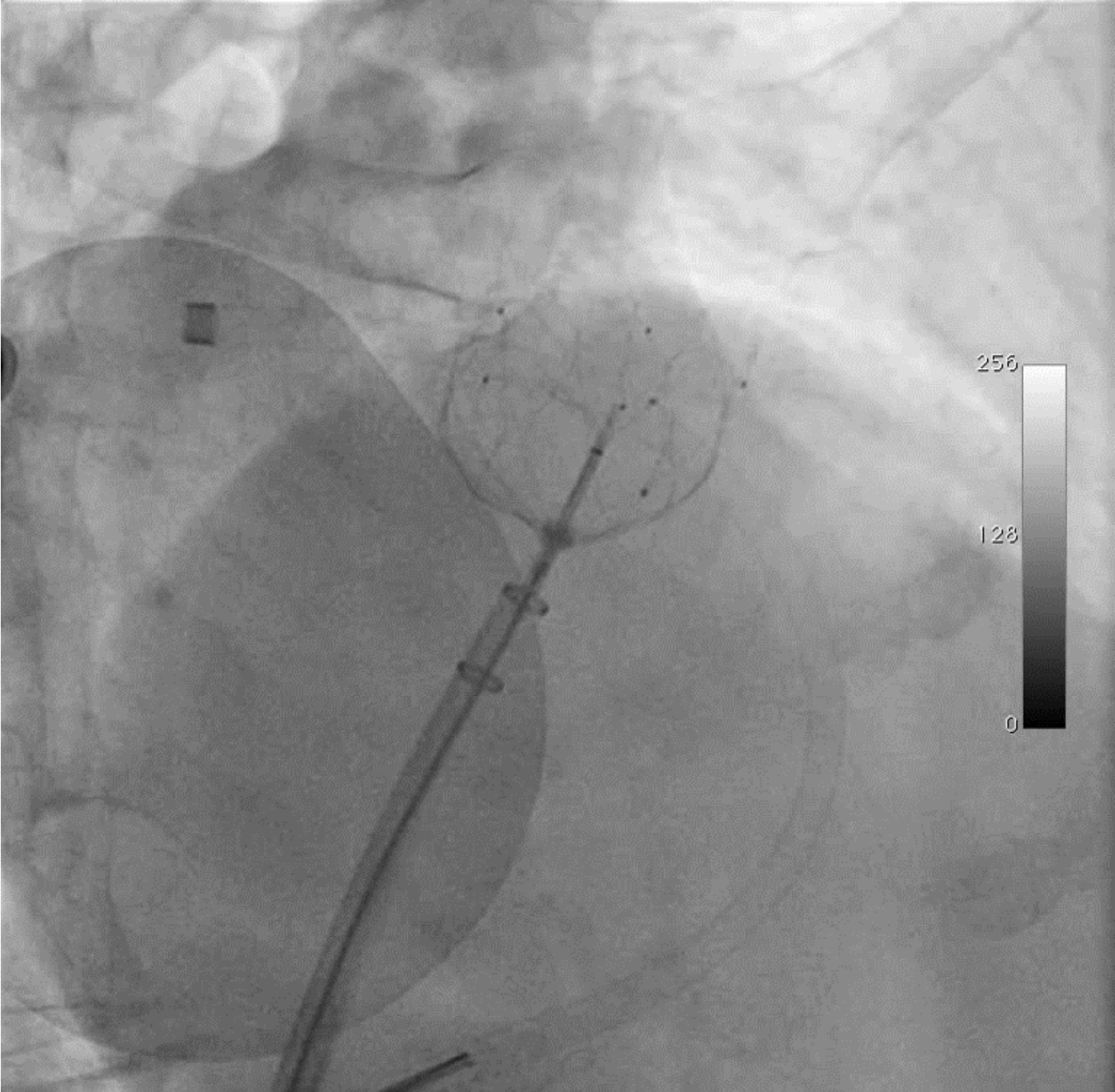
WATCHMAN™ Device

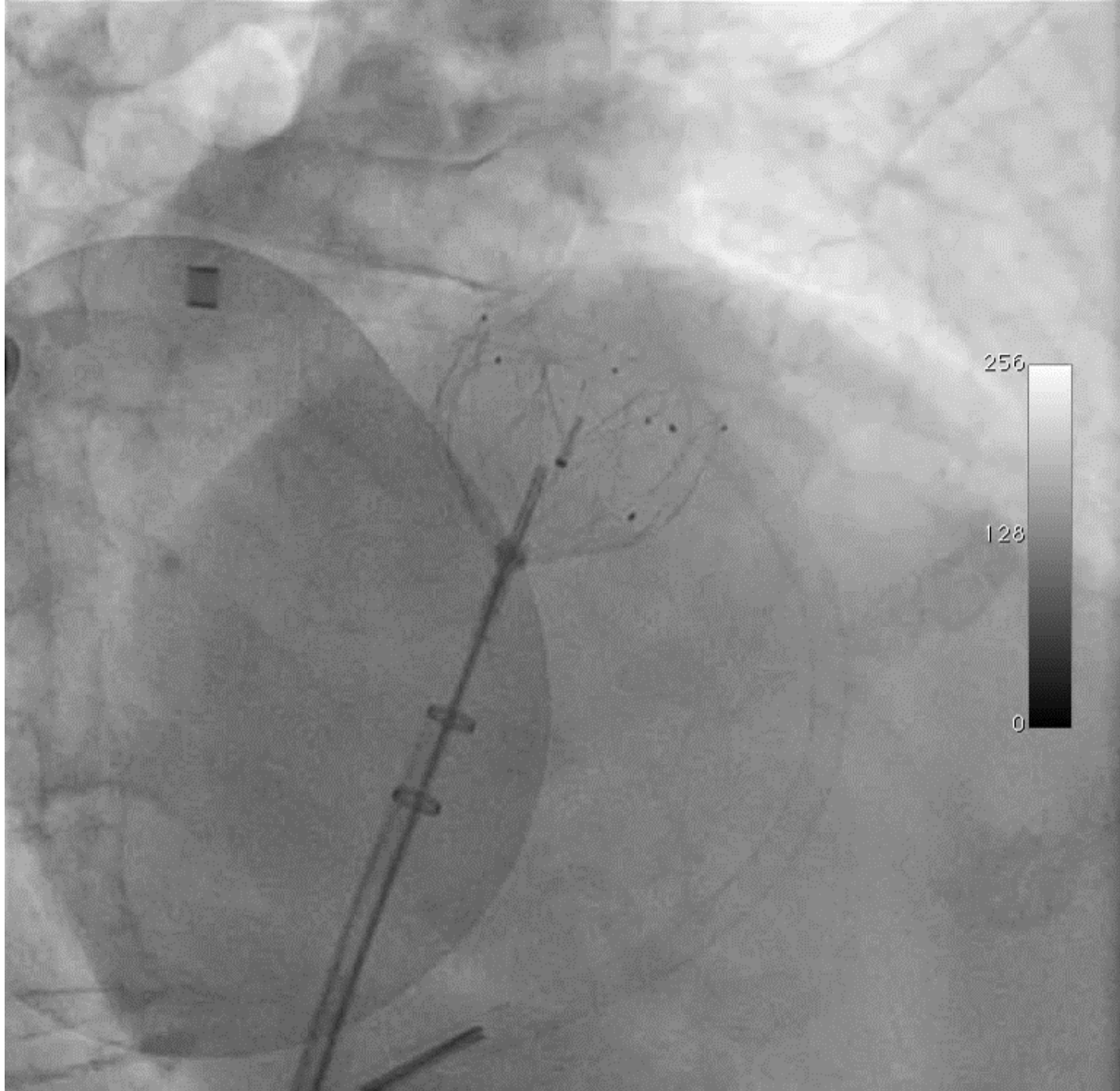
- ▶ CE Mark in 2005
- ▶ Purchased by Boston Scientific in 2011
- ▶ First device to undergo randomized clinical studies comparing stroke risk reduction following left atrial appendage closure versus oral anticoagulation (warfarin)

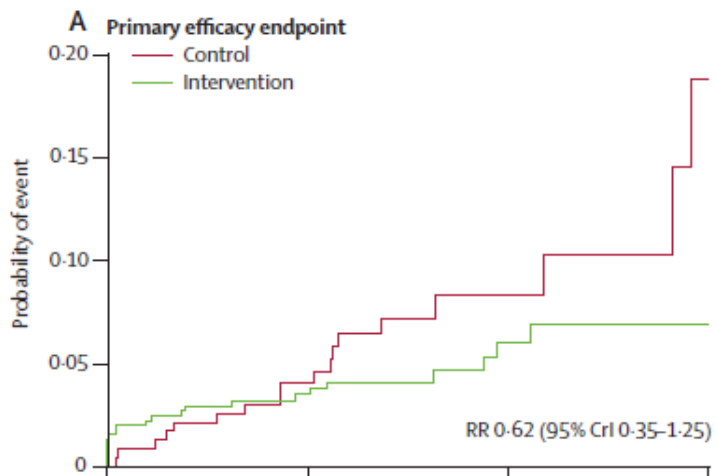


The PROTECT-AF trial (NCT00129545)
The PREVAIL trial (NCT01182441)



