

16th ANGIOPLASTY SUMMIT-TCTAP 2011
Seoul, Korea, April 27 – 29, 2011

Left Atrial Appendage Closure State of the Art

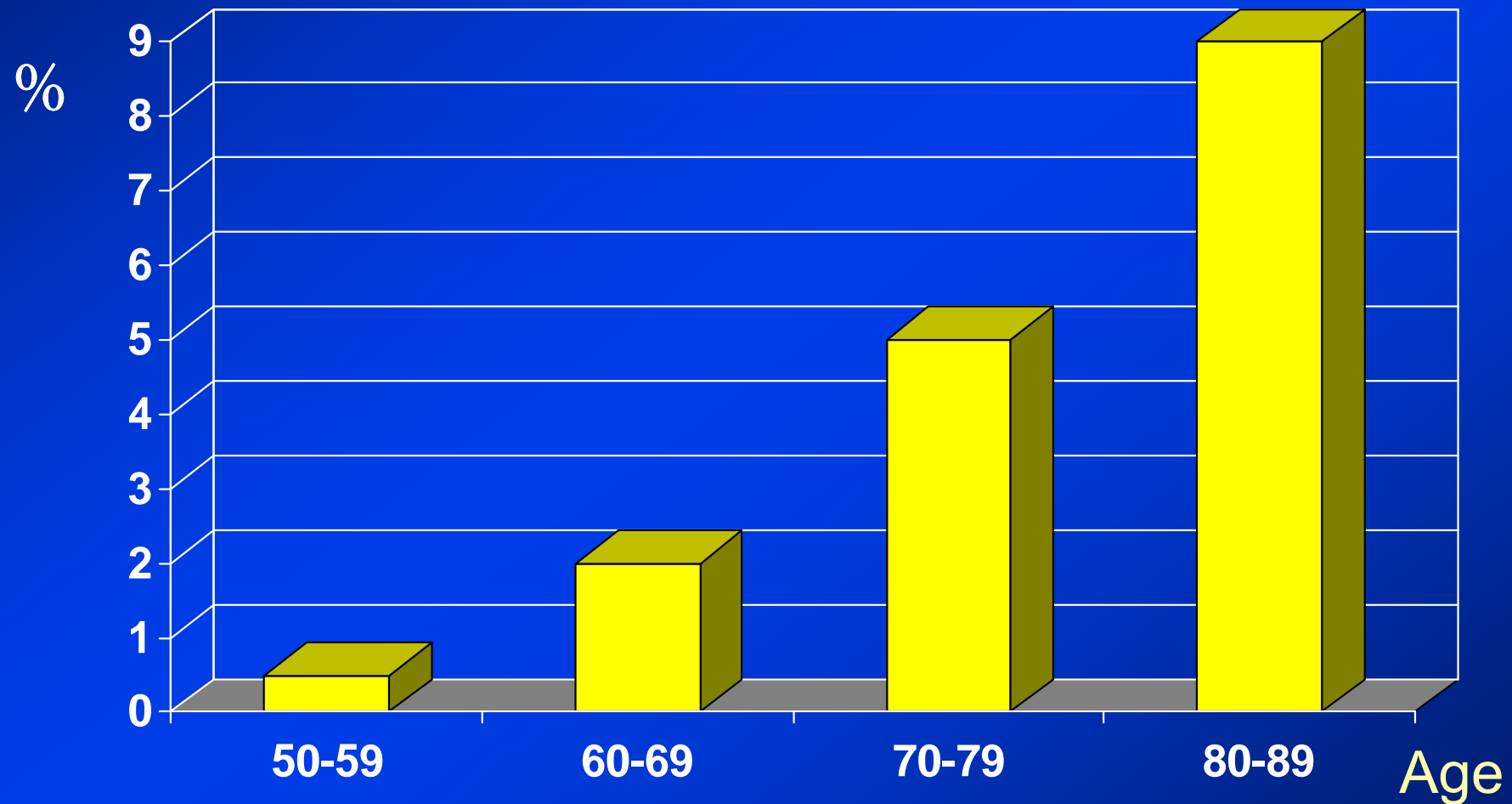
Horst Sievert, Nina Wunderlich,
Maik Gonzaga, Annkathrin Braut, Ilona Hofmann
CardioVascular Center Frankfurt
Frankfurt, Germany

Atrial Fibrillation is one of the Most Important Causes of Death/Stroke

- >15 % of all strokes are due to Atrial Fibrillation
- EU: > 3 mill. patients with AF
- > 1.5 million at high risk for stroke and require preventive therapy

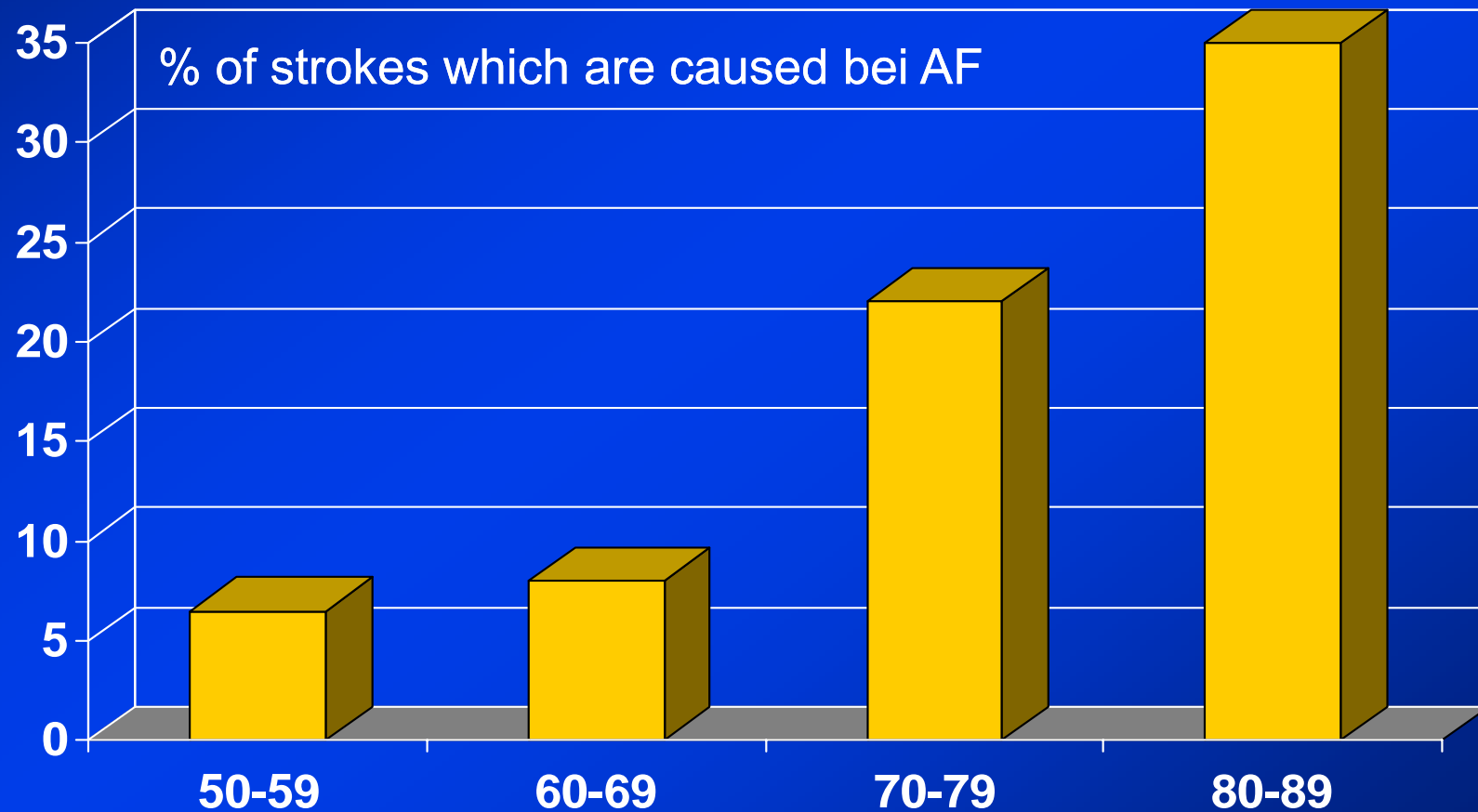
Prevalence of Atrial Fibrillation

Framingham Study, Wolf, 1991



Atrial fibrillation is one of the most important causes of stroke

Especially in elder patients



Framingham Study, Wolf, 1991

What is the stroke risk
in atrial fibrillation



Additional risk factors for an embolic stroke in atrial fibrillation

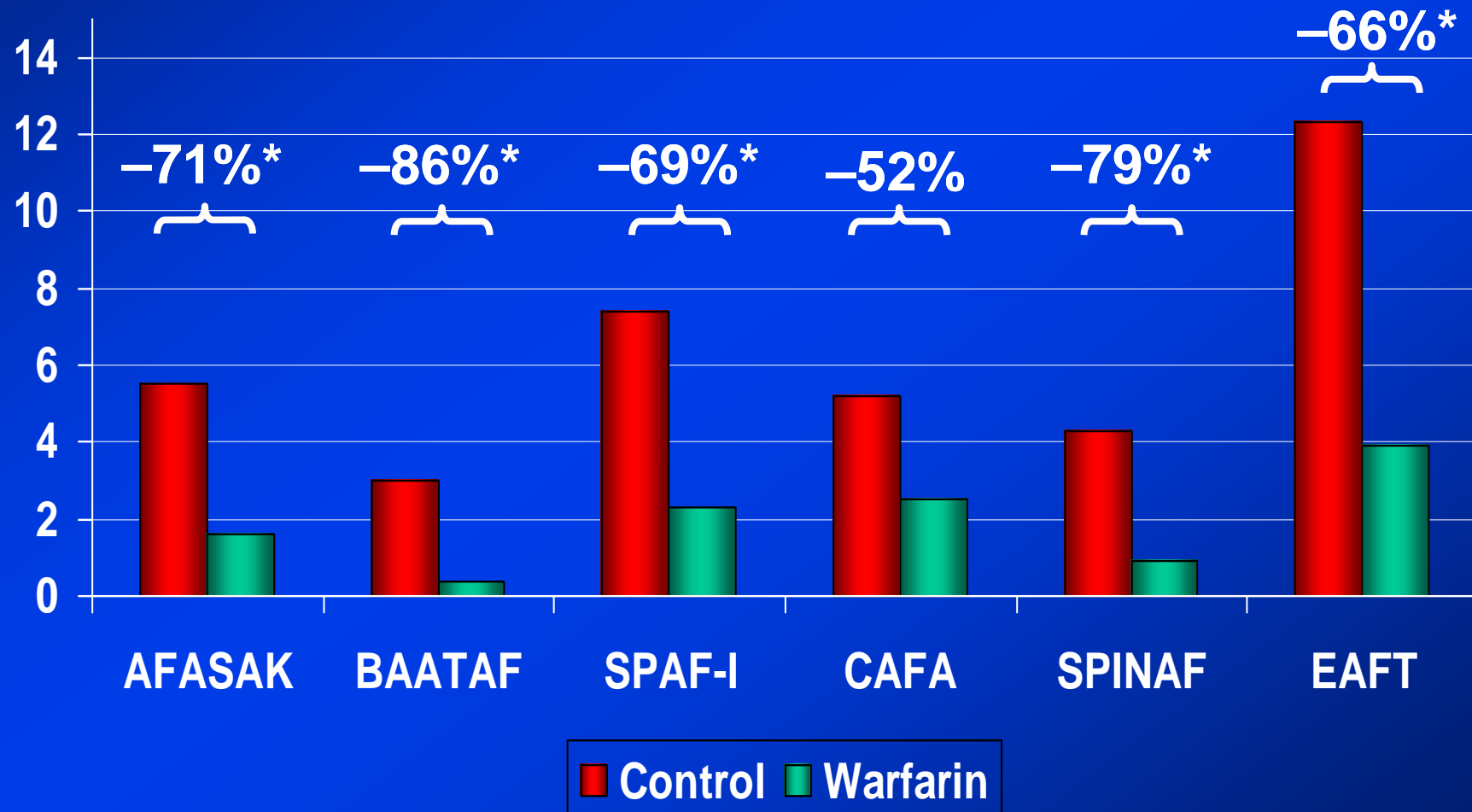
- Age >65
- Prior TIA / stroke
- Hypertension
- Diabetes
- Coronary heart disease
- Reduced LV function
- LAA flow velocity <20 cm/sec
- Spontaneous LAA echo contrast

What is the Annual Risk of Stroke?

