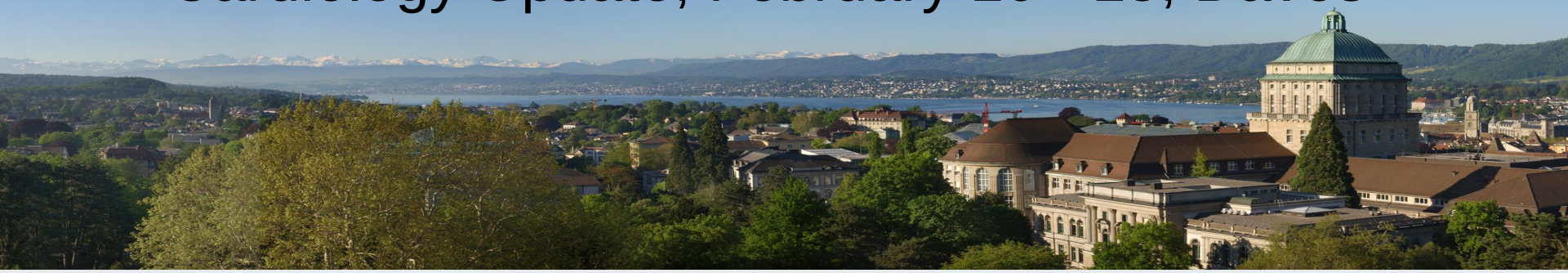
Cardiology Update, February 10 - 15, Davos



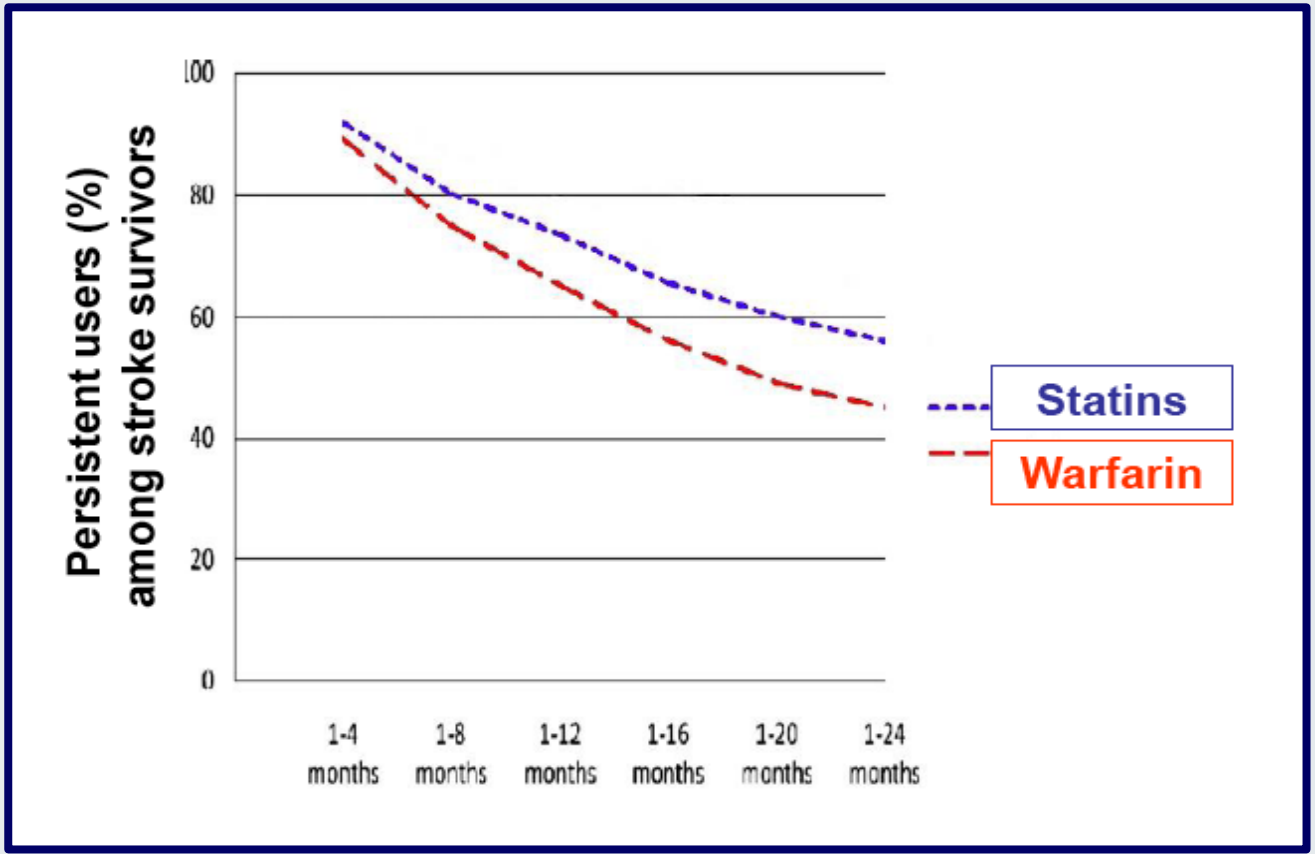
Catheter-based LAA occlusion: promising experiences