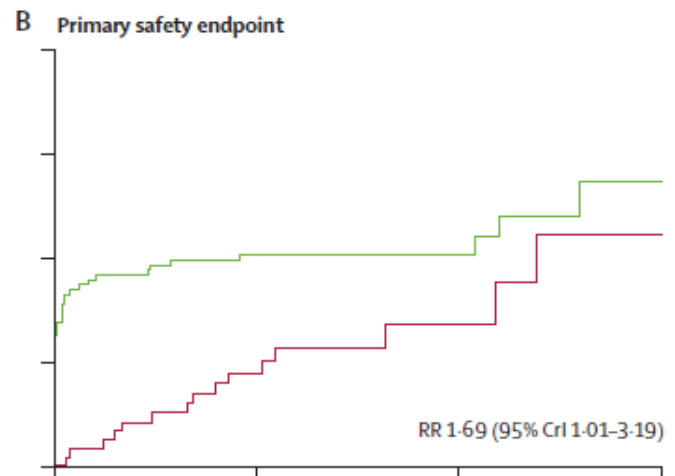




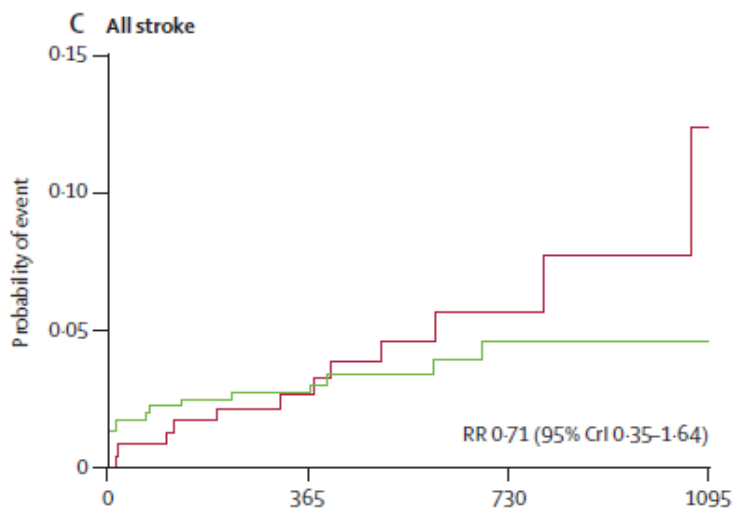


Number at risk

Control	244	174	67	17
Intervention	463	332	132	34

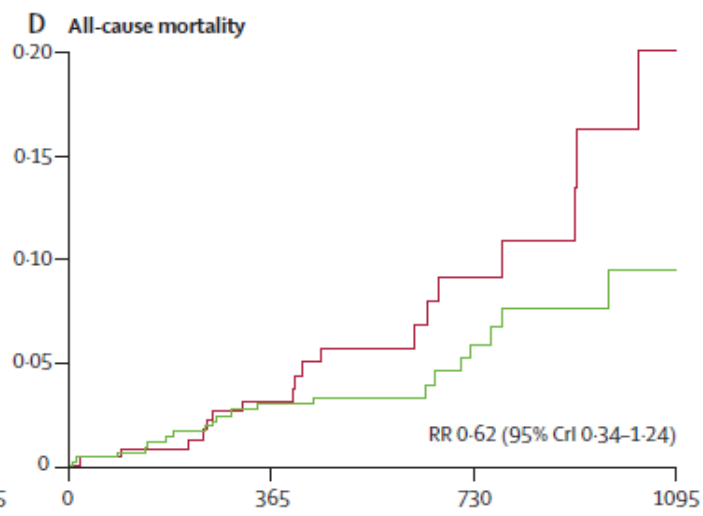


Control	244	171	65	16
Intervention	463	317	126	30



Number at risk

Control	244	174	67	17
Intervention	463	332	132	34

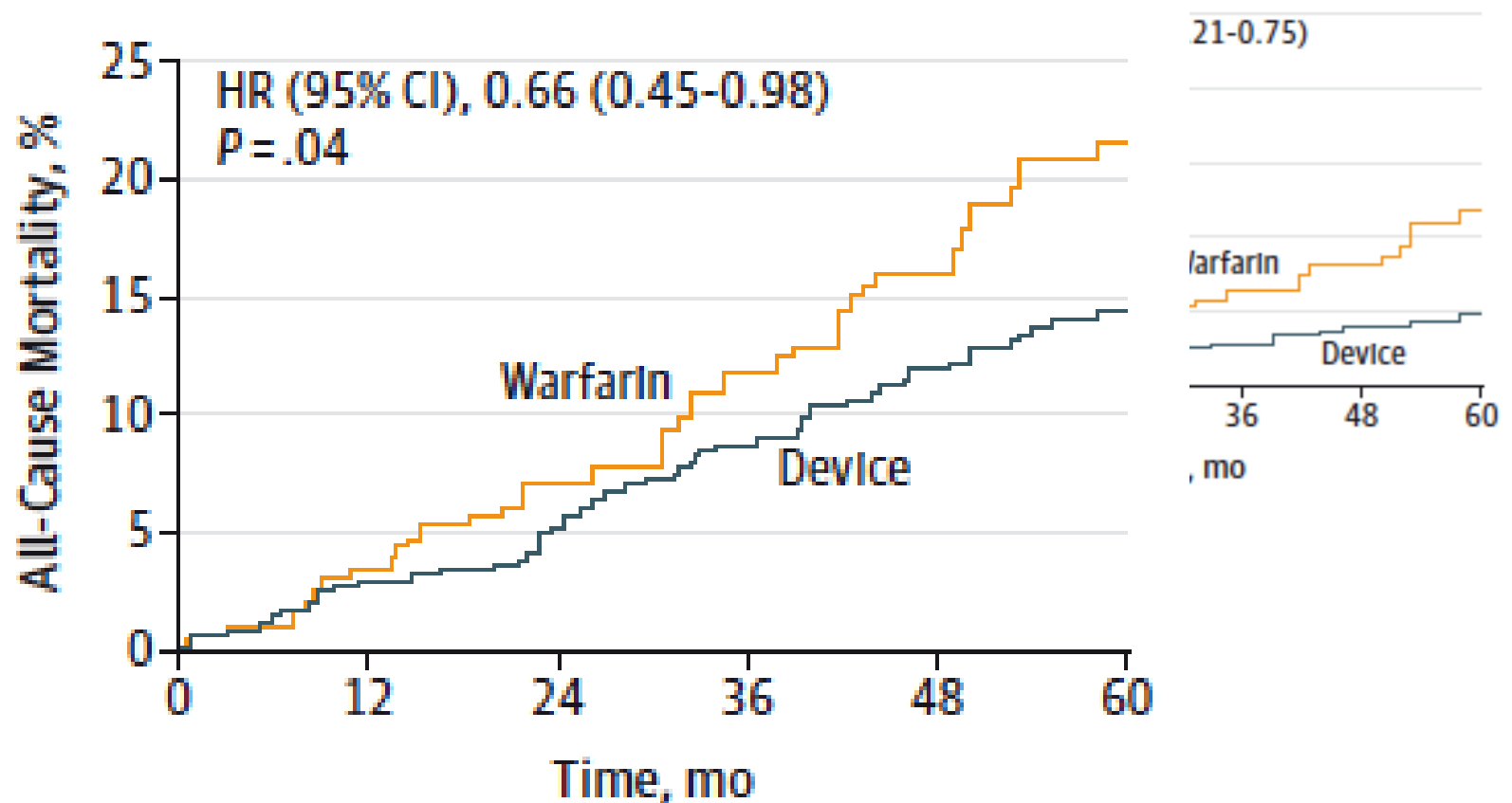


Control	244	176	68	17
Intervention	463	337	136	35

Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation

A Randomized Clinical Trial

C All-cause mortality



Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation

A Randomized Clinical Trial

	Device Group, No. (%) (n = 463)	Warfarin Group, No. (%) (n = 244)	P Value
Cardiovascular	17 (3.7)	22 (9.0)	.005
Heart failure	3 (0.6)	2 (0.8)	>.99
Hemorrhagic stroke	2 (0.4)	8 (3.3)	.004
Ischemic stroke	1 (0.2)	1 (0.4)	>.99
Myocardial infarction	2 (0.4)	2 (0.8)	.61
Sudden cardiac death	4 (0.9)	4 (1.6)	.46
Unexplained/other	5 (1.0)	5 (2.0)	.33
Cancer	10 (2.2)	3 (1.2)	.56
Pulmonary	9 (1.9)	9 (3.7)	.21
Neurologic	2 (0.4)	1 (0.4)	>.99
Multisystem organ failure	6 (1.3)	1 (0.4)	.43
Other	9 (1.9)	5 (2.0)	>.99
Renal failure	3 (0.6)	3 (1.2)	.42
Sepsis	2 (0.4)	1 (0.4)	>.99
Unexplained/other	4 (0.9)	1 (0.4)	.66

Several concerns were raised by the U.S. Food and Drug Administration regarding :

1. patient selection criteria (e.g., patients with CHADS2 = 1)
2. acute safety events, particularly in the early portion of the trial

A second trial was requested for CME approval.

	Intervention (n=463)	Control (n=244)
Serious pericardial effusion*	22 (4.8%)	0
Major bleeding†	16 (3.5%)	10 (4.1%)
Procedure-related ischaemic stroke	5 (1.1%)	0
Device embolisation	3 (0.6%)	0
Haemorrhagic stroke‡	1 (0.2%)	6 (2.5%)
Other§	2 (0.4%)	0

CHADS2 score*

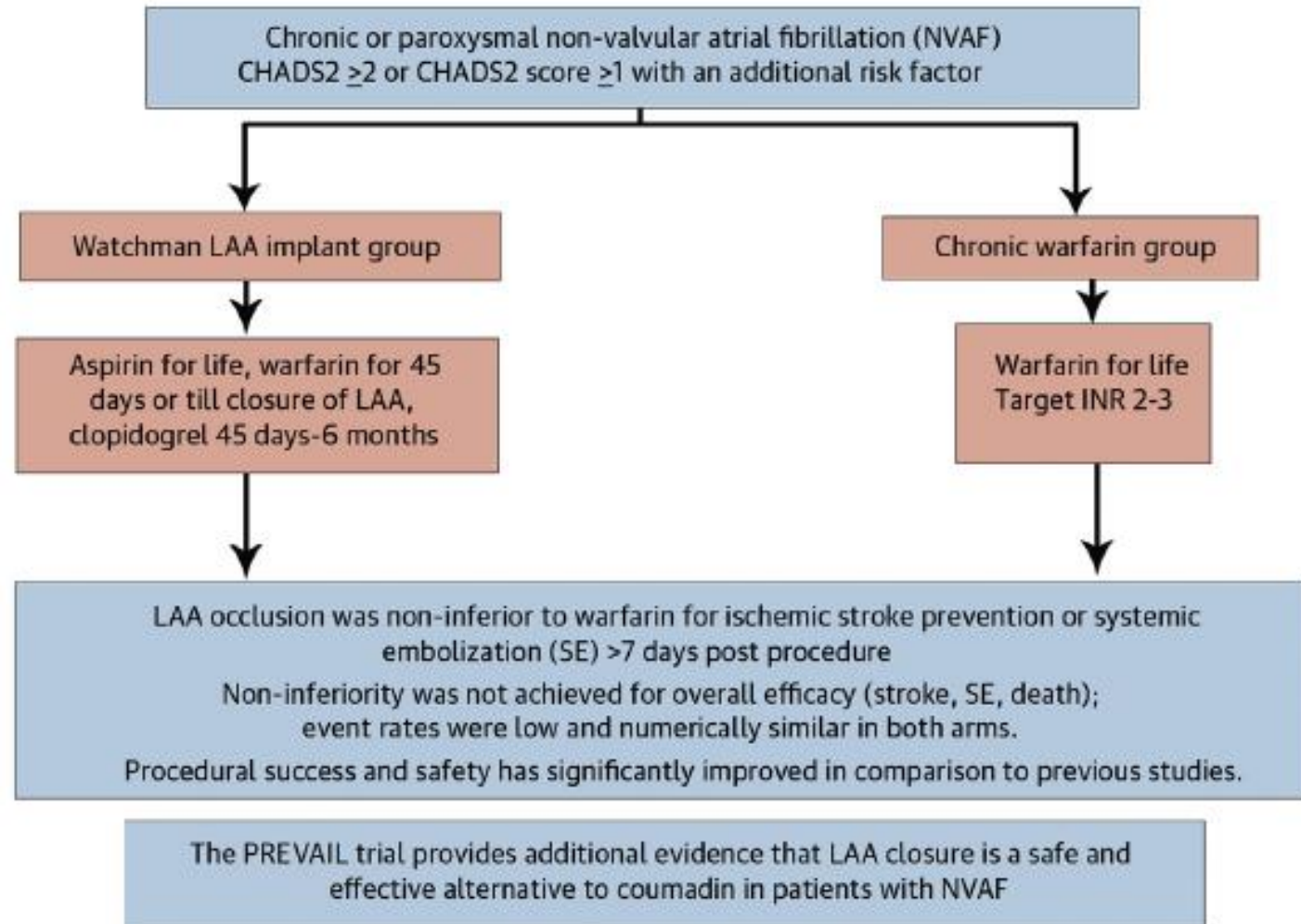
1	157 (33.9%)	66 (27.0%)
2	158 (34.1%)	88 (36.1%)
3	88 (19.0%)	51 (20.9%)
4	37 (8.0%)	24 (9.8%)
5	19 (4.1%)	10 (4.1%)
6	4 (0.9%)	5 (2.0%)



Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy



The PREVAIL Trial

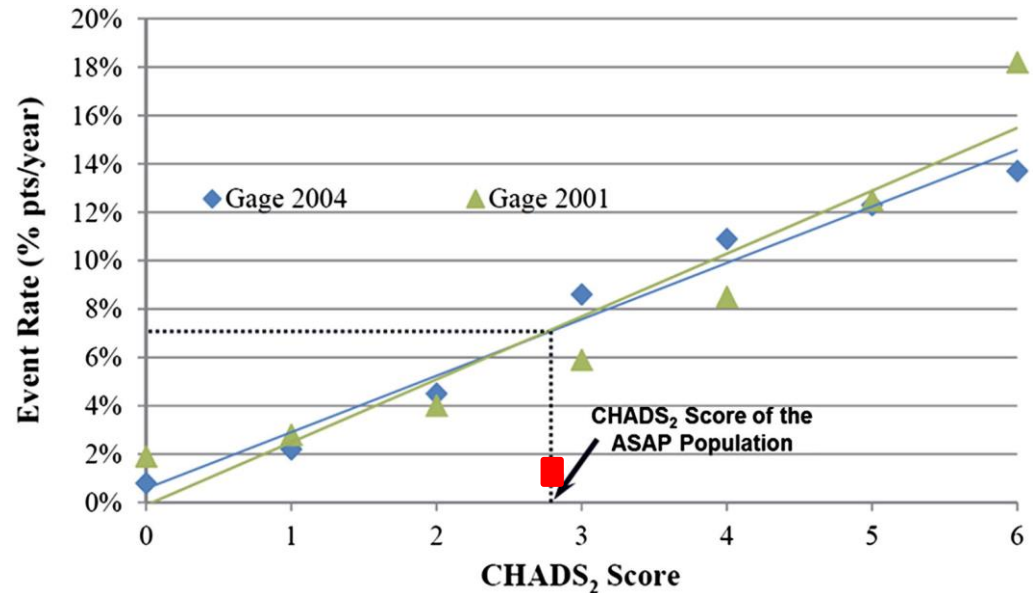


Left Atrial Appendage Closure With the Watchman Device in Patients With a Contraindication for Oral Anticoagulation

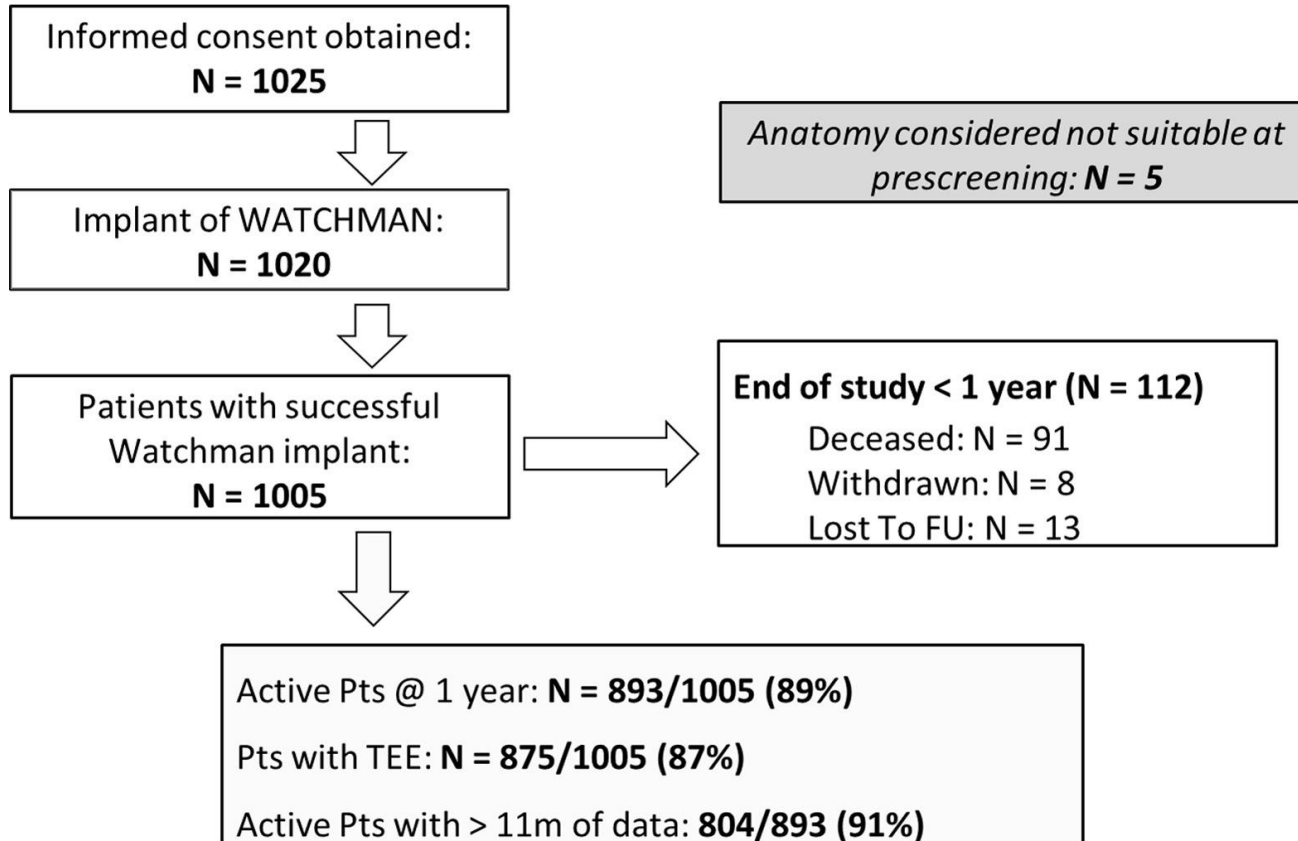
The ASAP Study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology)

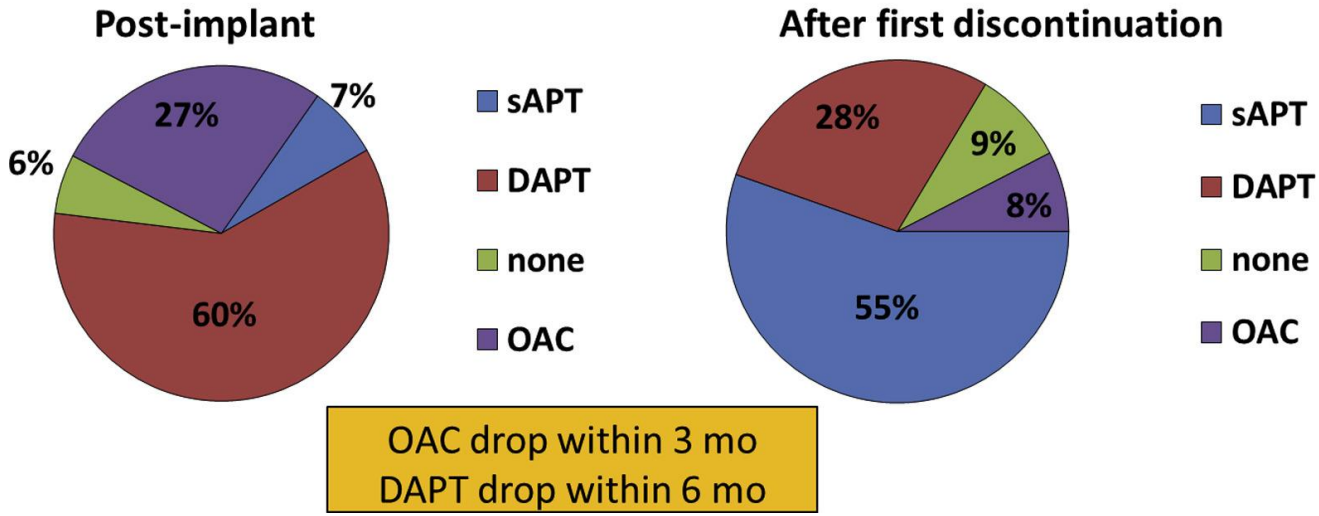
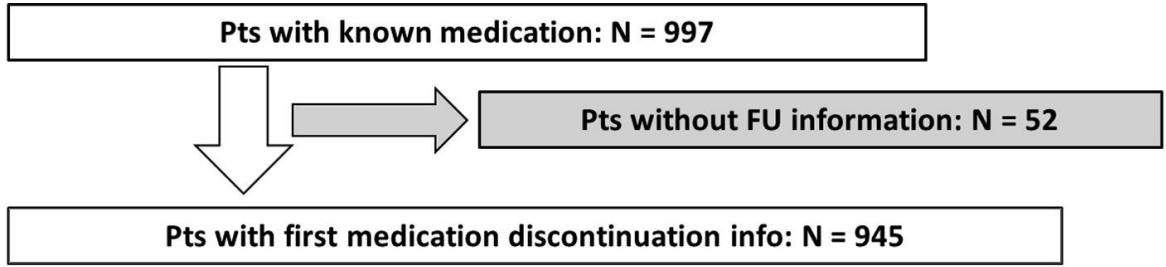
The mean CHADS₂ score in the ASAP study population was 2.8, which equates to a predicted ischemic stroke rate of 7.4% in patients, assuming no aspirin use, or to a predicted stroke rate of 7.3% assuming aspirin use.