Nat. Registry of AF: CHADS₂

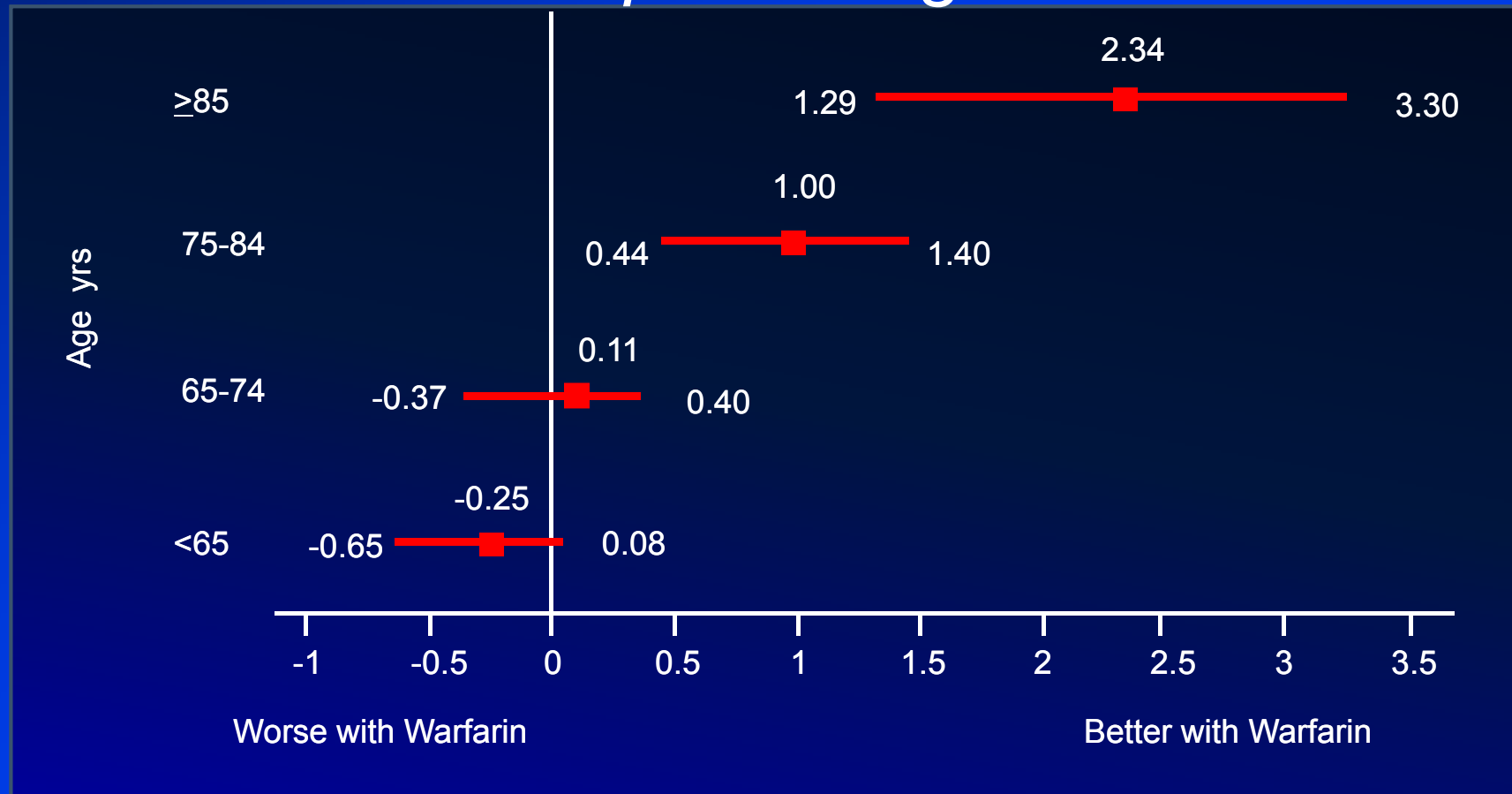
CHADS Score	# Pts n=1773	# Strokes n=94	NRAF adjusted Stroke Rate (95% CI)
0	120	2	1.9 (1.2-3.0)
1	463	17	2.8 (2.0-3.8)
2	523	23	4.0 (3.1-5.1)
3	337	25	5.9 (4.6-7.3)
4	220	19	8.5 (6.3-11.1)
5	65	6	12.5 (8.2-17.5)
6	5	2	18.2 (10.5-27.4)

Randomized Clinical Trials of Coumadin in Atrial Fibrillation



* $p < 0.05$

Warfarin Net Clinical Benefit: *Impact of Age*



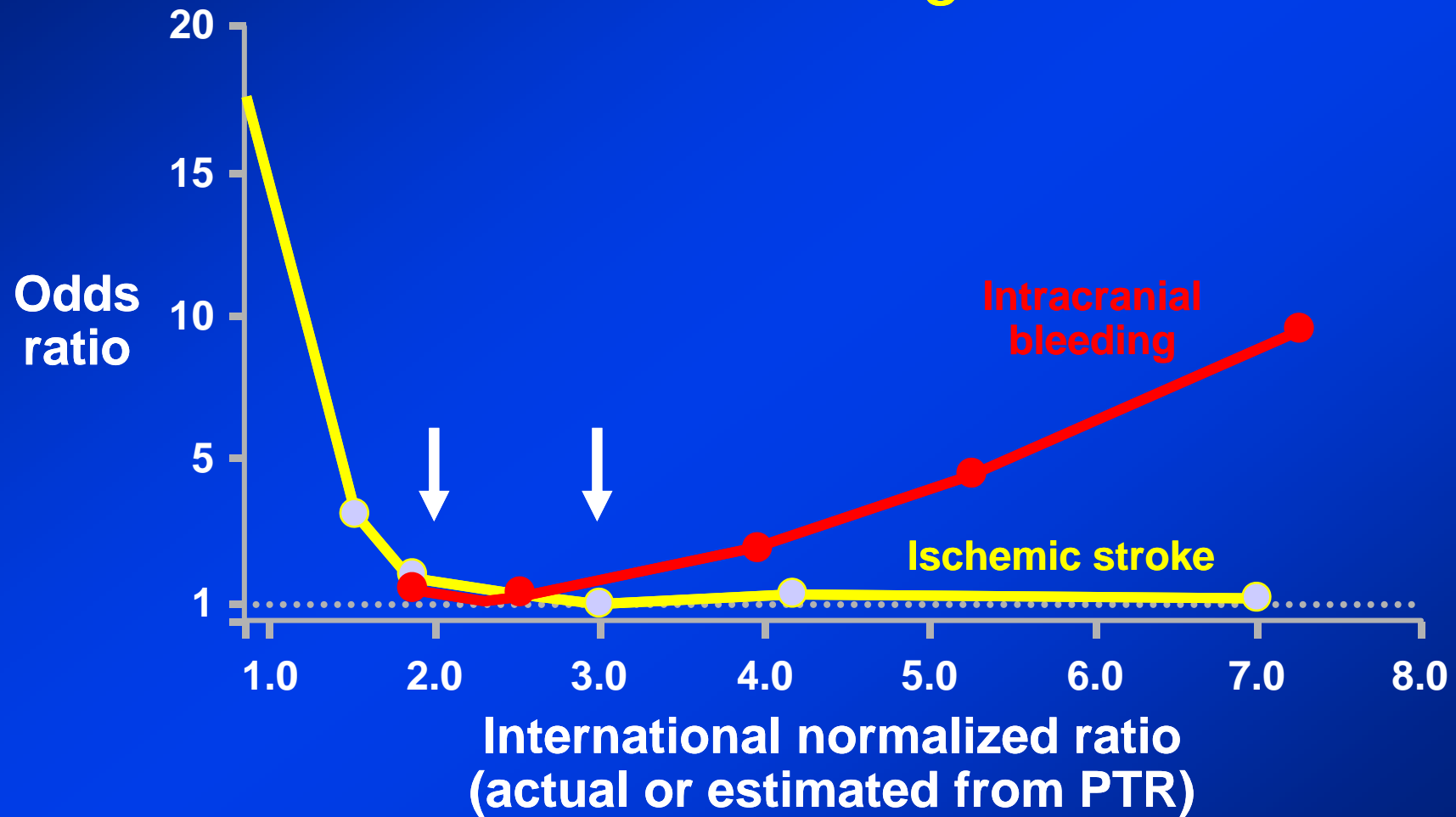
Net Clinical Benefit, Events Prevented per 100 Person – Years

Singer D, Ann Int Med. 2009; 2009;151:297-305

Almost nobody can
take Coumadin on the
long term

- Any localized or general physical condition in which the hazard of hemorrhage might be greater than the potential clinical benefits of anticoagulation
- Any personal circumstance in which the hazard of hemorrhage might be greater than the potential clinical benefits of anticoagulation
- Pregnancy
- Hemorrhagic tendencies
- Blood dyscrasias.
- Recent or contemplated surgery of central nervous system
- Recent or contemplated surgery of the eye
- Recent or contemplated traumatic surgery resulting in large open surfaces
- Gastrointestinal bleeding
- Genitourinary tract bleeding
- Respiratory tract bleeding
- Cerebrovascular hemorrhage
- Cerebral aneurysms
- Dissecting aorta
- Pericarditis
- Pericardial effusions
- Bacterial endocarditis
- Threatened abortion
- Eclampsia
- Preeclampsia
- Inadequate laboratory facilities
- Unsupervised patients
- Senility
- Alcoholism
- Psychosis
- Lack of patient cooperation
- Spinal puncture
- Other diagnostic procedures with potential for uncontrollable bleeding
- Therapeutic procedures with potential for uncontrollable bleeding
- Major regional anesthesia
- Lumbar block anesthesia
- Malignant hypertension

Effect of Intensity of Anticoagulation on Stroke and Bleeding in AF

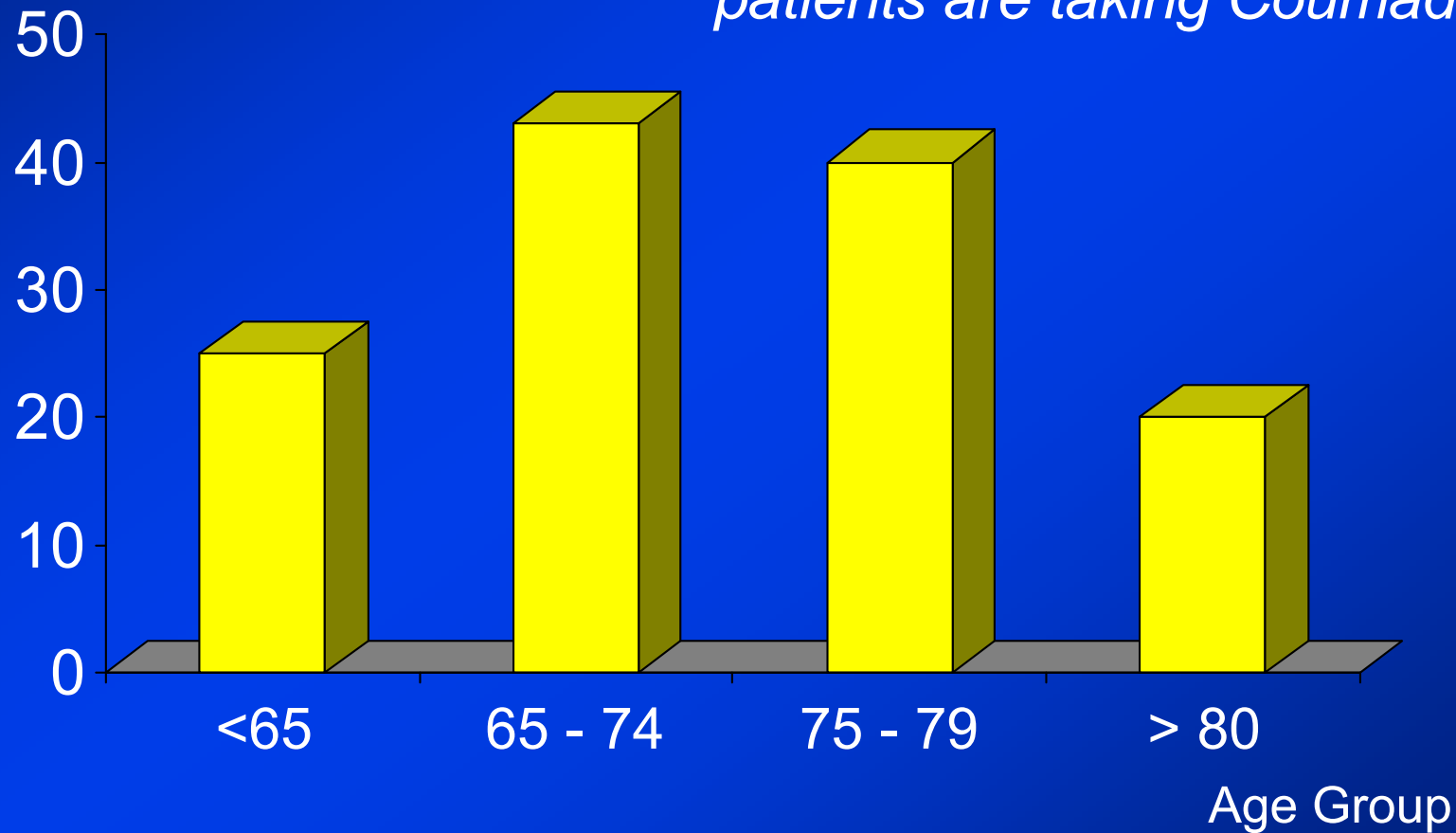


Hylek EM and Singer DE: Ann Intern Med 120:897, 1994

Hylek EM et al: N Engl J Med 335:540, 1996

Anticoagulation Underuse

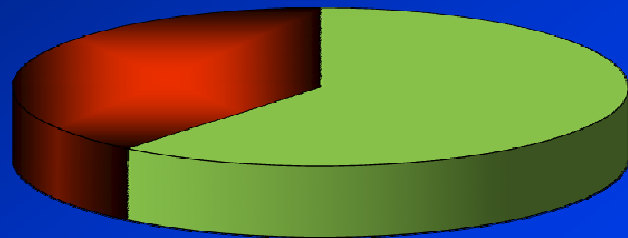
Only about 1/3 of all eligible patients are taking Coumadin