Ulf Landmesser, MD
Cardiology, Cardiovascular Center,
University Hospital Zürich, Switzerland

UniversityHospital Zurich

University of Zurich[UZH]

Persistent use of anticoagulation in clinical practice ?

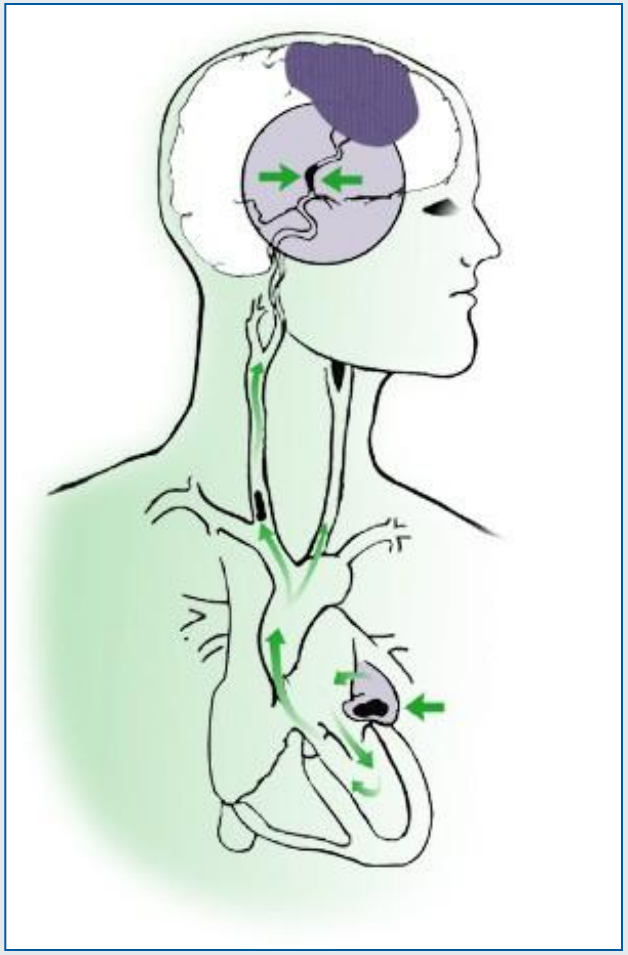


21 077 stroke survivors: the persistent use of anticoagulation with warfarin declined to 45 % after 2 years

Glader EL et al.; *Stroke* 2010; 41: 397-401

Left atrial appendage closure in atrial fibrillation – the hypothesis

Ischemic stroke in patients with AFib has mostly a cardiac thromboembolic genesis, the main origin of these thrombi is the LAA.