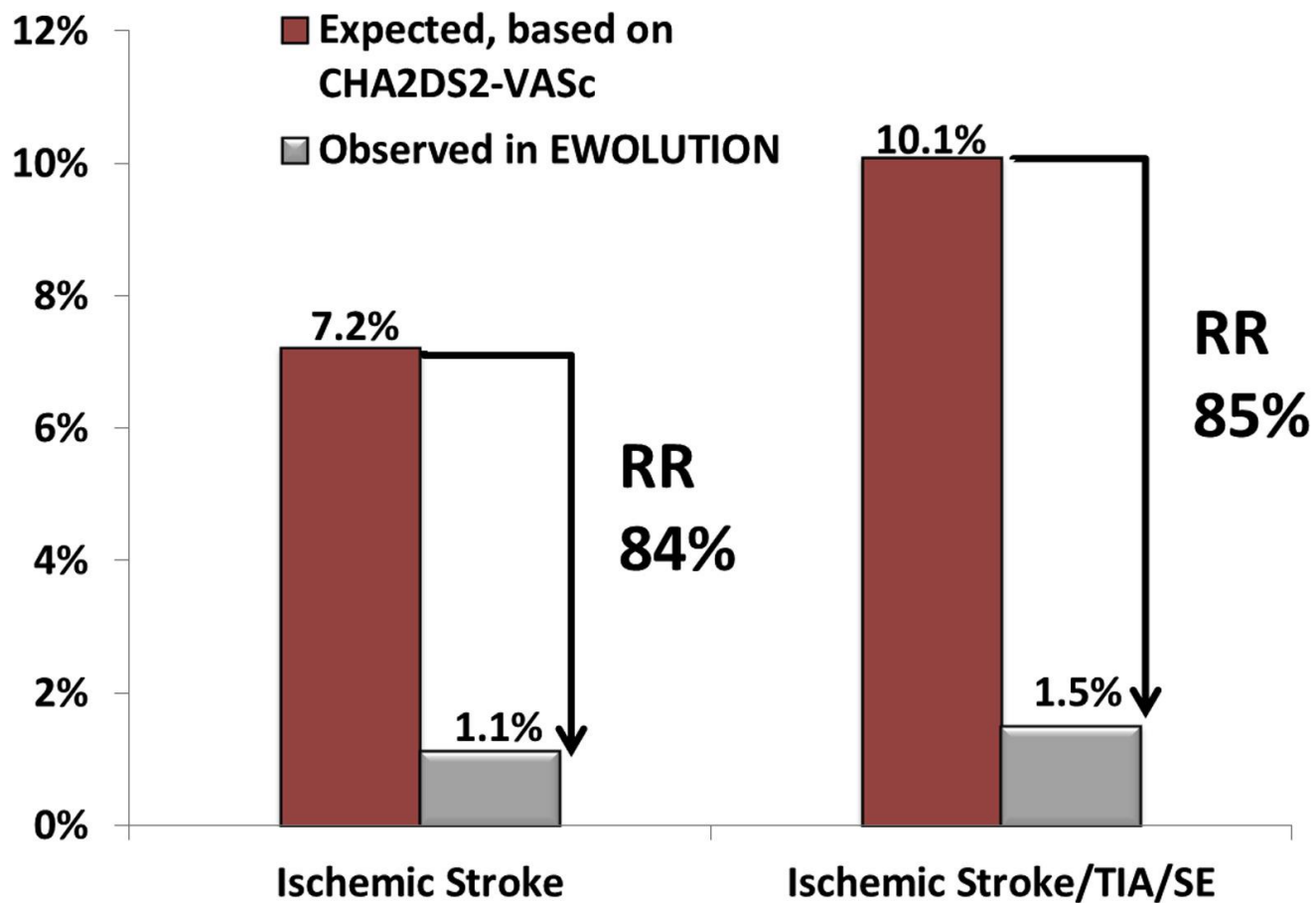
Clopidogrel has been reported to reduce ischemic stroke by 32%, so the expected stroke rate would be 5.0% per year. But the observed rate of **1.7%** per year would still represent a robust reduction in the ischemic stroke rate.

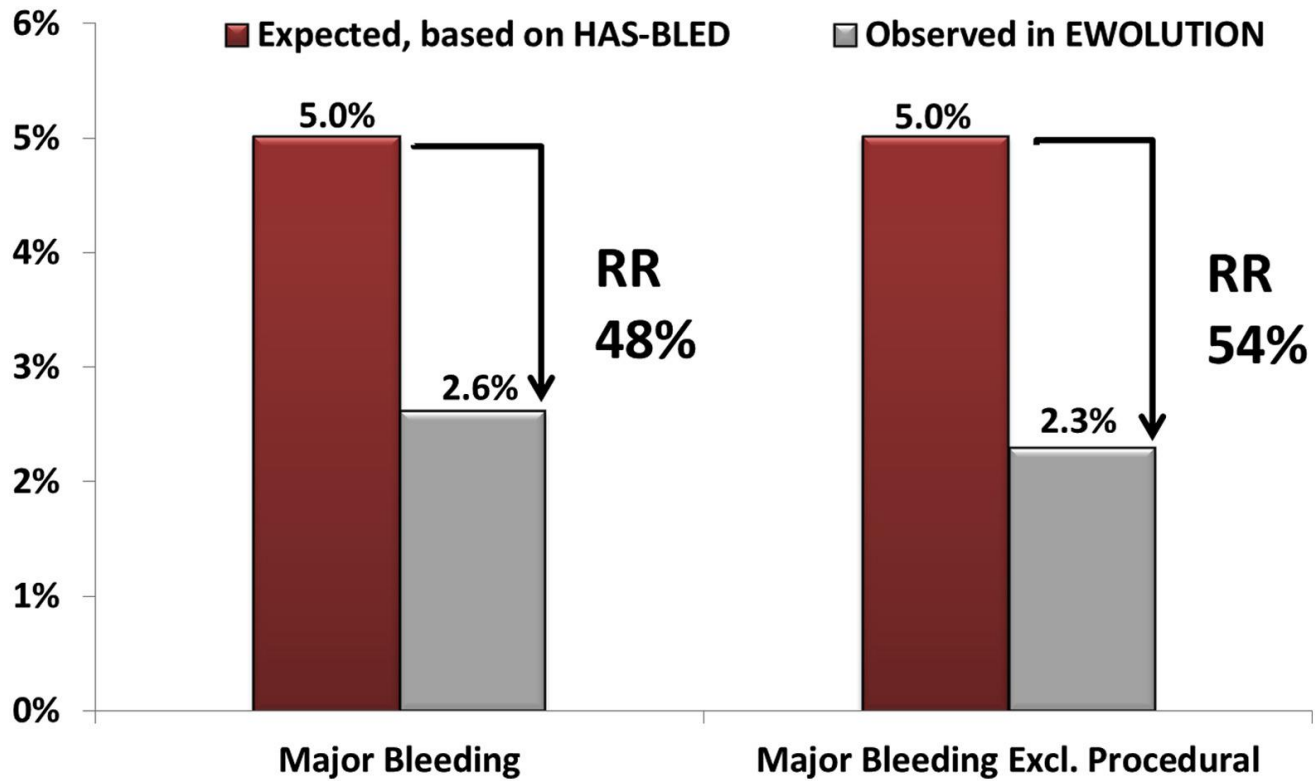


	Entire Cohort Events/Patient-Years*
Primary efficacy	8/175.0 (4.6%)
Death, all cause	9/180.0 (5.0%)
All stroke	4/176.0 (2.3%)
Ischemic stroke	3/176.9 (1.7%)
Hemorrhagic stroke	1/179.1 (0.6%)







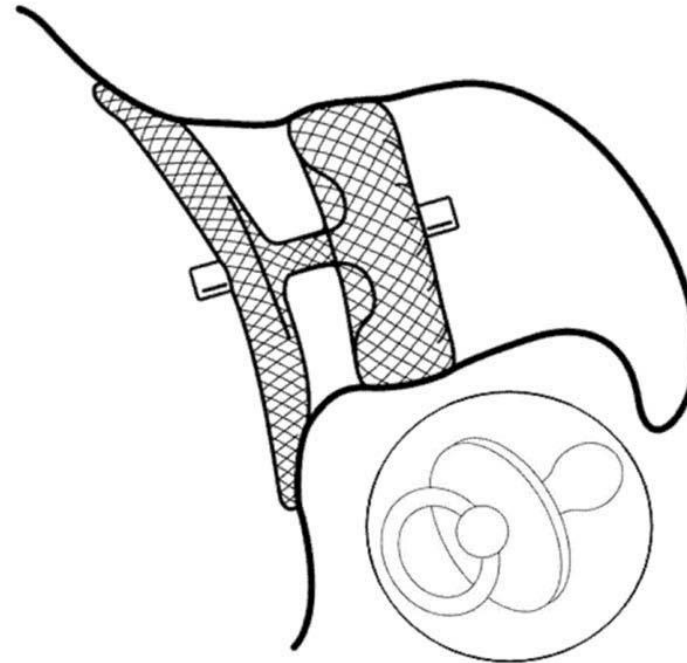
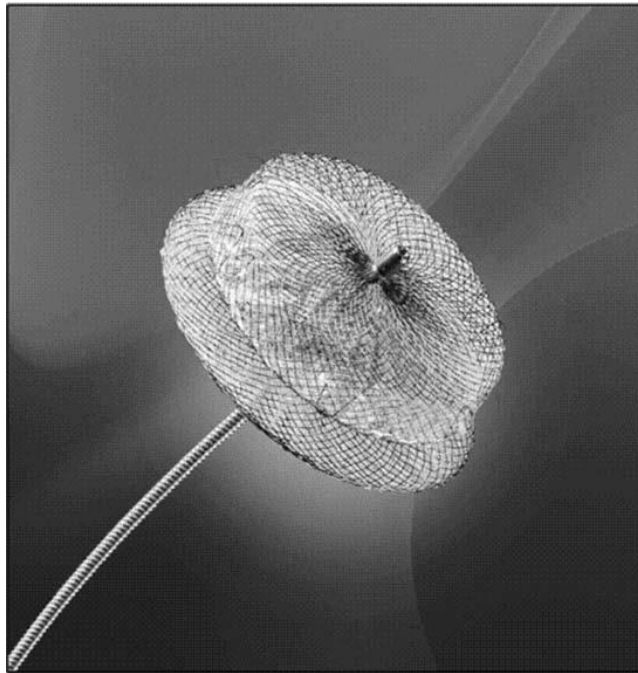


AMPLATZER™ Left Atrial Appendage Occluders

- ▶ AMPLATZER™ Cardiac Plug (ACP) introduced in 2008
- ▶ AGA Medical purchased by St. Jude Medical in 2010
- ▶ Second-generation AMPLATZER™ Amulet™ Left Atrial Appendage Occluder introduced in 2013