Stafford and Singer, Arch Int Med, 1996

Management of AF in Clinical Practice

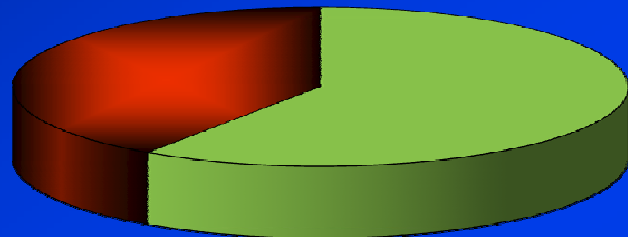
Prescription of Anticoagulation



n = 23,657

Medicare cohort, USA

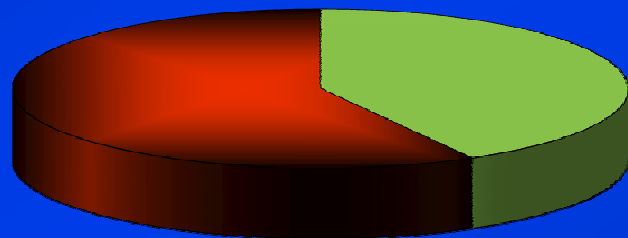
Birman-Deych E, et al. Stroke 2006;37:1070



n = 5,333

EuroHeart survey

Nieuwlaat, R et al. Eur Heart J 2005;29:1181



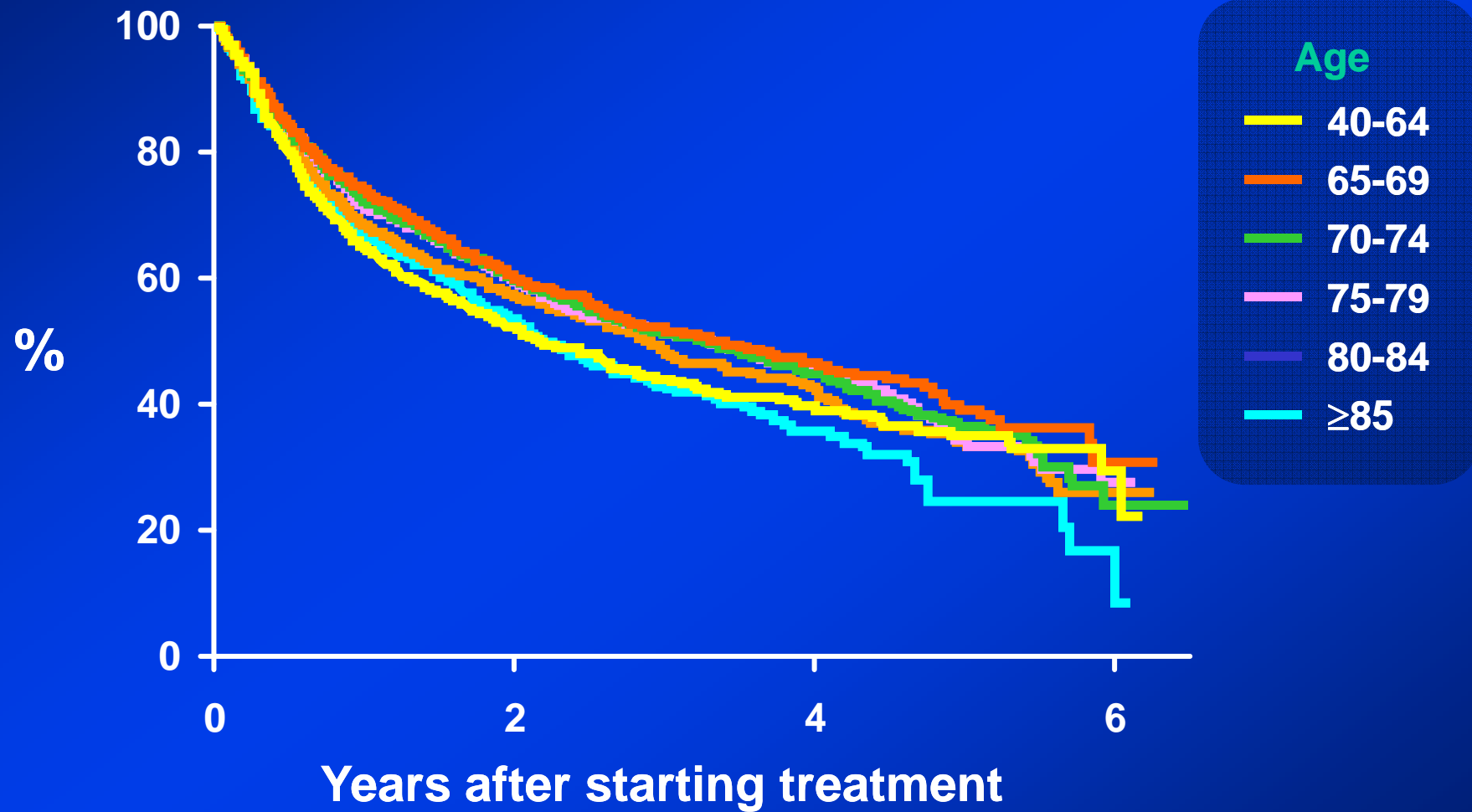
n = 11,379

ATRIA cohort (managed care system, California, USA)

Go AS, et al. JAMA 2003;290:2685

■ No Anticoagulation
■ Vitamin K antagonists

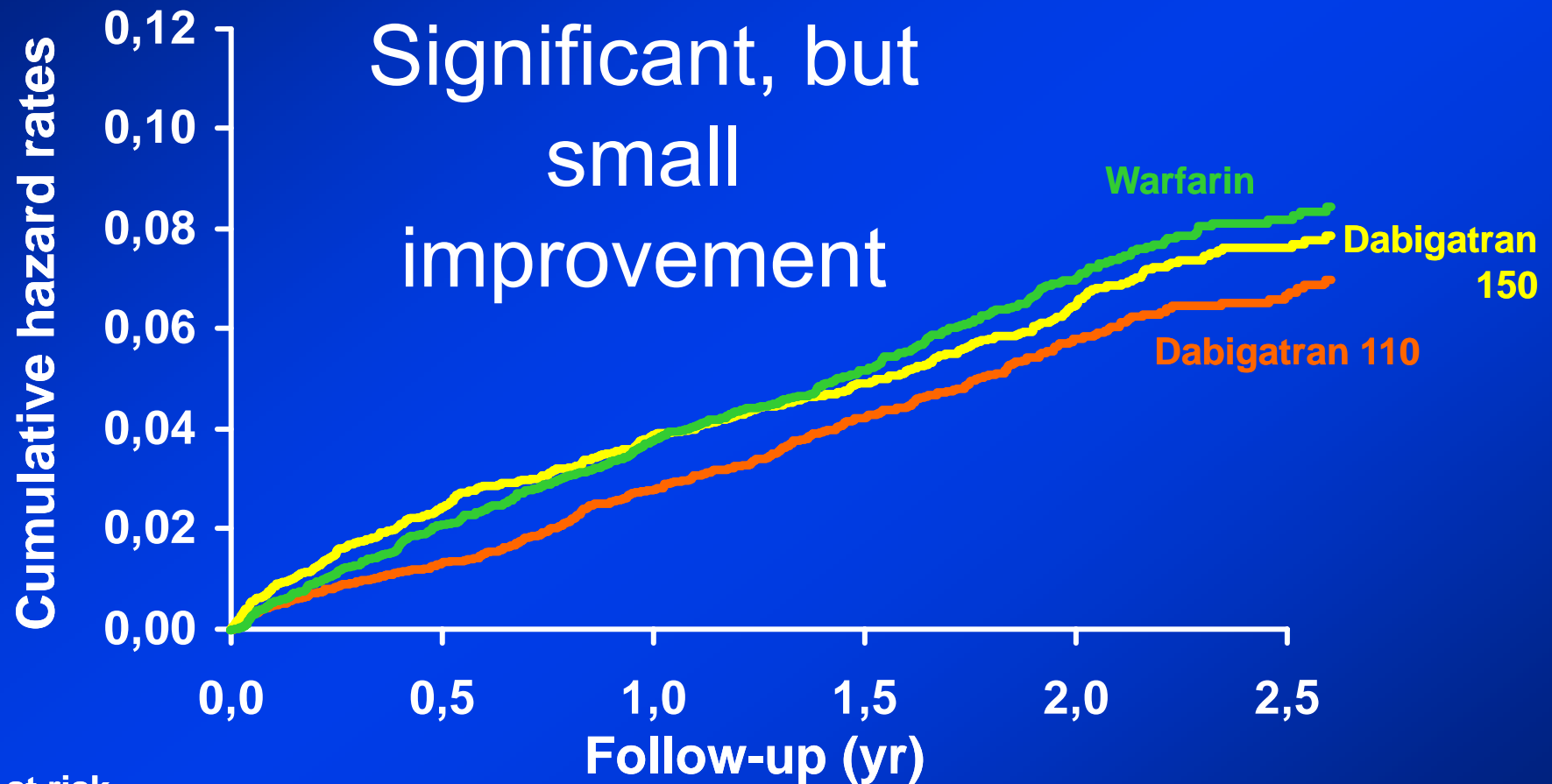
Anticoagulation Use in General Practice Discontinuation



Gallagher AM et al: J Thromb Haemost 6:1500, 2008

Other drugs?

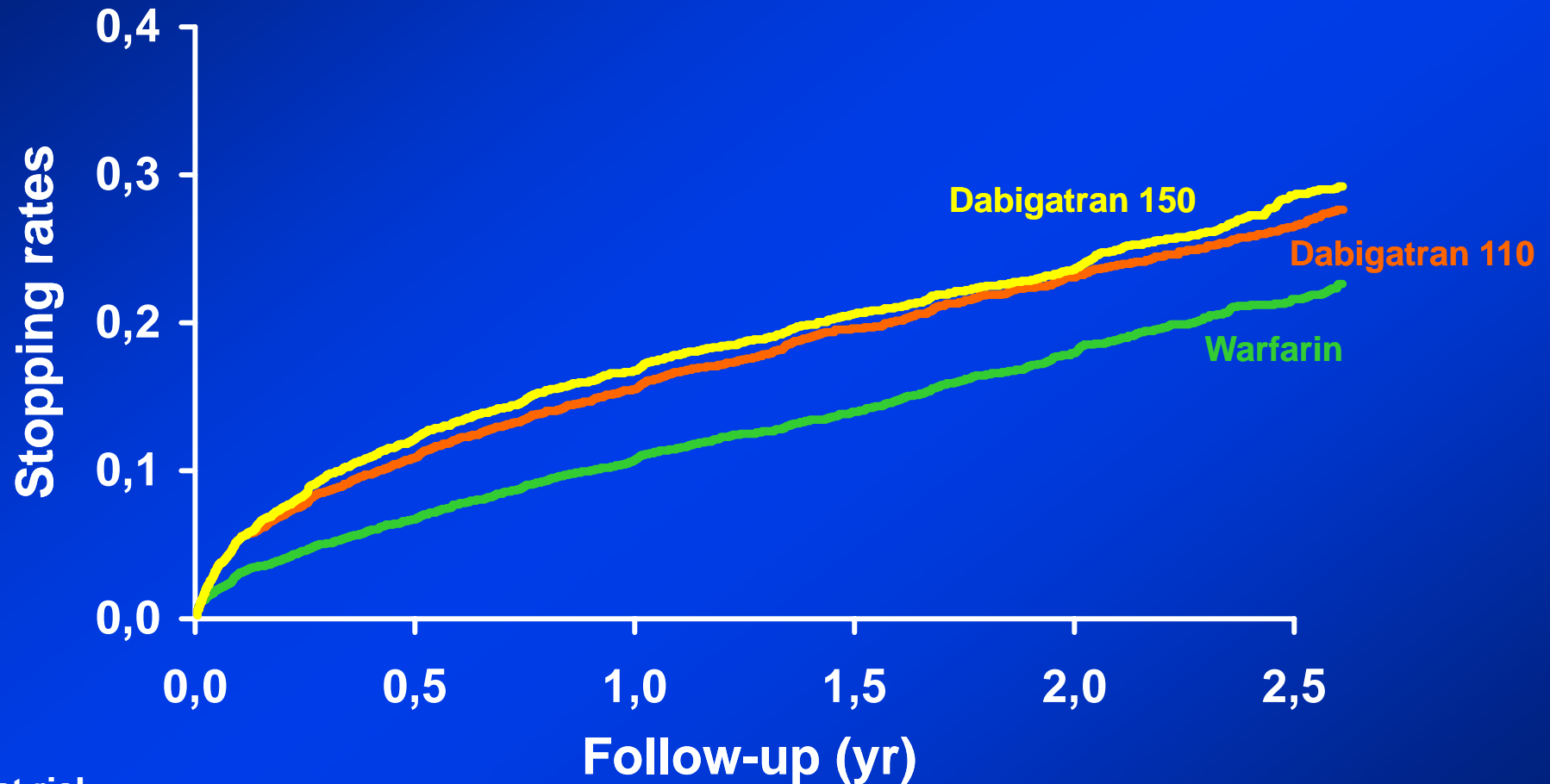
Dabigatran - Major Bleeding



No. at risk

—	6,015	5,835	5,640	4,510	2,872	1,349
—	6,076	5,839	5,638	4,557	2,928	1,366
—	6,022	5,801	5,600	4,474	2,797	1,269