AMPLATZER™
Amulet™ Device



PHILIPS

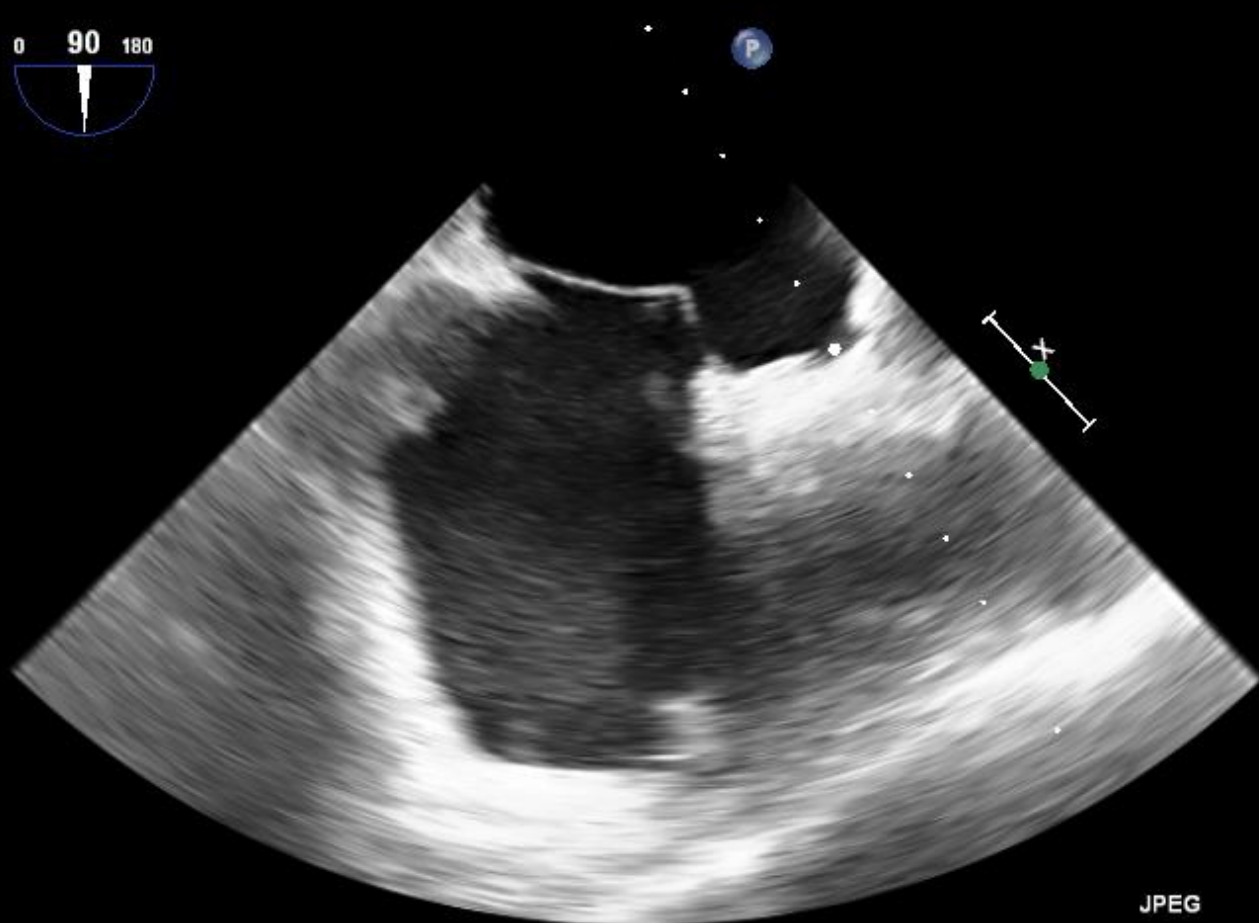
TIS0.1 MI 0.5

X7-2t/Adulti

FR 50Hz
12cm

M4

2D
70%
C 50
P Off
Gen.



JPEG

Temp. PAZ.: 37.0C
Temp. TEE: 38.6C

*** bpm

PHILIPS

TIS0.1 MI 0.5

X7-2t/Adulti

FR 50Hz
12cm

M4

2D
70%
C 50
P Off
Gen.



G
P R

A small diagram showing a triangle with vertices labeled G (top), P (left), and R (right).



JPEG

Temp. PAZ.: 37.0C
Temp. TEE: 38.7C

*** bpm

PHILIPS

TIS0.1 MI 0.6

X7-2t/Adulti

FR 8Hz
7.1cm

Battiti 3D 1

M4

3D
3D 52%
3D 40dB



JPEG

Temp. PAZ.: 37.0C
Temp. TEE: 38.6C

*** bpm

Image size: 512 x 512
View size: 876 x 876
WL: 128 WW: 256

GRZGPP71L59F839T (- 42 y , 39 y)
Coro Rec. 15fps FI 15fps - unnamed
34100
1



Zoom: 171% Angle: 0
Im: 1/89

NOT FOR MEDICAL USAGE

18/02/11 16:20:40
Made in Ostrix

JPEGLossless.Non-hierarchical-1stOrderPrediction

Image size: 512 x 512
View size: 876 x 876
WL: 128 WW: 256

GRZGPP71L59F839T (42 y , 39 y)
Coro Rec 15fps FI 15fps — unnamed
34100
1

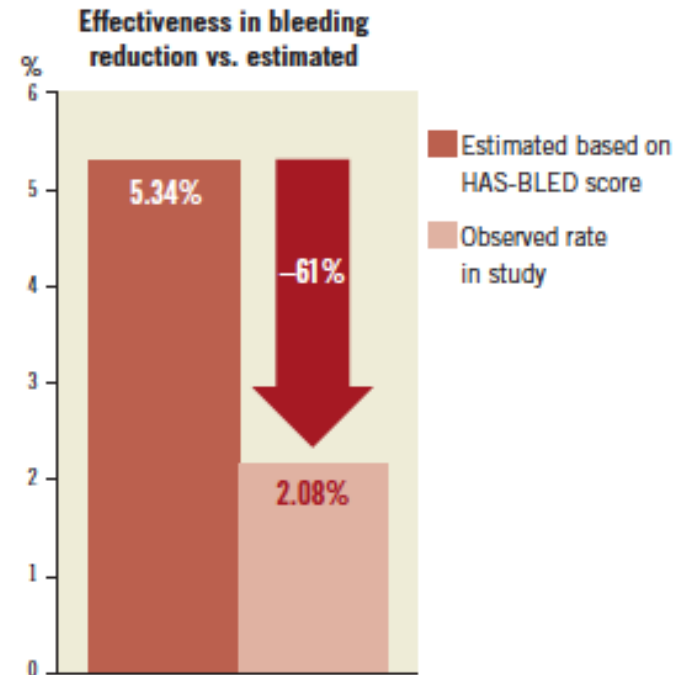
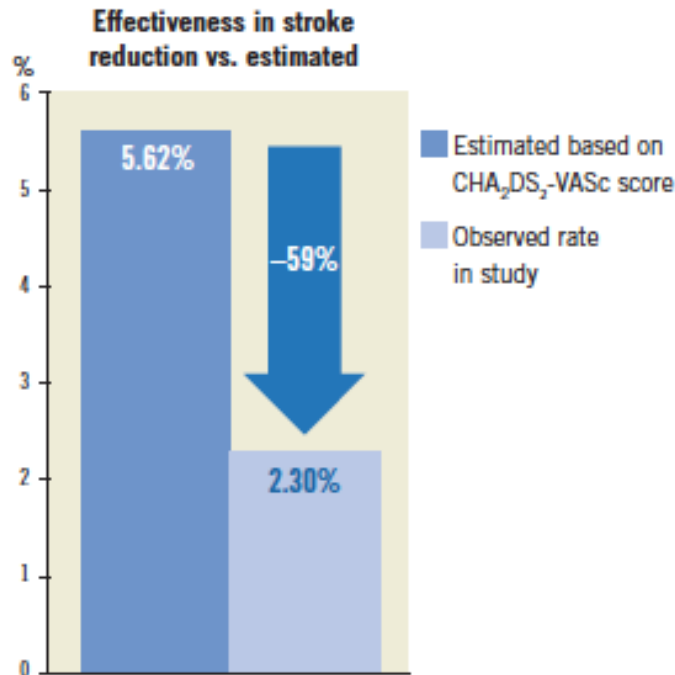


Zoom: 171% Angle: 0
Im: 1/68
JPEG Lossless Non-hierarchical-1stOrderPrediction

NOT FOR MEDICAL USAGE

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Made In Osirix

Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug



Total patients	Total patient-years	CHA ₂ DS ₂ -VASc score
1,001	1,349	4.43
Estimated stroke rate per CHA₂DS₂-VASc		Actual annual stroke rate (No. strokes+TIA)
5.62%		2.30% (31)

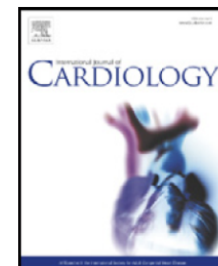
Total patients	Total patient-years	HAS-BLED score
1,001	1,349	3.12
Estimated bleeding rate per HAS-BLED		Actual annual bleeding rate (No. major bleeds)
5.34%		2.08% (28)



Contents lists available at [ScienceDirect](#)

International Journal of Cardiology

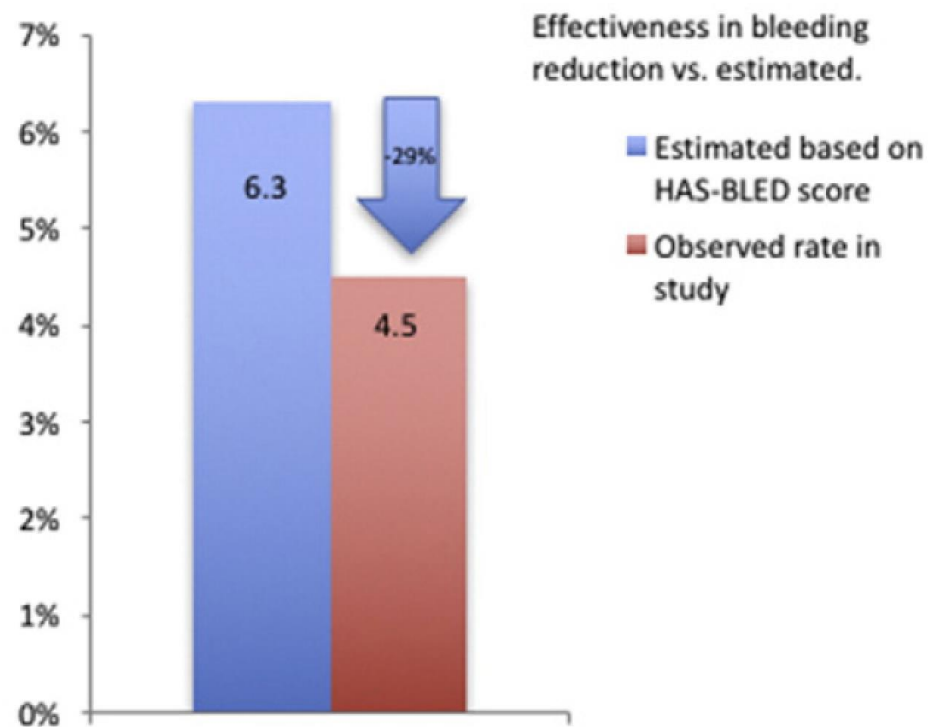
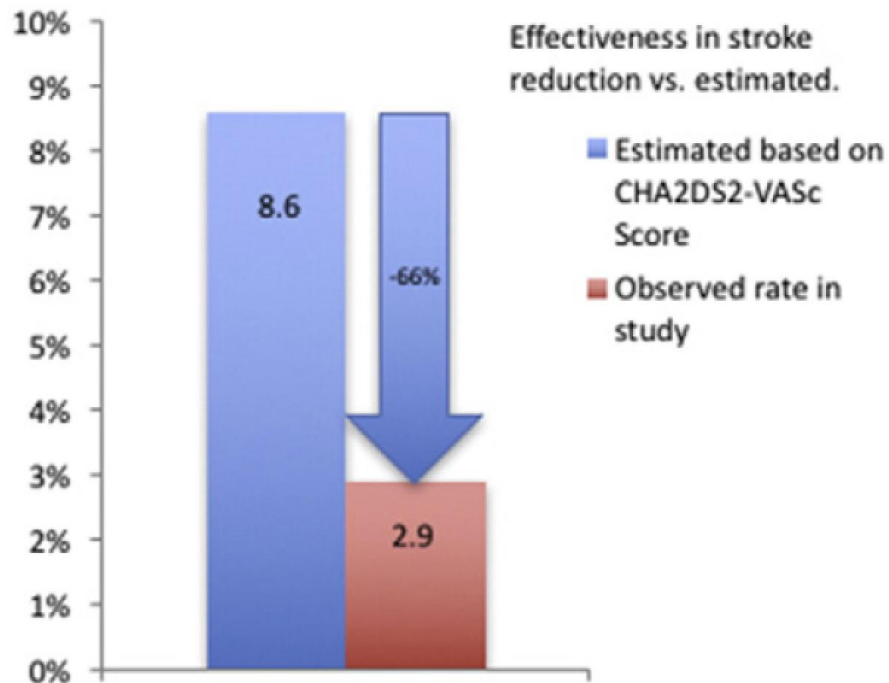
journal homepage: www.elsevier.com/locate/ijcard