Dabigatran Permanent Discontinuation



No. at risk

—	6,015	5,336	5,026	3,950	2,491	1,176
—	6,076	5,329	5,015	3,955	2,528	1,172
—	6,022	5,563	5,269	4,158	2,561	1,187

Dabigatran

- NNT 357
- 1.3 million US \$ to prevent 1 stroke

All Antigoagulants

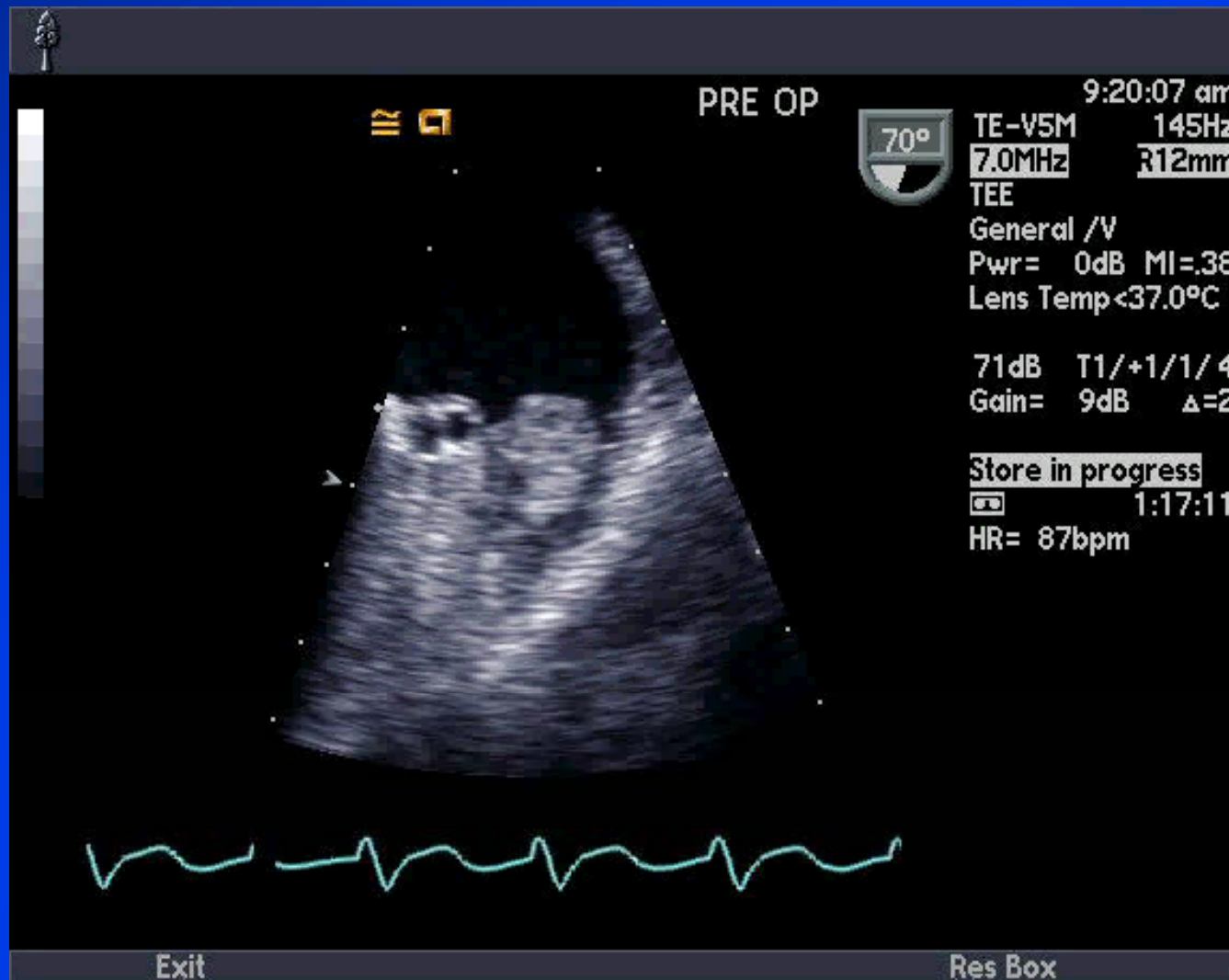
- Per definition
 - have to be given lifelong
 - have a bleeding risk
- Bleeding risk increases with age
- At some point Anticoagulants have to be stopped
- What does that mean in clinical practice?
 - You should avoid anticoagulants in elderly patients because of higher bleeding risk
 - You should avoid anticoagulants in younger patients because they would have to take it for a longer time period

Where do
the thrombi arise ?

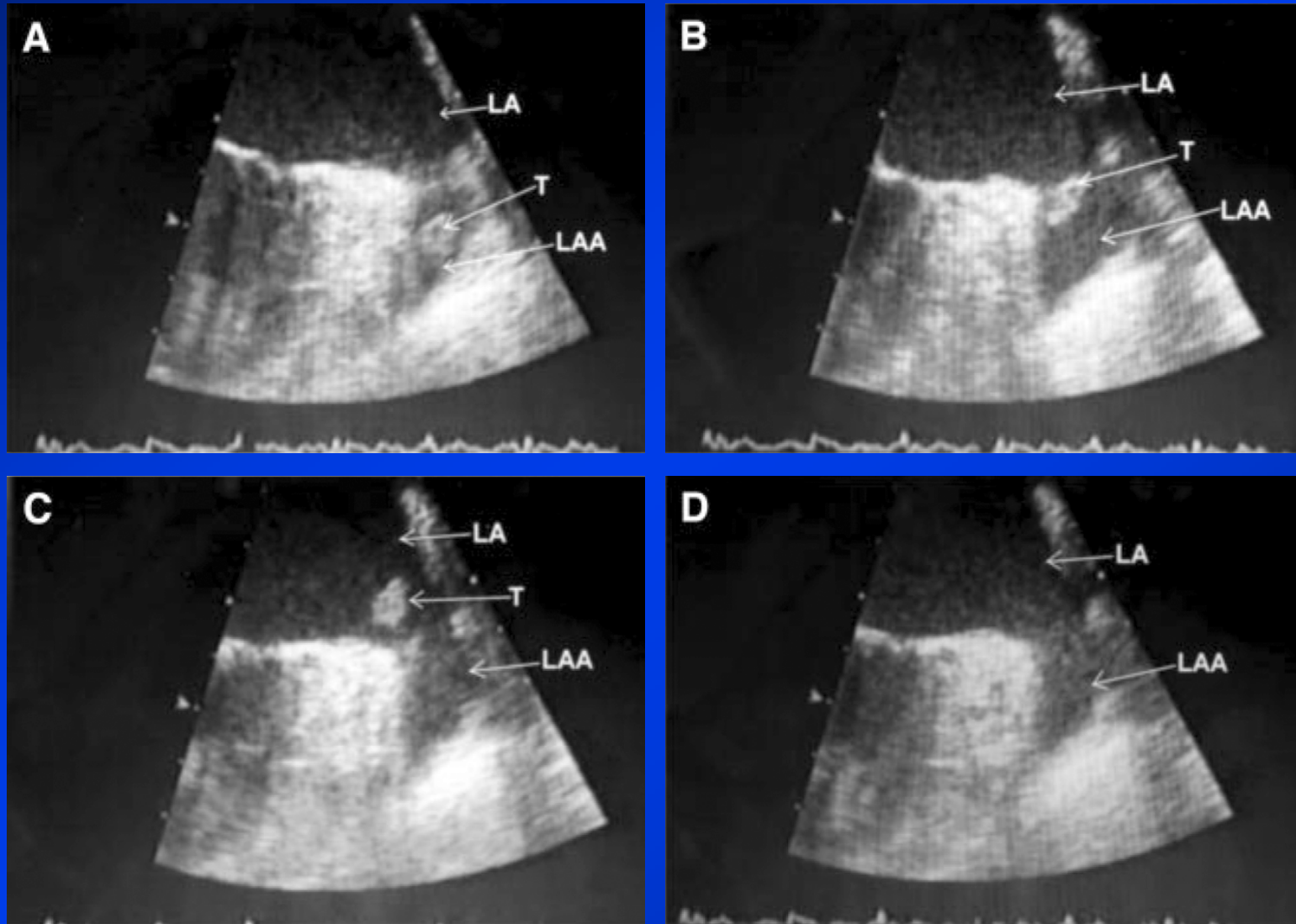
Thrombus in the left atrial appendage



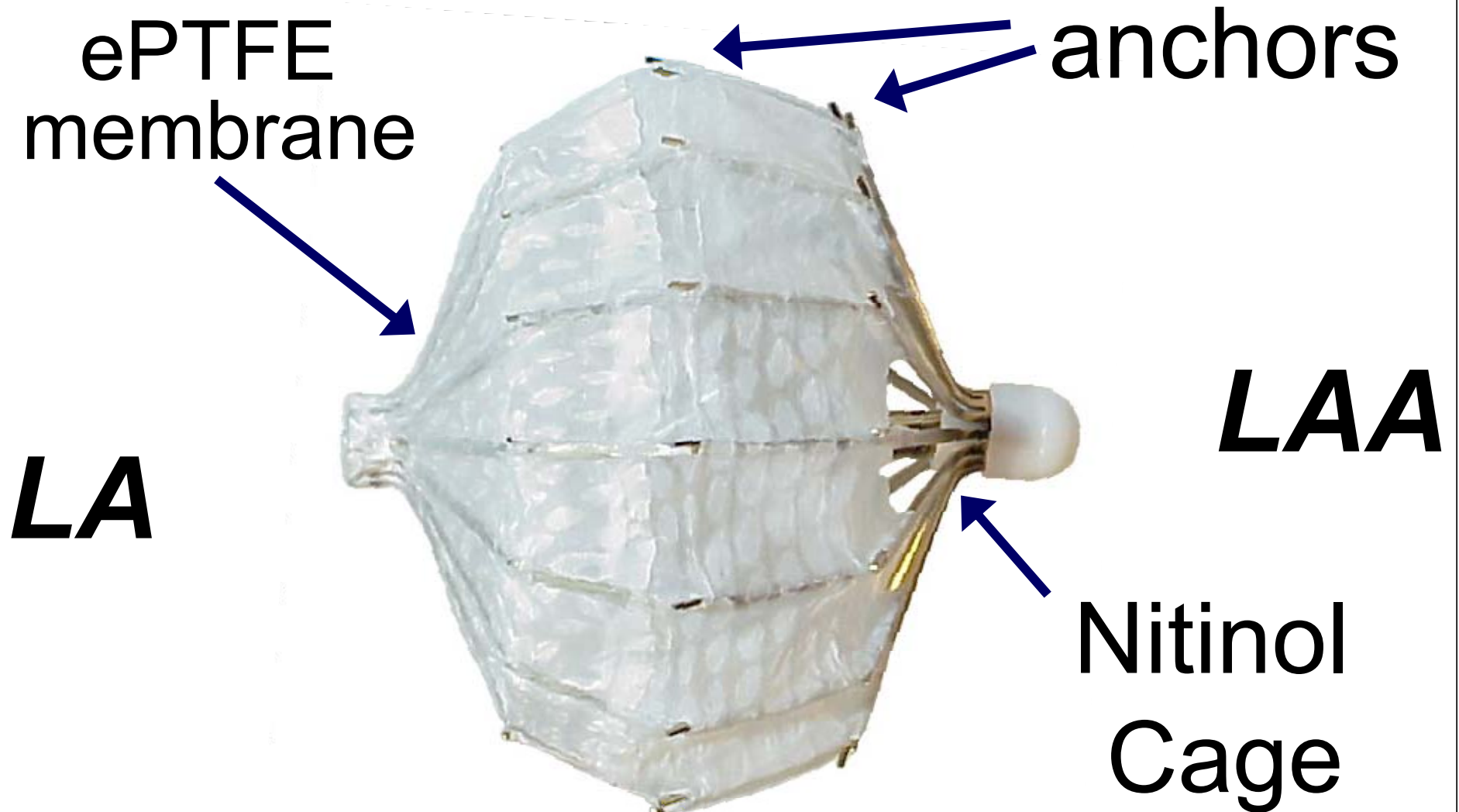
Thrombus in the LAA



Disappearing LAA Thrombus Resulting in Stroke



PLAATO™ Device

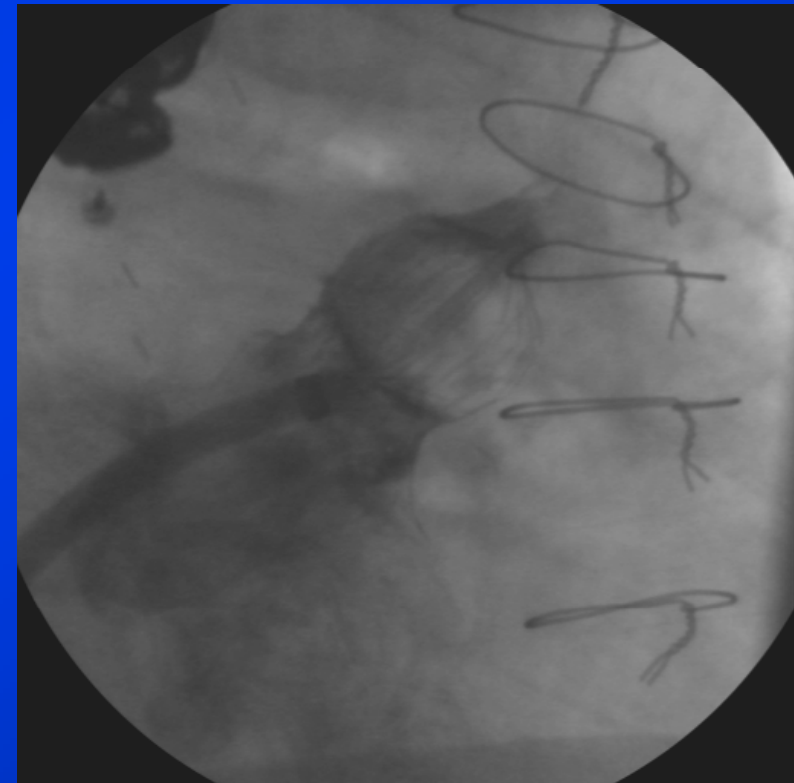


The first patient who underwent successful closure of the LAA

- Aug 30, 2001
- A.S., 72 y/o, male
- AF since 2 years
- Multiple contraindications for coumadin
- Very unstable INR
- CHADS score 3