Left atrial appendage closure using AMPLATZER™ devices: A large, multicenter, Italian registry☆



Sergio Berti ^{a,*}, Gennaro Santoro ^b, Elvis Brscic ^c, Matteo Montorfano ^d, Luigi Vignali ^e, Paolo Danna ^f, Claudio Tondo ^g, Gianpiero D'Amico ^h, Amerigo Stabile ⁱ, Salvatore Saccà ^j, Giuseppe Patti ^k, Antonio Rapacciuolo ^l, Arnaldo Poli ^m, Paolo Golino ⁿ, Paolo Magnavacchi ^o, Alberto De Caterina ^a, Francesco Meucci ^b, Bruno Pezzulich ^c, Marco Rezzaghi ^a, Miroslava Stolcova ^b, Giuseppe Tarantini ^h



Total Patients	Total Patient-Years	CHA ₂ DS ₂ -VASc score
542	896	4.2

Total Patients	Total Patient-Years	HAS-BLED score
542	896	3.2

Estimated stroke rate per CHA ₂ DS ₂ -VASc	Actual annual stroke rate (No. Strokes+TIA)
8.6%	2.9%

Estimated stroke rate per HAS-BLED	Actual annual stroke rate (No. Strokes+TIA)
6.3%	4.5%



Primary Outcomes of the Amplatzer™ Amulet™ IDE Randomized Controlled Trial

Dhanunjaya Lakkireddy, MD - David Thaler, MD, PhD - Christopher Ellis, MD - Vijendra Swarup, MD
Lars Sondergaard, MD - John Carroll, MD - Michael R. Gold, MD, PhD - James Hermiller, MD
Hans-Christoph Diener, MD, PhD - Boris Schmidt, MD - Lee MacDonald, MD - Moussa Mansour, MD
Brijeshwar Maini, MD - Stephan Windecker, MD

on behalf of the Amulet IDE investigators

ESC CONGRESS 2021
THE DIGITAL EXPERIENCE

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otherwise noted.

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AMULET IDE TRIAL DESIGN

PATIENT ELIGIBILITY

- Paroxysmal, persistent, or permanent non-valvular atrial fibrillation
- High risk of stroke or systemic embolism defined as CHA₂DS₂-VASc score of ≥3 or CHADS₂ score of ≥2
- Suitable for short term warfarin therapy but deemed unable to take long term oral anticoagulation
- Imaging indicated Watchman device and Amulet LAA occluder were able to be implanted

CLINICAL FOLLOW-UP

- Discharge, 45d (+TEE), 6mo, 12mo (+TEE), 18mo, 24mo and annually for 5 years*

DISCHARGE MEDICATIONS

- Amulet LAA occluder: aspirin + clopidogrel (DAPT) or aspirin + OAC
- Watchman device: aspirin + warfarin (mandatory per the DFU)

AMULET IDE TRIAL ENDPOINTS

PRIMARY ENDPOINTS (ALL ENDPOINTS TO BE MET FOR TRIAL SUCCESS)

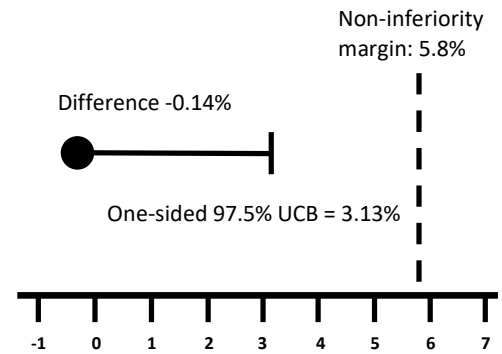
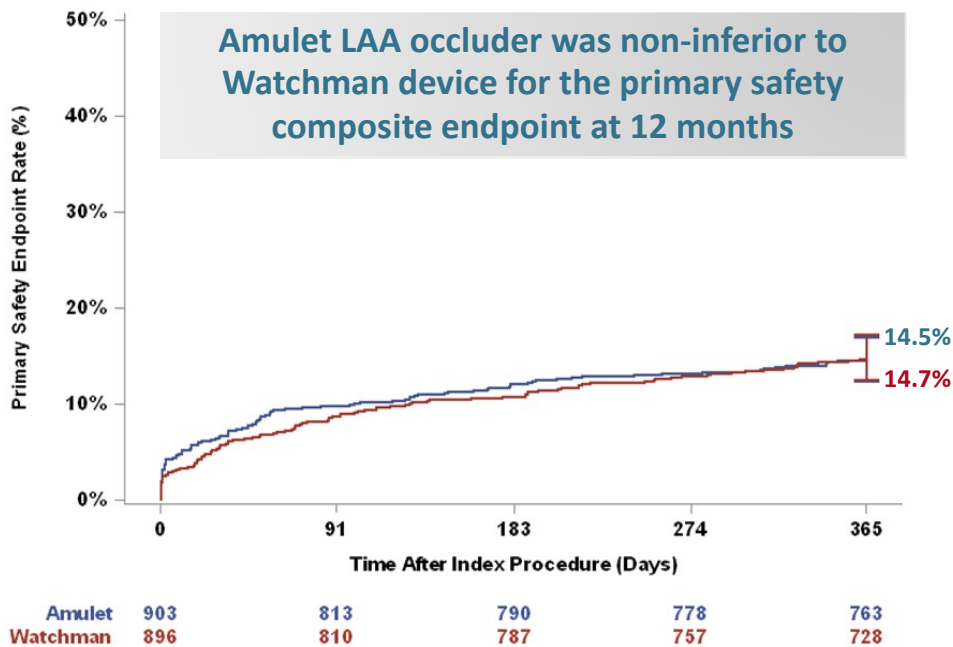
- **Mechanism of action** (45 days): Residual jet around the device $\leq 5\text{mm}$ Non-inferiority margin: -3%
- **Safety** (12 months): Composite of procedure-related complications, or all cause death, or major bleeding Non-inferiority margin: 5.8%
- **Effectiveness** (18 months): Composite of ischemic stroke or systemic embolism Non-inferiority margin: 3.2%

SECONDARY ENDPOINTS (NON-HIERARCHICAL TEST BASED ON HOCHBERG ADJUSTMENT¹ FOR MULTIPLE TESTING)

- Mechanism of action (45 days) Superiority test
- Primary safety endpoint (12 months) Superiority test
- Primary effectiveness endpoint (18 months) Superiority test
- Major bleeding (18 months) Superiority test
- Composite of stroke/systemic embolism/cardiovascular death (18 months) Non-inferiority margin: 4.5%

PRIMARY SAFETY ENDPOINT

COMPOSITE OF PROCEDURE-RELATED COMPLICATIONS, ALL-CAUSE DEATH, OR MAJOR BLEEDING AT 12 MONTHS



Difference in Primary Safety Endpoint Event Rates
 p (non-inferiority) = 0.0002

Primary Safety Endpoint	Amulet	Watchman
Composite	14.5%	14.7%
Procedure-Related Complications	4.5%	2.5%
All-Cause Death	3.9%	5.1%
Major Bleeding (Type 3 or greater)	10.6%	10.0%
Non-Procedure Related	7.9%	8.0%

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 THE DIGITAL EXPERIENCE

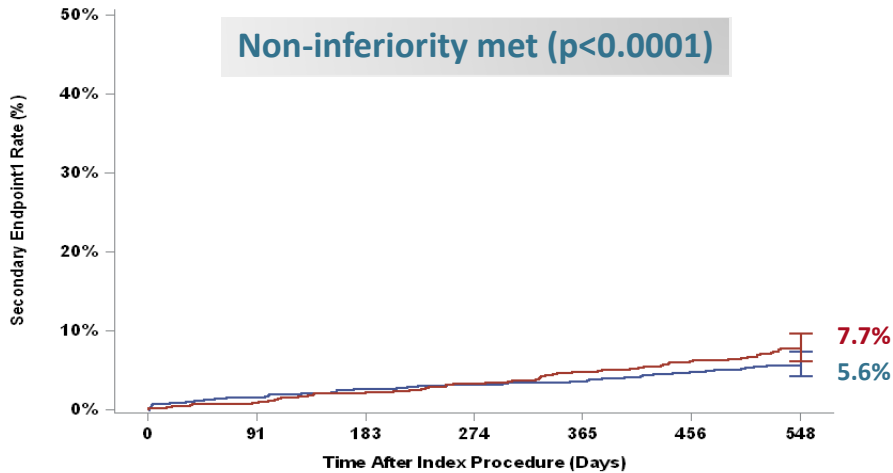
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SECONDARY ENDPOINTS

Stroke, Systemic Embolism & CV Death

Non-inferiority met ($p < 0.0001$)

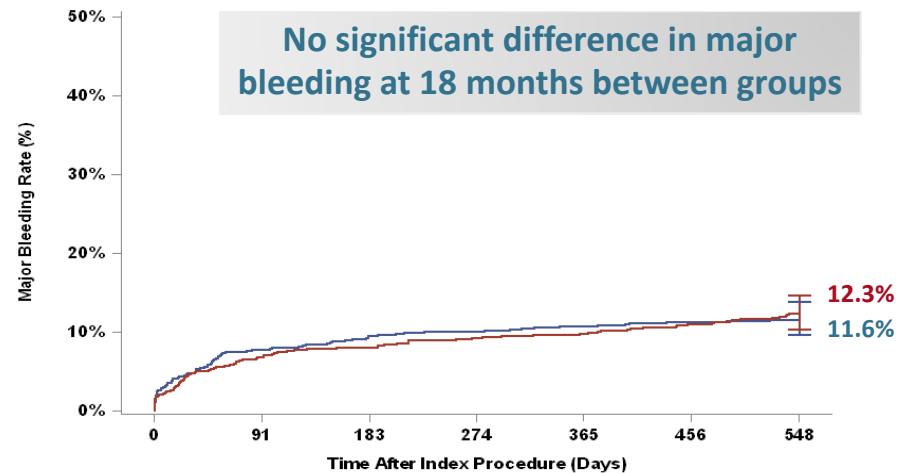


	915	893	876	863	851	832	783
Amulet	915	893	876	863	851	832	783
Watchman	916	894	873	843	811	790	726

Stroke, Systemic Embolism, CV Death	Amulet	Watchman
Composite	5.6%	7.7%
- Ischemic or Hemorrhagic Stroke	2.7%	3.4%
- Systemic Embolism	0.3%	0.2%
- Cardiovascular/Unexplained Death	3.1%	4.8%

Major Bleeding

No significant difference in major bleeding at 18 months between groups



	917	834	811	798	782	760	719
Amulet	917	834	811	798	782	760	719
Watchman	916	836	812	782	753	731	669

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Two secondary endpoints were met based on the Hochberg criteria
Other content provided by Dhanunjaya Lakkireddy, MD unless otherwise noted.