First successful attempt of LAA closure



- Procedure time 85 min
- Complete seal
- No complications
- Coumadin off since 2001
- No neurological events
- Participated in other FIM trials
- Had his 80th birthday in Jan 2009

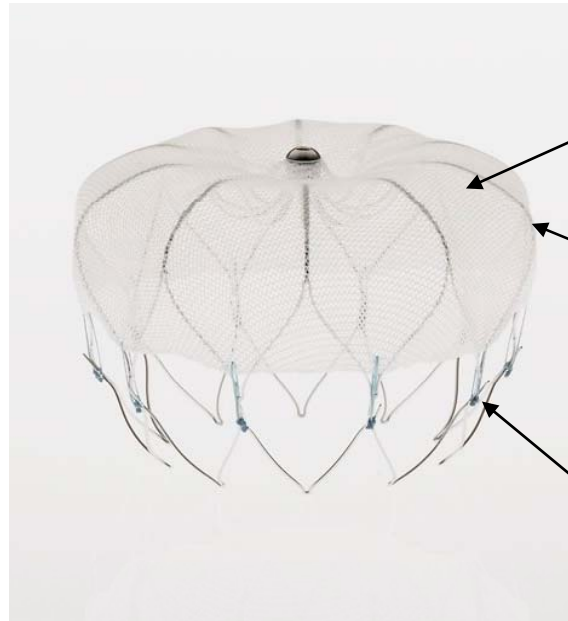
Watchman Device



- Nitinol frame
- PET membrane
- row of fixation barbs around the mid perimeter
- 21, 24, 27, 30, 33 mm

CE mark

WATCHMAN Device – Current vs Gen 4*

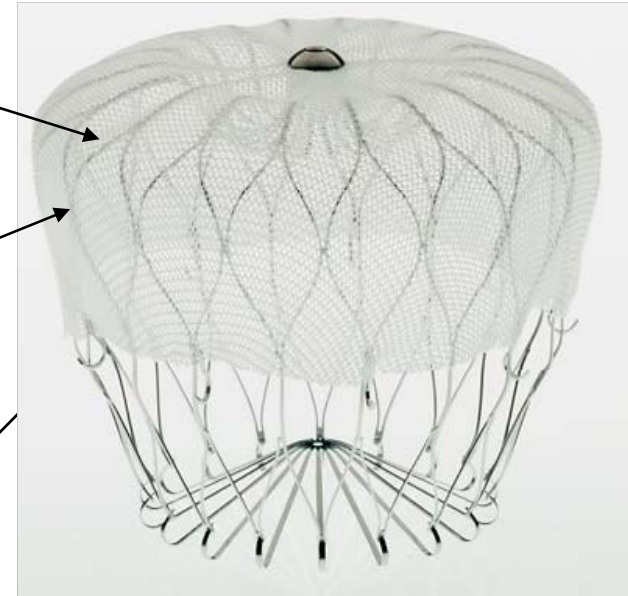


21, 24, 27, 39, 33 mm
(diameter)
10 cells
Oversize 8 – 20%
Fixation barbs (allow recapture)

160 μ PET
Fabric

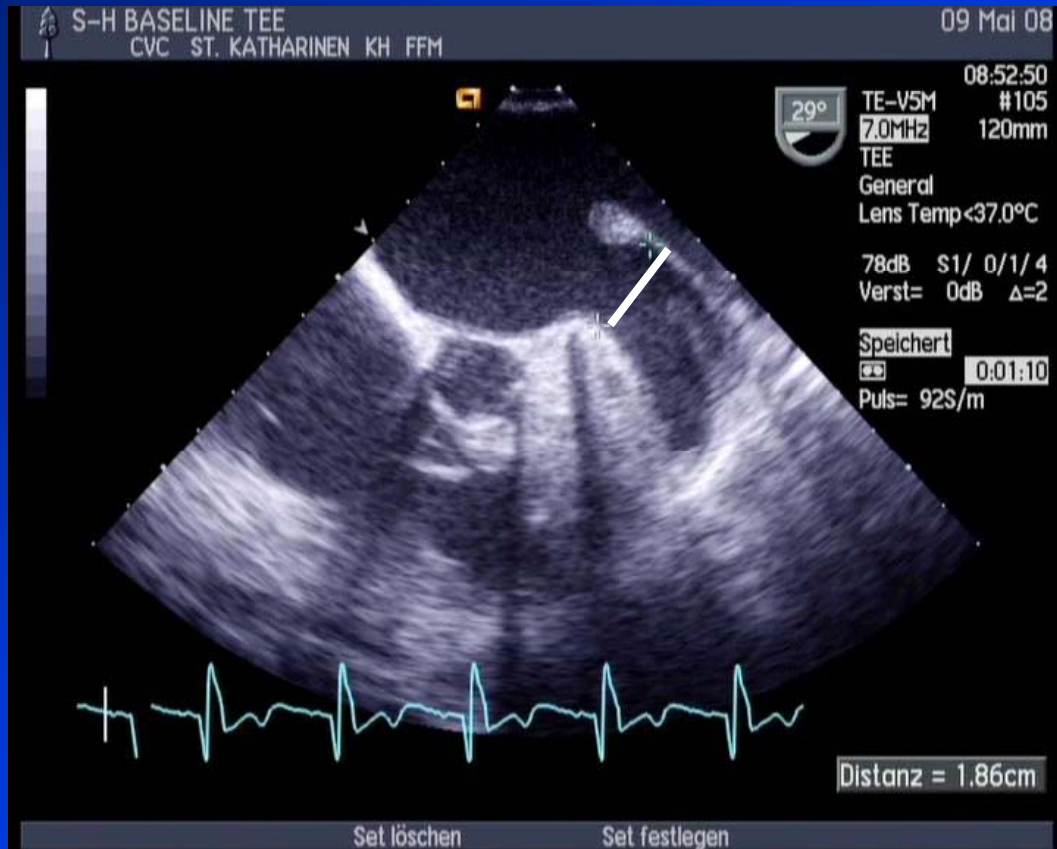
Nitinol
Frame

Barbs

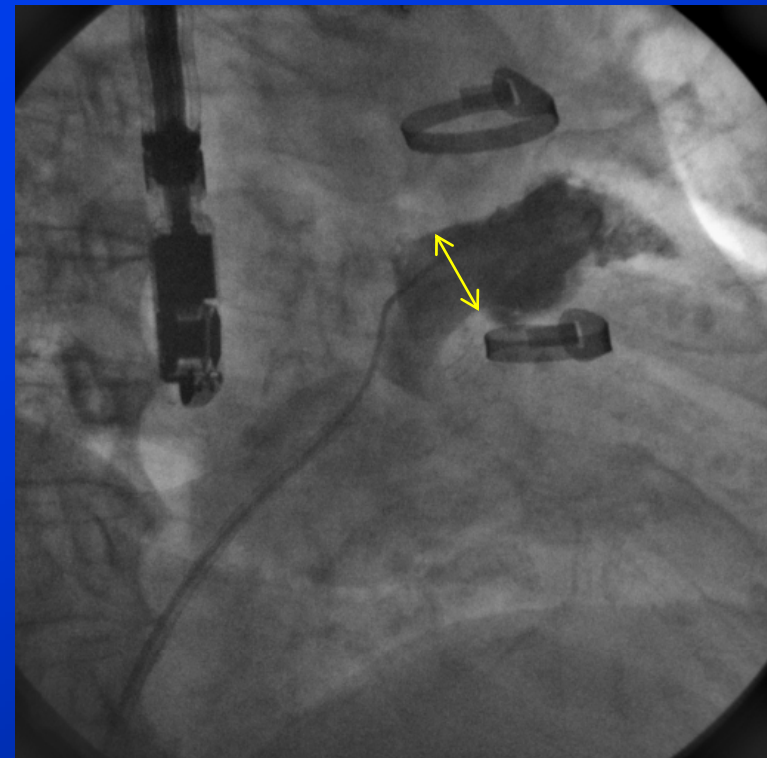


22, 26, 31 mm (diameter)
18 cells
Oversize 7 – 28%
Bumper Stabilizer
Prolapsed fixation barbs (allow
multiple full recaptures and
redeployments)

Watchman Implantation



- LAA diameter in TEE
19 mm



- anatomy of LAA in TEE
and fluoro

Watchman Implantation

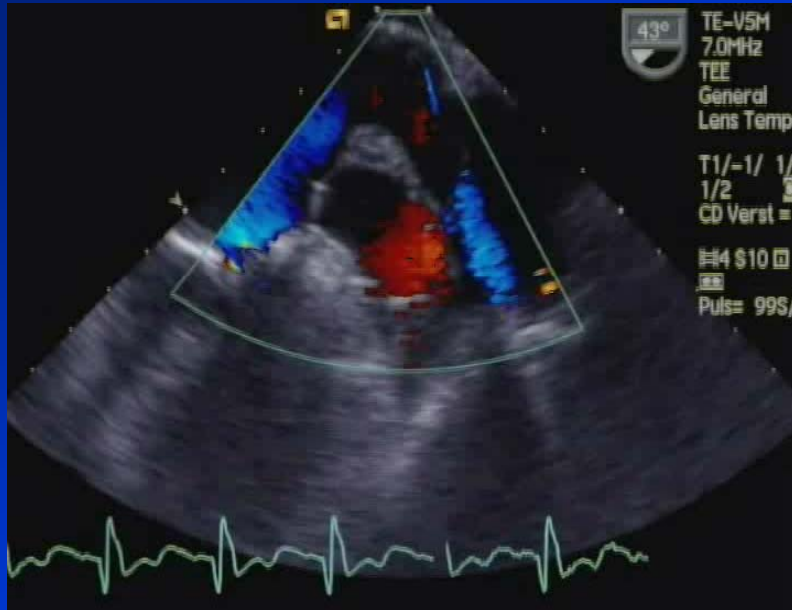
Maximum measured LAA ostium (mm)	Implant diameter (mm)
17 - 19.5	21
20 - 22.9	24
23 - 25.9	27
26 - 28.9	30
29 - 31.9	33



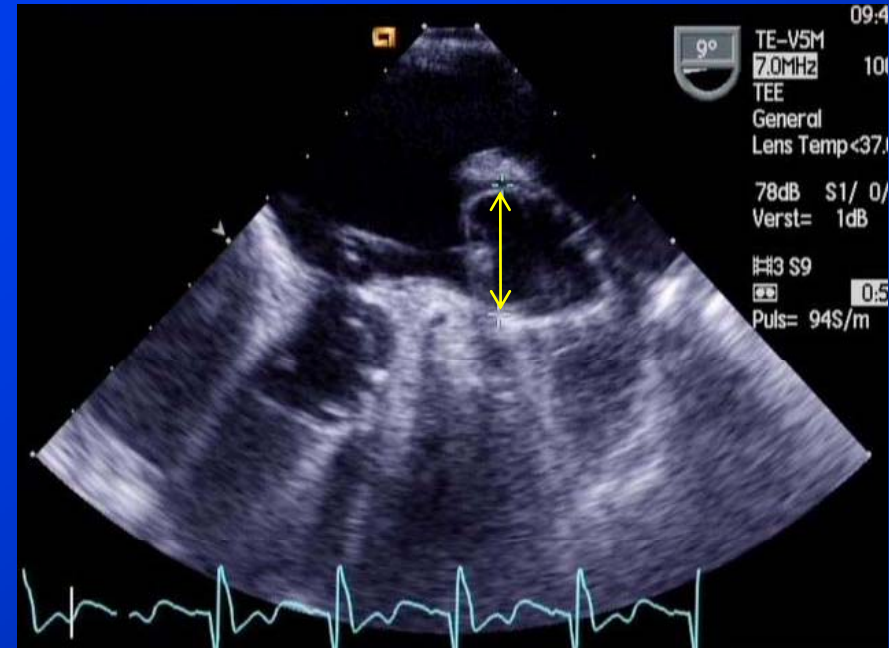
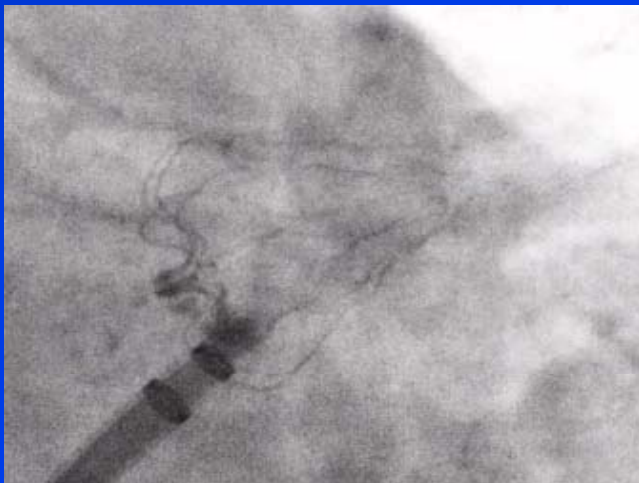
- device selection according to measurements