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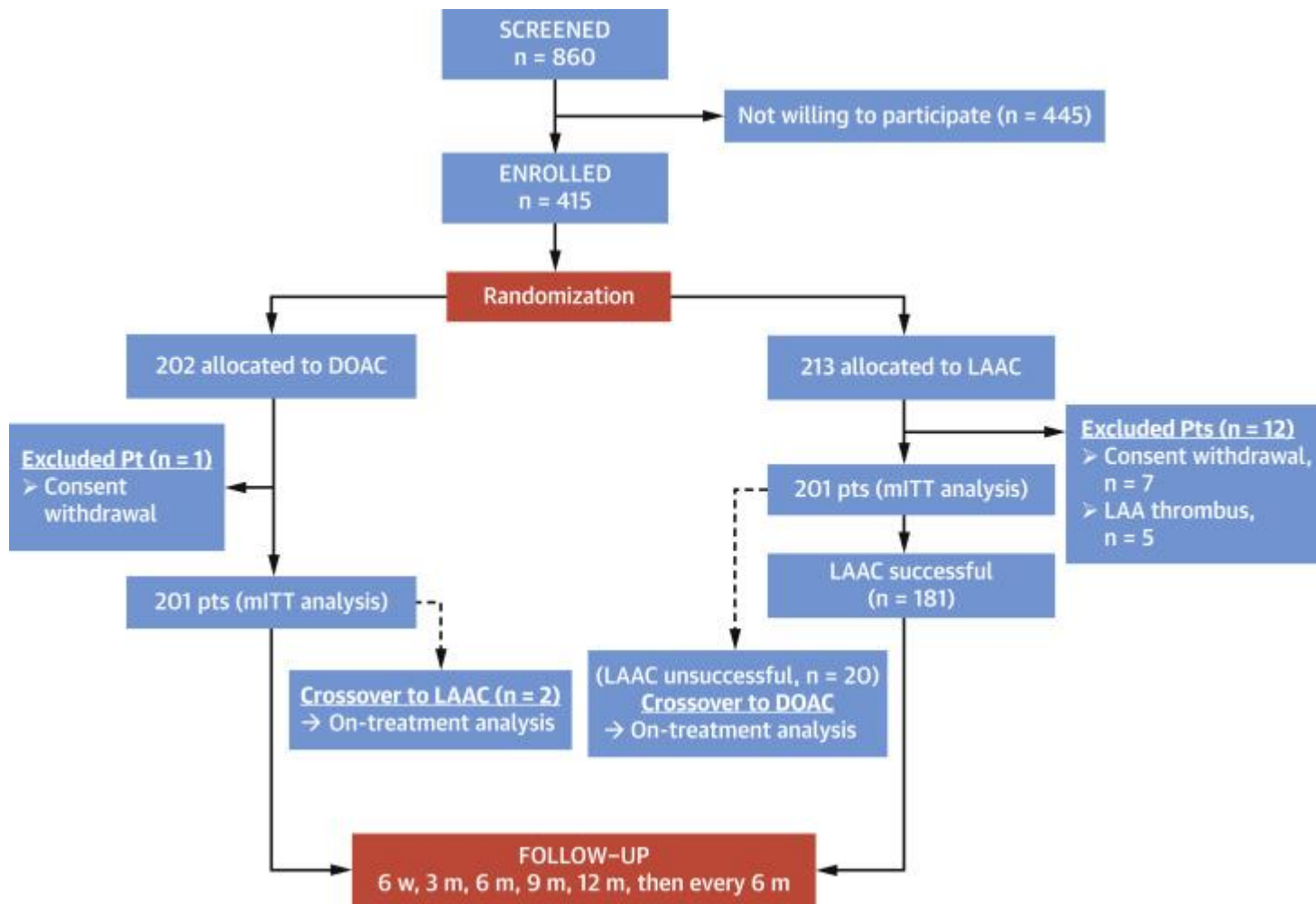
Journal of the American College of Cardiology

Volume 75, Issue 25, 30 June 2020, Pages 3122-3135



Original Investigation

Left Atrial Appendage Closure Versus Direct Oral Anticoagulants in High-Risk Patients With Atrial Fibrillation

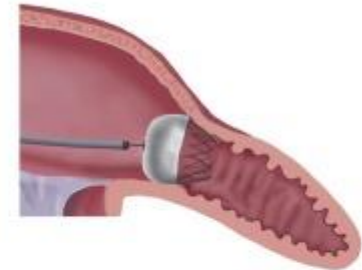


CENTRAL ILLUSTRATION: The PRAGUE-17 Trial

PRAGUE-17 Randomized Clinical Trial

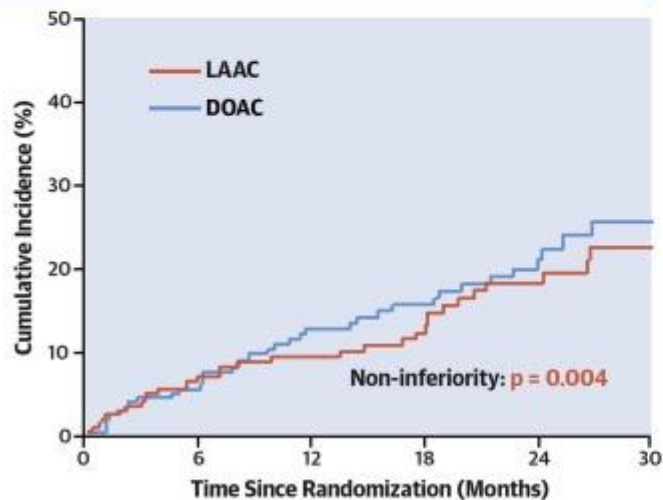


- 402 High-Risk AF Pts → Randomized
 $CHA_2DS_2-VASc = 4.7 \pm 1.5$
 $HAS-BLED = 3.1 \pm 0.9$
- Follow-up: 20.8 ± 10.8 mo (695 pt-year)



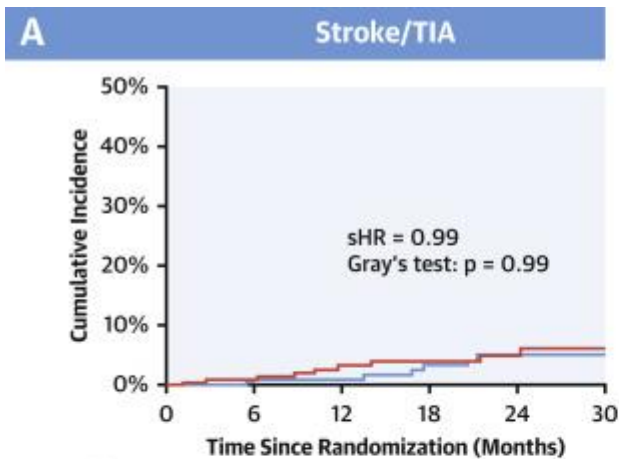
Primary Endpoint

Stroke, TIA, SE, CV Death, Bleeding, or Complications



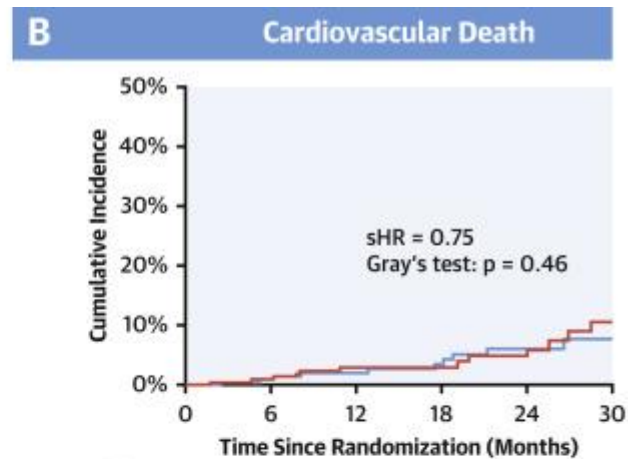
	sHR (95% CI)	p value
Primary Endpoint		
mITT	0.84 (0.53-1.31)	0.44
Per Protocol	0.82 (0.52-1.30)	0.40
On-Treatment	0.79 (0.49-1.25)	0.31
All-Stroke/TIA	1.00 (0.40-2.51)	0.99
CV Death	0.75 (0.34-1.62)	0.46
Major + NMCR Bleeding		
All	0.81 (0.44-1.52)	0.51
Nonprocedural	0.53 (0.26-1.06)	0.07

Osmancik, P. et al. J Am Coll Cardiol. 2020;75(25):3122-35.



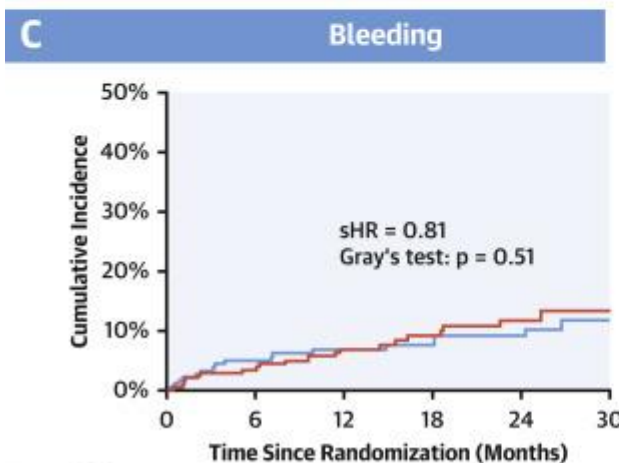
No. at Risk*

— LAAC 201 (0) 186 (4) 155 (7) 115 (11) 81 (13) 45 (15)
— DOAC 201 (0) 187 (2) 142 (9) 109 (10) 76 (14) 39 (17)



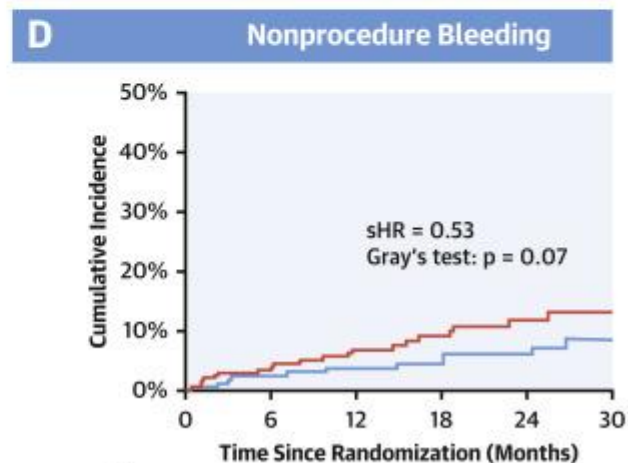
No. at Risk*

— LAAC 201 (0) 188 (2) 156 (4) 117 (7) 84 (7) 48 (8)
— DOAC 201 (0) 188 (0) 147 (3) 114 (5) 81 (7) 42 (7)