- Implantation of 21mm Watchman Occluder

Watchman Implantation



- Check position
- Check device compression
- Check residual flow
- Tug test
- Release

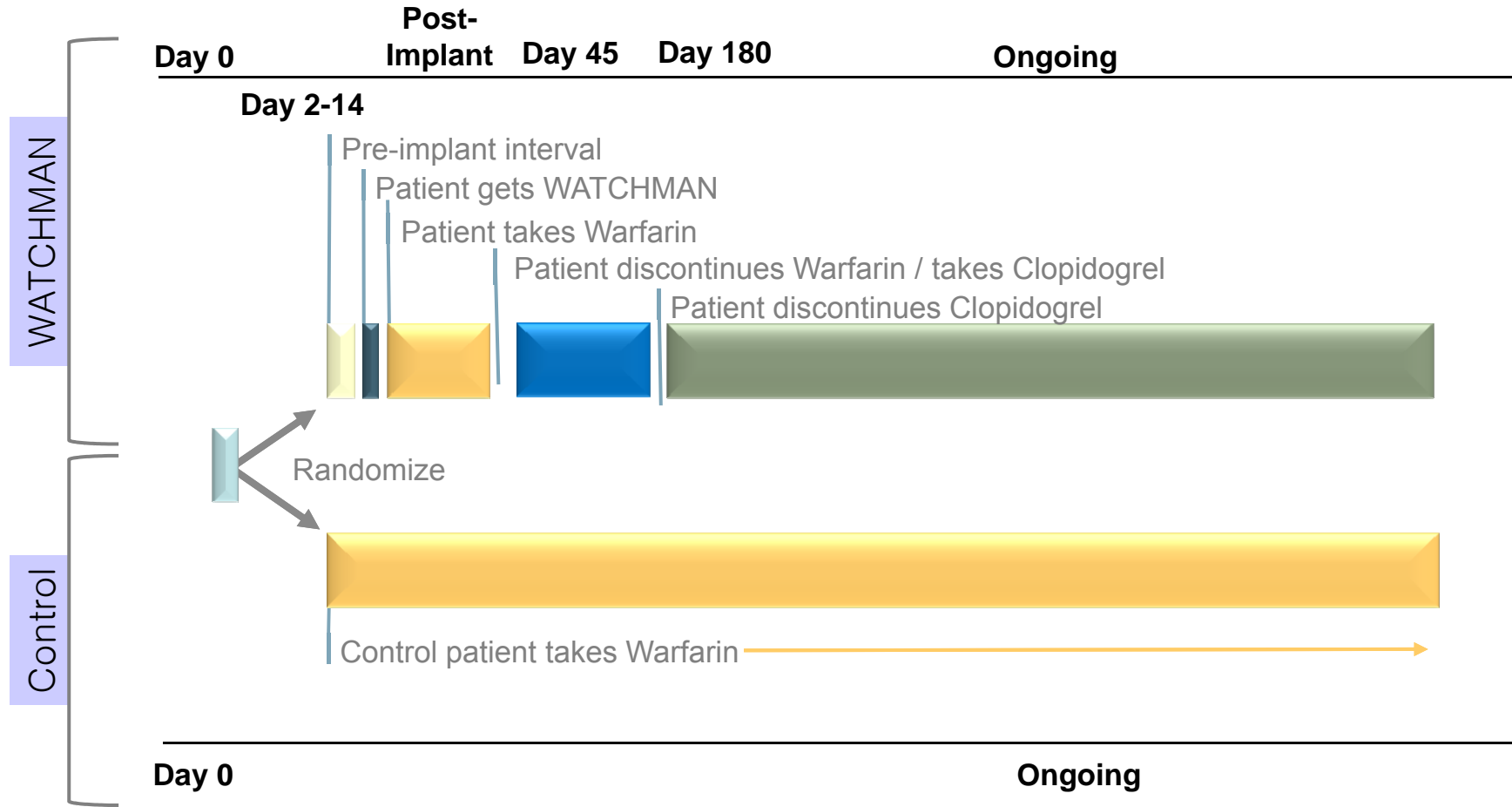


Protect AF

(System for Embolic PROTECTION
in Patients with Atrial Fibrillation)

- Multicenter
- Prospective randomized
- WATCHMAN vs coumadin 2:1
- Non-inferiority trial
- 800 pts (enrollment closed June 2008)
- > 900 patient-years

Patient Study Timeline



In- & Exclusion

Major inclusion criteria

- Non valvular AF with Chads2 score ≥ 1
- No contraindications to coumadin
- No co-morbidities mandating chronic warfarin use other than AF

Major exclusion criteria

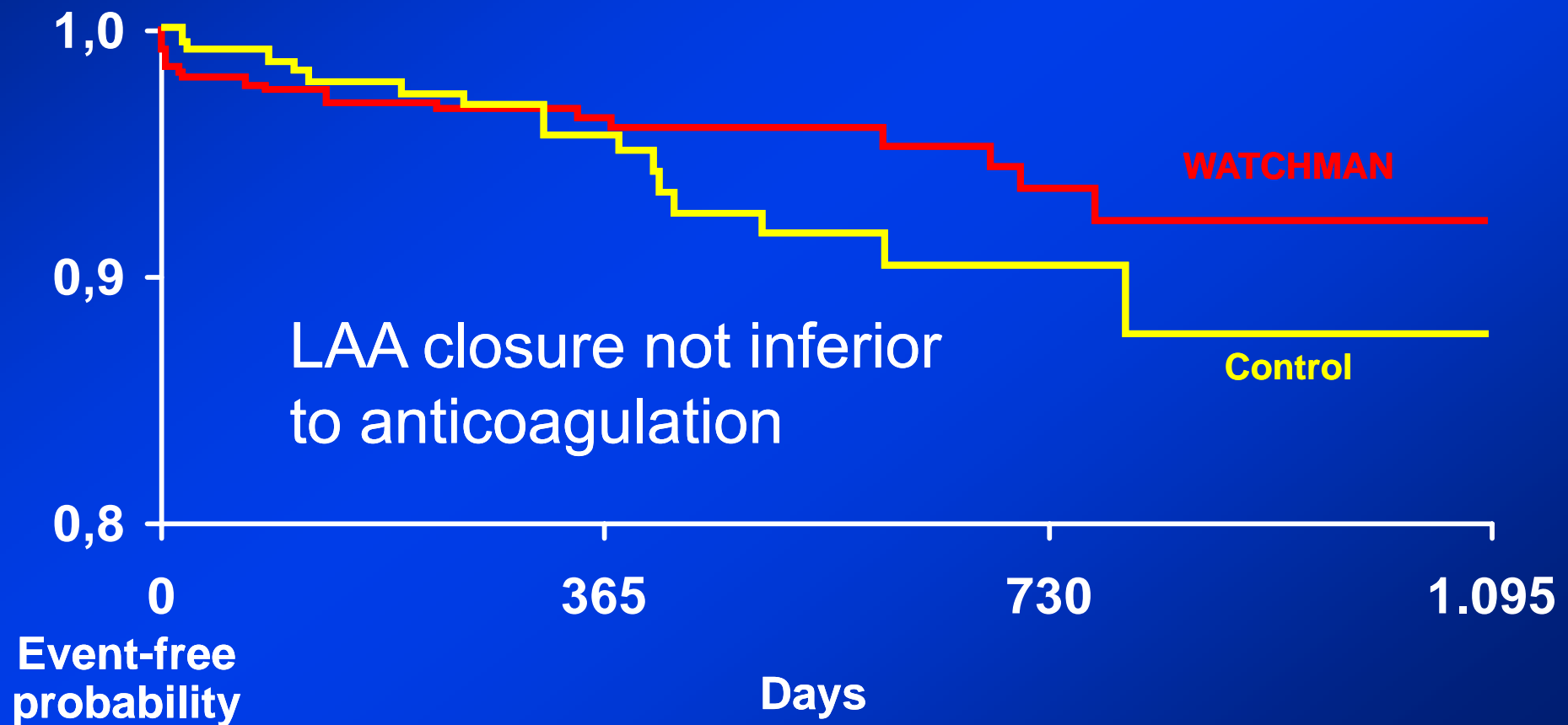
- LAA thrombus
- Large PFO with significant atrial septal aneurysm
- Mobile aortic atheroma
- Symptomatic carotid artery disease

PROTECT AF Trial Endpoints

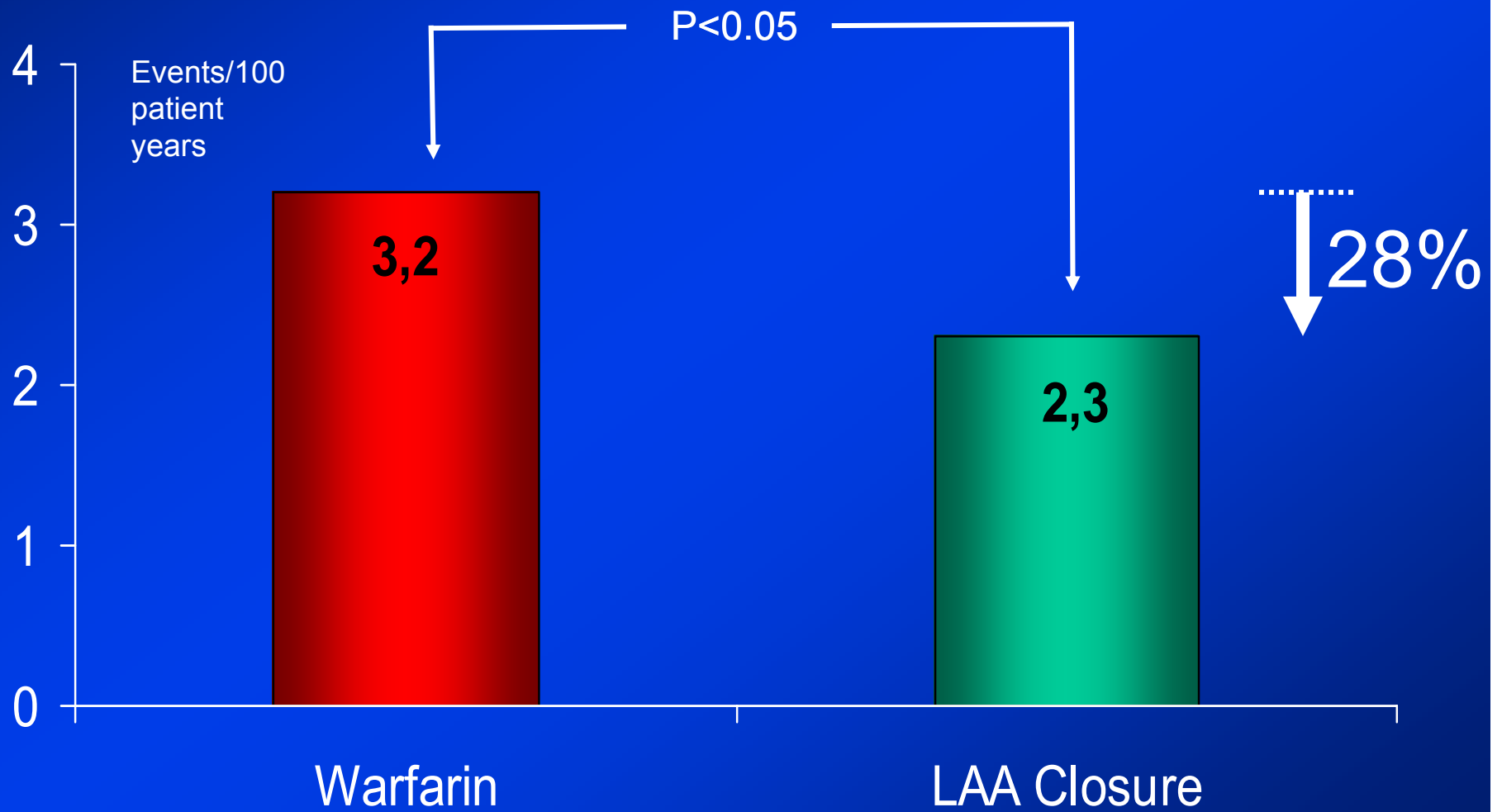
- Primary Efficacy Endpoint
 - All stroke
 - Cardiovascular and unexplained death
 - Systemic embolization
- Primary Safety Endpoint
 - Device embolization requiring retrieval
 - Pericardial effusion requiring intervention
 - Cranial bleeds and gastrointestinal bleeds
 - Any bleed that requires ≥ 2 uPRBC