No. at Risk*

— LAAC 199 (0) 179 (2) 145 (5) 109 (9) 78 (11) 45 (13)
— DOAC 201 (0) 182 (2) 140 (7) 106 (9) 71 (12) 34 (15)



No. at Risk*

— LAAC 201 (0) 184 (4) 150 (8) 113 (12) 81 (14) 45 (16)
— DOAC 201 (0) 182 (2) 140 (7) 106 (9) 71 (12) 34 (15)

Documento di posizione GISE/AIAC sui requisiti di processo diagnostico ed interventistico riferiti al trattamento della chiusura percutanea dell'auricola sinistra in pazienti affetti da fibrillazione atriale non valvolare

Sergio Berti^{1*} (Chairman), Sakis Themistoclakis²⁵ (Co-Chairman), Gennaro Santoro^{3*}, Roberto De Ponti⁴⁵, Paolo Danna^{5*}, Massimo Zecchin⁶⁵, Francesco Bedogni^{7*}, Luigi Padeletti⁸⁵

- Impiego principale: trattamento per la prevenzione dell'ictus in pazienti con controindicazione alla terapia anticoagulante orale (TAO), o ad elevato rischio emorragico (HASBLED \geq 3).
- Pazienti anziani con FA e DES
- Prevenzione secondaria di evento ischemico: pazienti che hanno presentato un ictus durante TAO in range terapeutico, dopo workup diagnostico che escluda la presenza di altre sorgenti emboligene

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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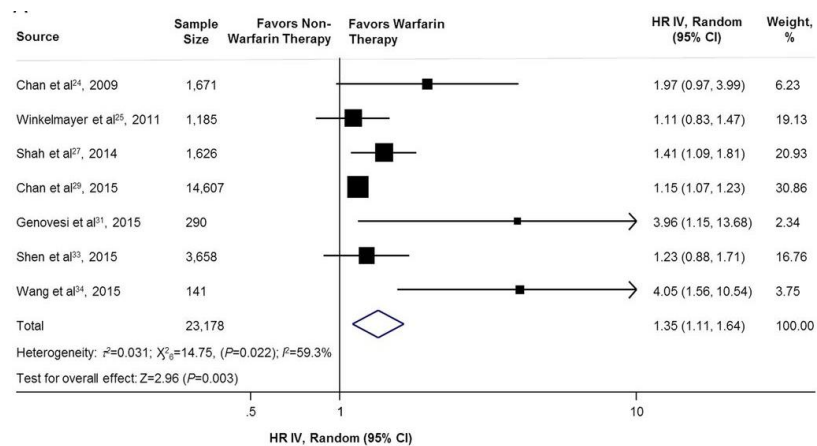
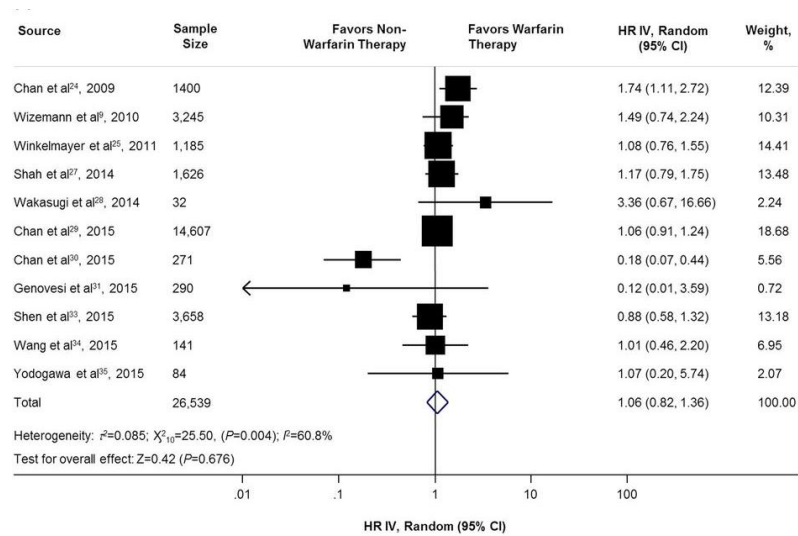
Warfarin Use and the Risk for Stroke and Bleeding in Patients With Atrial Fibrillation Undergoing Dialysis

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

Conclusions—Our results suggest that warfarin use is not beneficial in reducing stroke risk, but it is associated with a higher bleeding risk in patients with AF undergoing dialysis. (*Circulation*. 2014;129:1196-1203.)

La chiusura percutanea dell'auricola sinistra potrebbe rappresentare la modalita ideale di prevenzione dell'ictus nei pazienti in FA in emodialisi.

Adjusted and unadjusted of stroke/thromboembolism comparing warfarin users versus non-warfarin users.

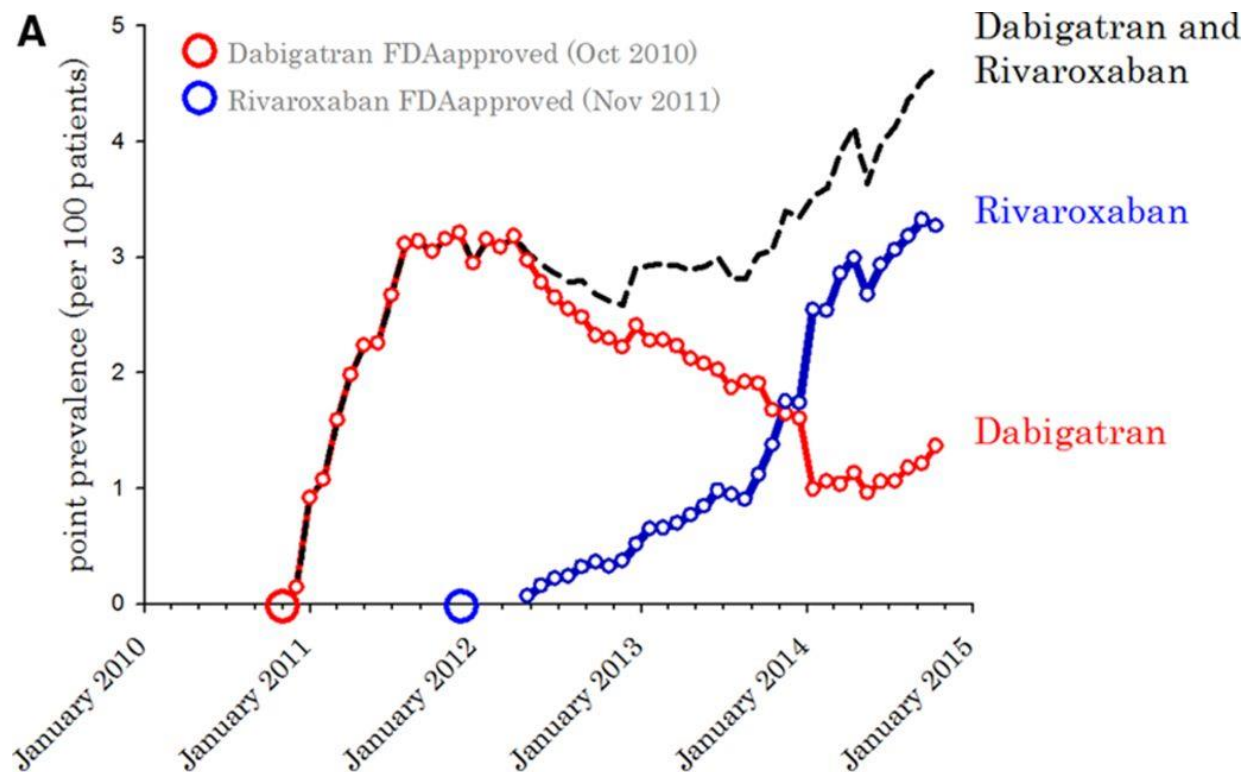


Surapon Nochaiwong et al. Open Heart 2016;3:e000441

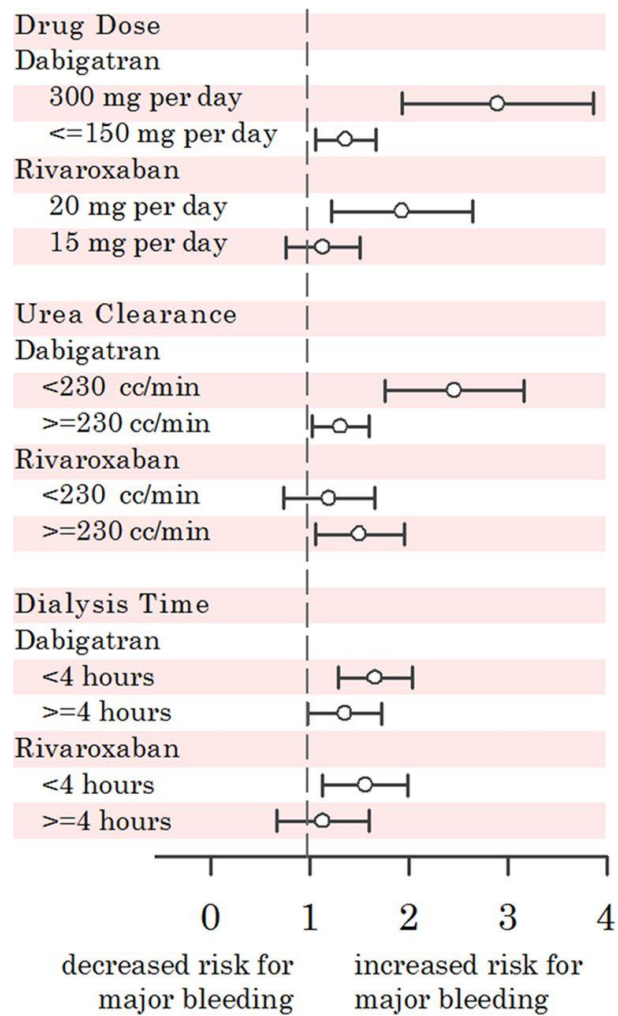
Epidemiology and Prevention

Dabigatran and Rivaroxaban Use in Atrial Fibrillation Patients on Hemodialysis

Kevin E. Chan, MD, MSc; Elazer R. Edelman, MD, PhD; Julia B. Wenger, MPH;
Ravi I. Thadhani, MD, MPH; Franklin W. Maddux, MD



Rate ratio of major bleeding with dabigatran and rivaroxaban when compared with warfarin, by drug dose, urea clearance, and dialysis time.



Kevin E. Chan et al. *Circulation*. 2015;131:972-979