Primary Efficacy Endpoint

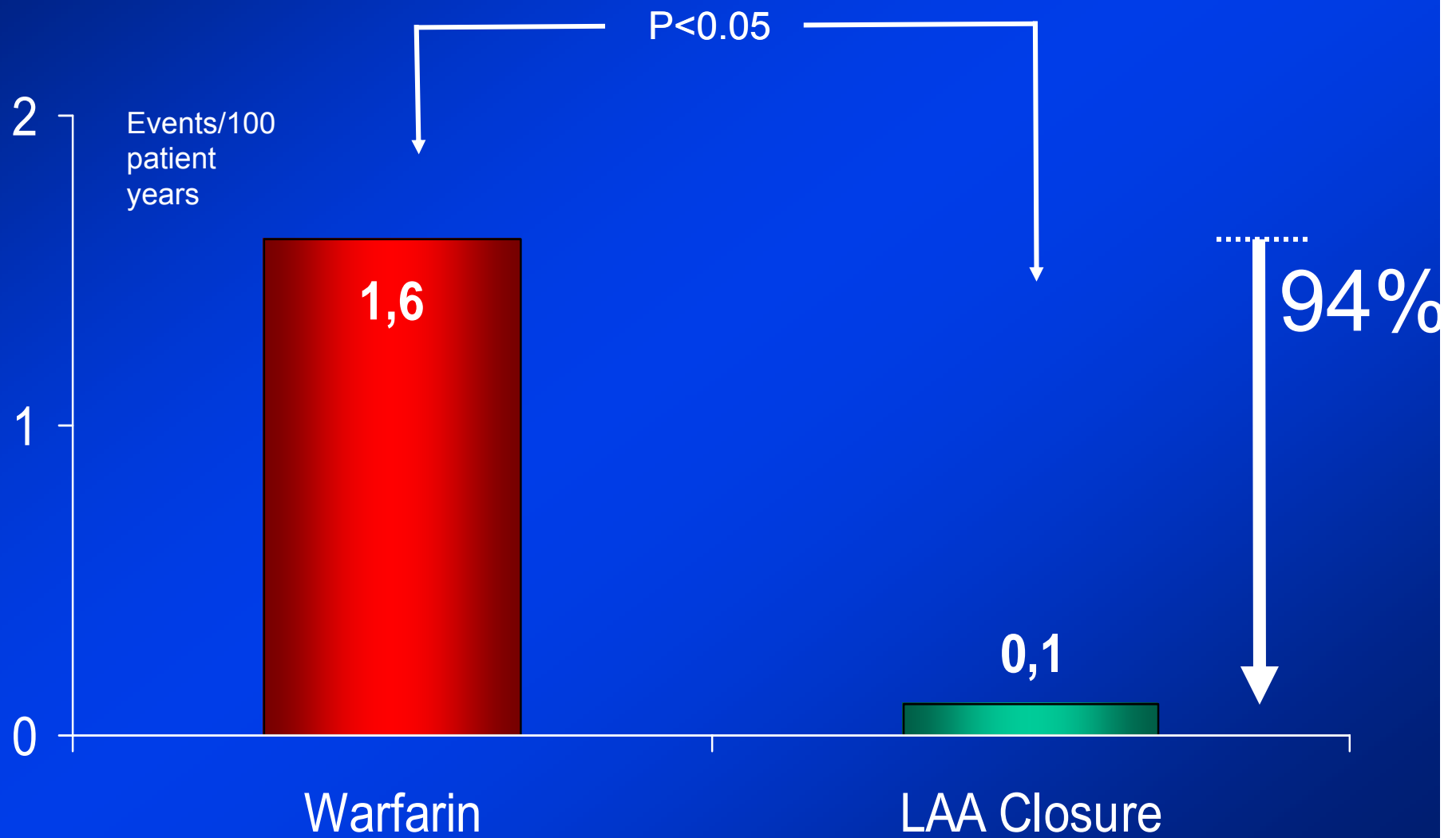
Freedom from Stroke, Death, Systemic Embolization



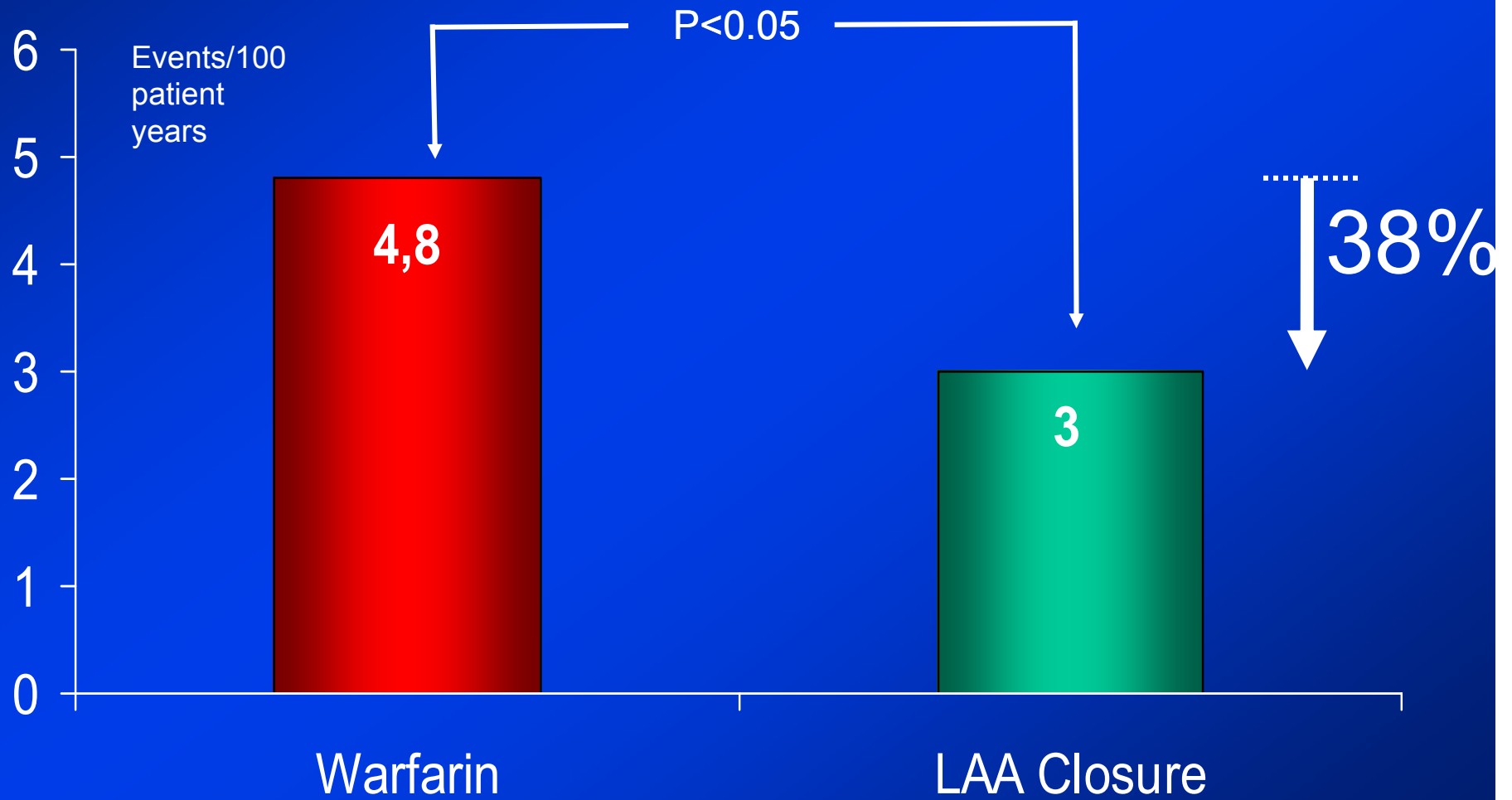
All Stroke



Hemorrhagic Stroke

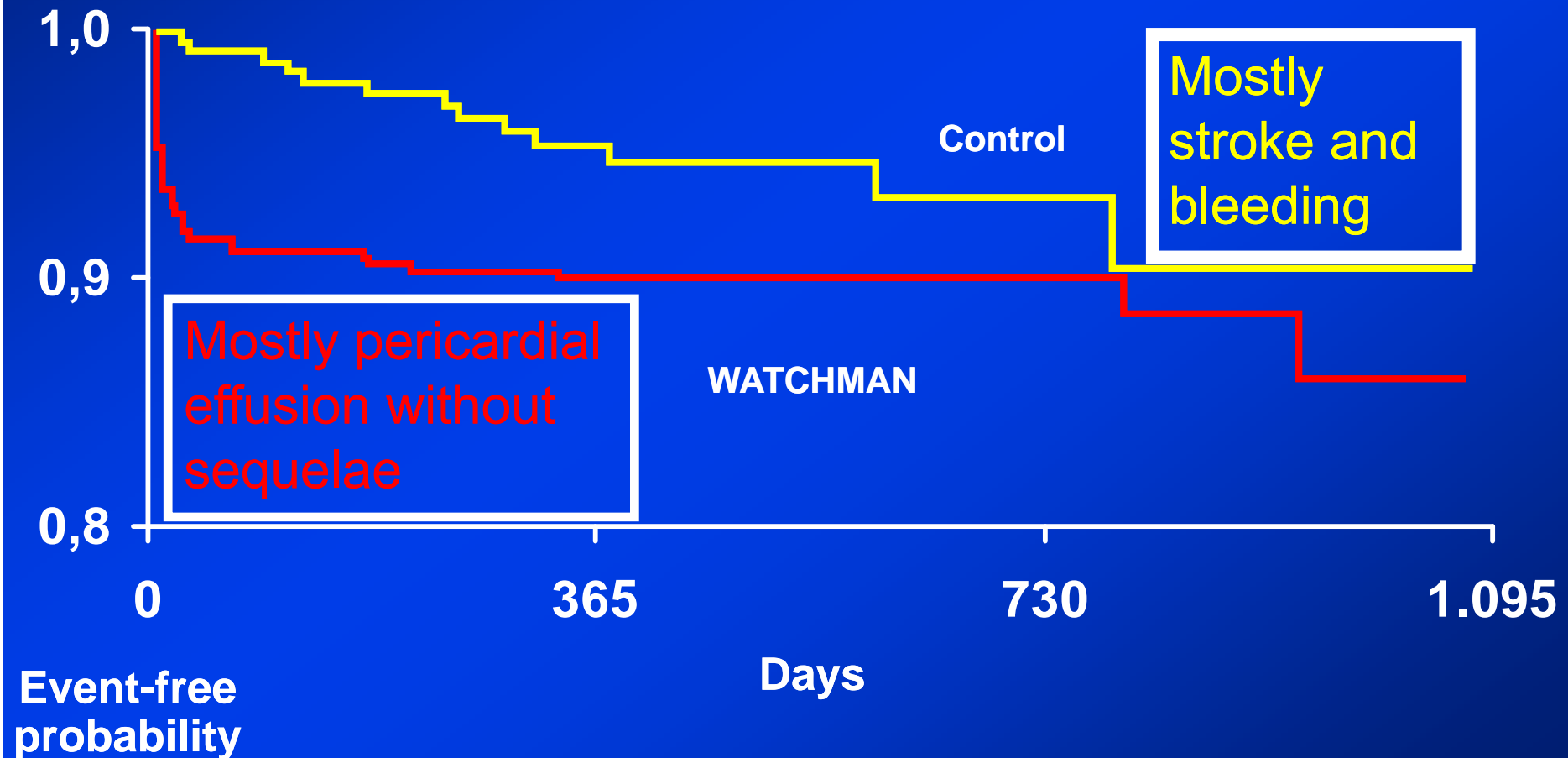


Mortality



Safety

Freedom from device embolization, pericardial effusion, Severe bleeding



Performance Metrics PROTECT AF vs CAP

	PROTECT AF	PROTECT AF		CAP	p-value*	p-value±
		Early	Late			
Procedure Time (Mean ± SD)	62 ± 34	67 ± 36	58 ± 33	50 ± 21	<0.001	<0.001
Implant Success	485/542 (89.5%)	239/271 (88.2%)	246/271 (90.8%)	437/460 (95.0%)	0.001	0.001
45-day Warfarin Discontinuation Among Implanted	414/478 (86.6%)	194/235 (82.6%)	220/243 (90.5%)	352/371 (94.9%)	<0.001	<0.001

*From tests comparing the PROTECT AF cohort with CAP

±From tests for differences across three groups (early PROTECT AF, late PROTECT AF, and CAP)

- Improvements seen over time in PROTECT AF
 - Shorter implant time, higher implant success rate, higher warfarin discontinuation rate
- Trends confirmed in CAP



Safety Event Rates

PROTECT AF vs CAP

	PROTECT AF	PROTECT AF Early	PROTECT AF Late	CAP	p-value*	p-value±
Procedure/Device Related Safety Adverse Events within 7 Days	42/542 (7.7%)	27/271 (10.0%)	15/271 (5.5%)	17/460 (3.7%)	0.007	0.006
Serious Pericardial Effusions within 7 Days	27/542 (5.0%)	17/271 (6.3%)	10/271 (3.7%)	10/460 (2.2%)	0.019	0.018
Procedure Related Stroke	5/542 (0.9%)	3/271 (1.1%)	2/271 (0.7%)	0/460 (0.0%)	0.039	0.039

Improvements seen over time for acute safety events

Fewer total procedure/device related events



ASAP Results

- 113 patients enrolled @ 4 centers in Europe
- Average CHADS₂ = 2.7
- Successful implantation in 105/113 pts (93%)
- Device or procedure related AE
 - 1 pericardial effusion - resolved
 - 1 device embolisation – retrieved
 - 1 pseudo-aneurysm – resolved
- Follow-up 7.9 mo
 - 43 patients @ 1 year
- 2 patients with device related thrombus @ 45 days and 3 mo TEE
 - Resolved w/ 2 mo SQ heparin
- 2 strokes during FU

Concept of PLAATO and Watchman

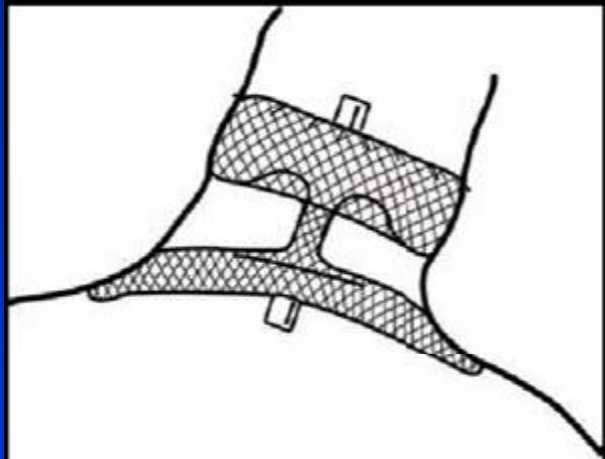
- To close the LAA like with a ball



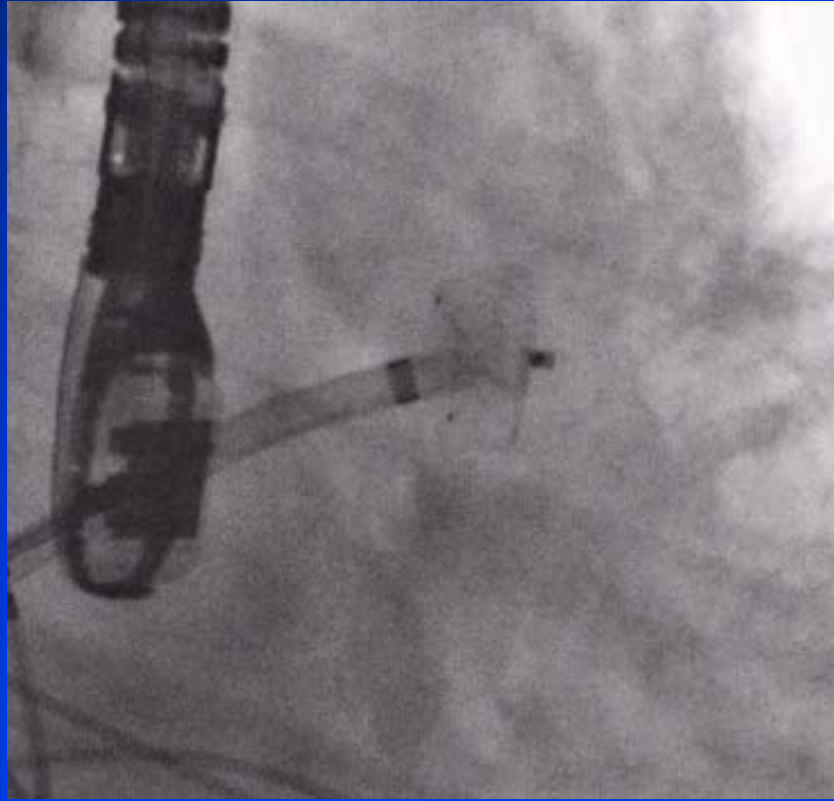
Amplatzer Cardiac Plug ACP



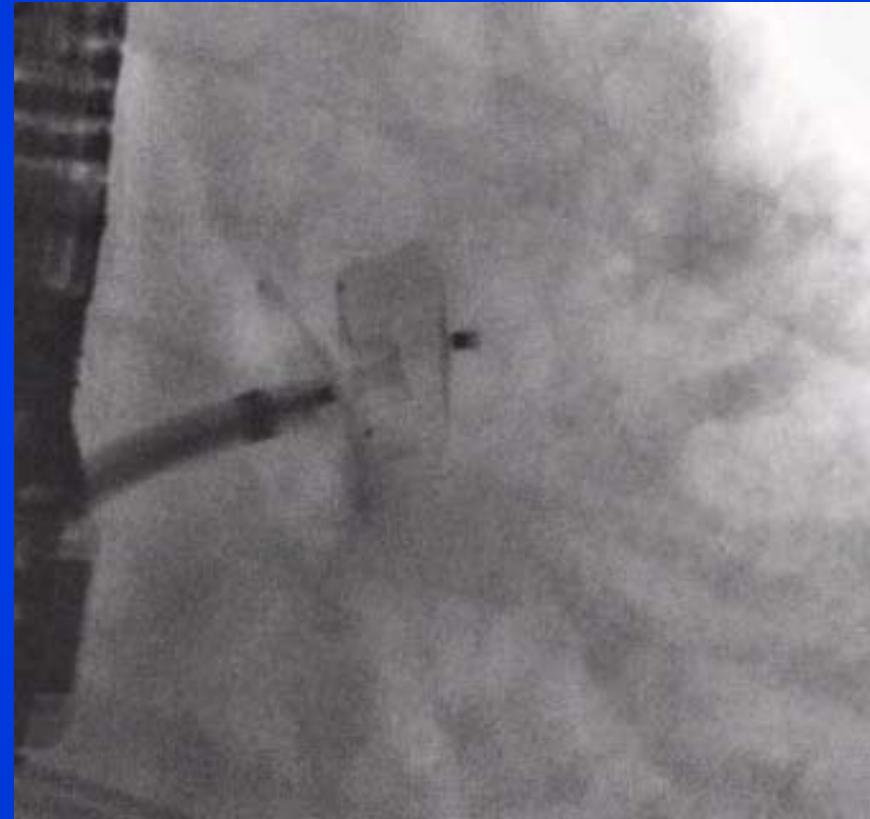
Concept of Amplatzer Cardiac Plug ACP



M.I., female, 66 years



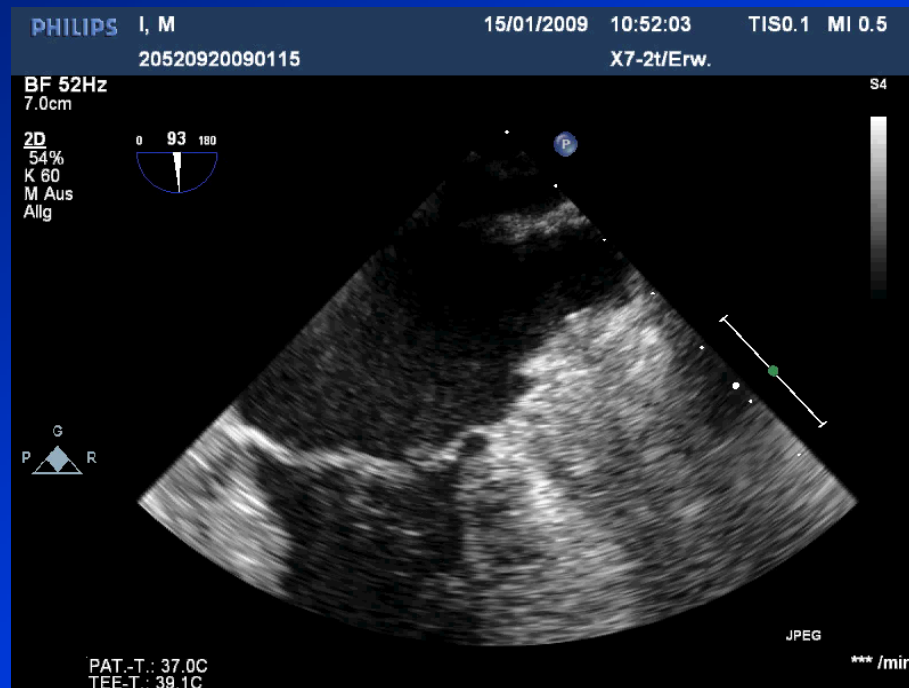
- Implantation



- Angiographic confirmation of correct position

M.I., femal, 66 years

Final position



- 2D TEE 93°

- 3D TEE: LA en-face view of the occluder



New Approaches

- Endocardial

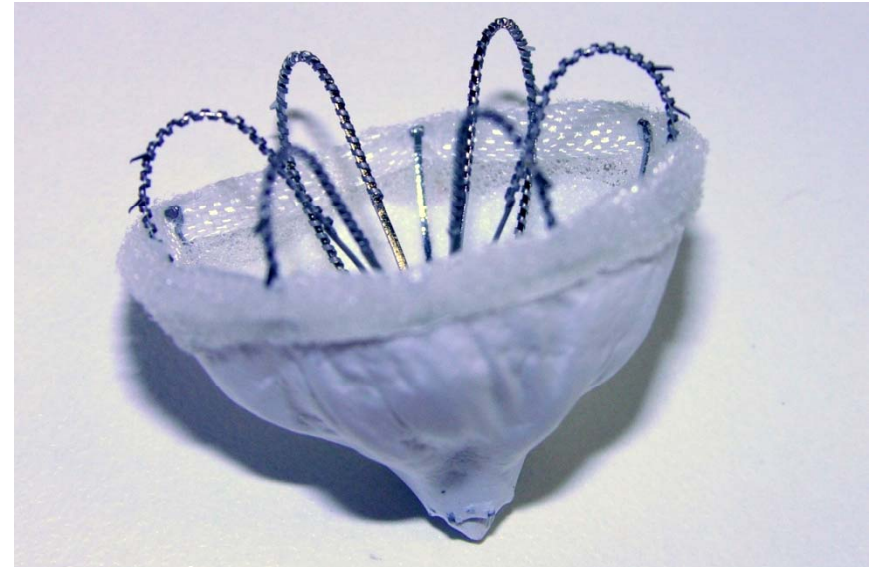
- Occlutech
- Coherex
- Gore

- Epicardial

- Epitec
- AtriCure
- SentreHeart
- Aegis Medical

Coherex WaveCrest LAA Occlusion System

- Soft Nitinol frame
- Covered by polyurethane foam and e-PTFE
- 22, 27, 33 mm



- Special features
 - Separation of occlusion and anchoring
 - Occluder is completely re-positionable

Coherex WaveCrest

- “Roll-out” anchors
 - Separate structure from the occluder
 - Rolled out only when the occluder is in position



Coherex WaveCrest

- Anchoring is completely reversible
 - Anchor
 - Adjust / re-sheath
 - Re-anchor
- Detachment does not disrupt implant position
 - No torque transferred to implant during detachment



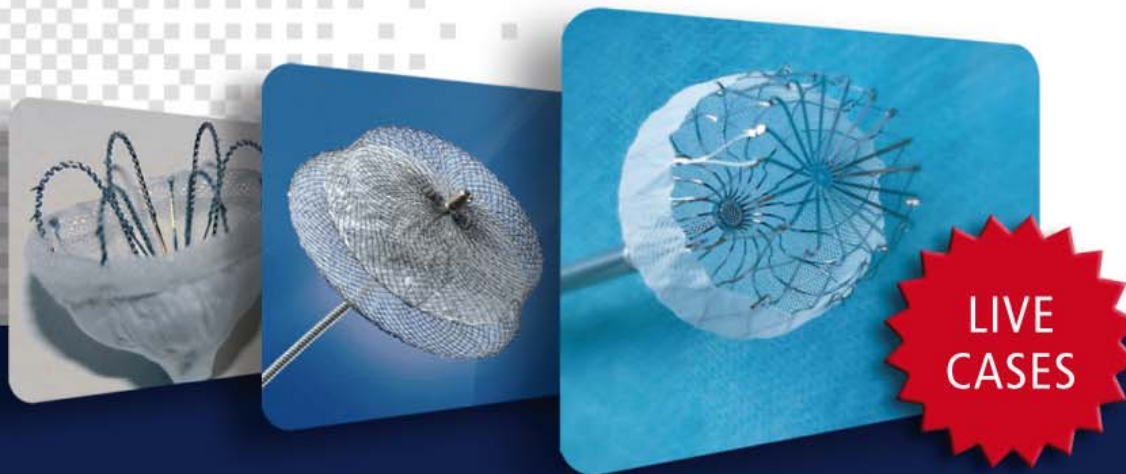


June 23 – 25, 2011 | Frankfurt, Germany

CSI 2011 – Catheter Interventions in Congenital & Structural Heart Disease

www.csi-congress.org





November 19, 2011 | Frankfurt, Germany

LAA 2011 – How to Close the Left Atrial Appendage



www.csi-laa.org

Take Home Messages

- Atrial fibrillation is a frequent cause of stroke
- Anticoagulation therapy is effective but difficult
- Thrombi originate from the left atrial appendage
- Catheter closure of the left atrial appendage is feasible, relatively safe and according to the PROTECT AF Trial equivalent to anticoagulation
- Two devices for LAA closure are available and there are more to come