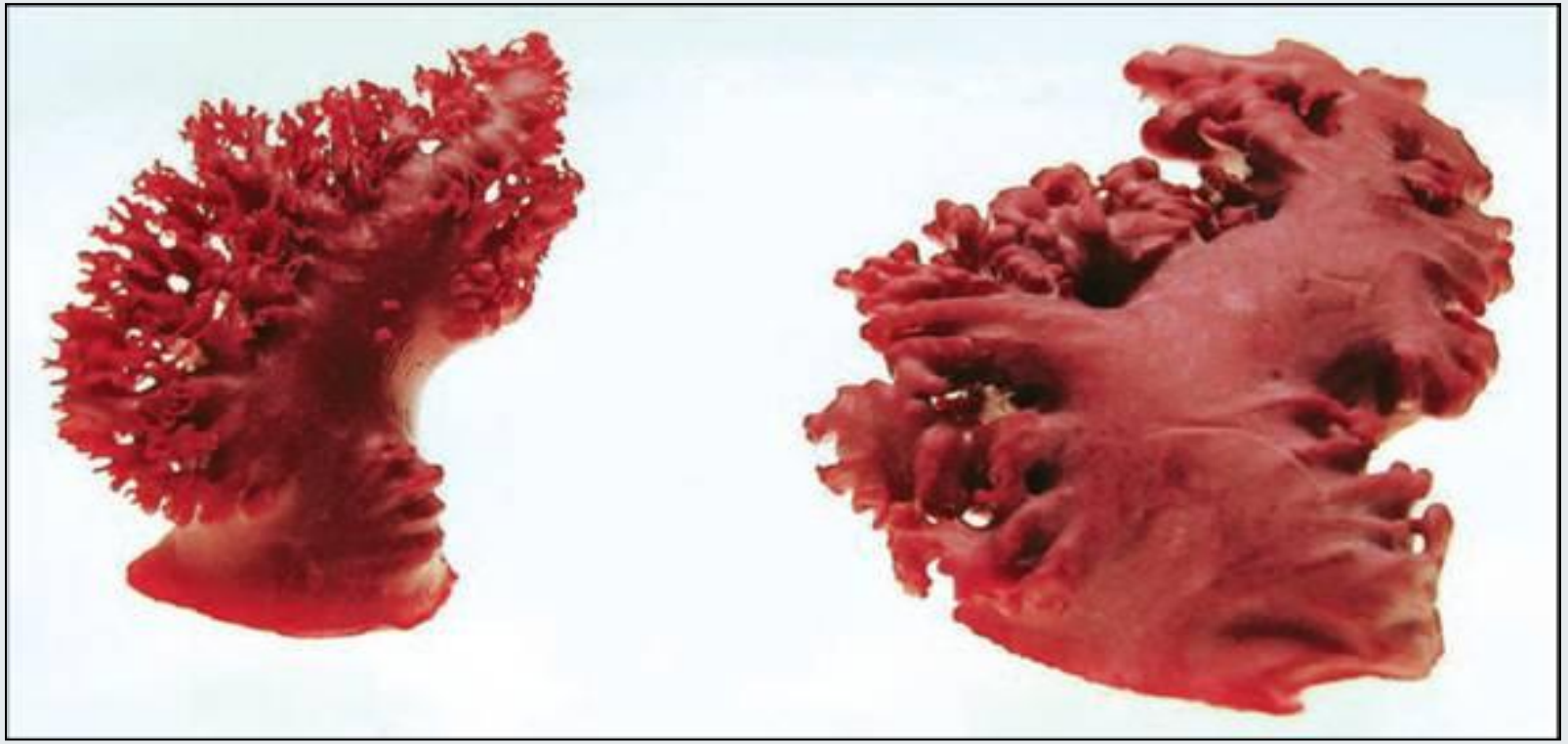
Location of thrombus in left atrium in non-valvular atrial fibrillation

Setting	N	Appendage	Percent	LA Body	Percent	Reference
TEE	317	66	21	1	0.3	Stoddard; JACC, 1995
TEE	233	34	15	1	0.4	Manning; Circ, 1994
Autopsy	506	35	7	12	2.4	Aberg; Acta Med Scan, 1969
TEE	52	2	4	2	3.8	Tsai; JFMA, 1990
TEE	48	12	25	1	2.1	Klein; Int J Card Image, 1993
TEE & Operation	171	8	5	3	1.8	Manning; Circ, 1994
SPAF III TEE	359	19	5	1	0.3	Klein; Circ, 1994
TEE	272	19	7	0	0.0	Leung; JACC, 1994
TEE	60	6	10	0	0.0	Hart; Stroke, 1994
Total Thrombus		201		21		

91% (201/222) of Left Atrial Thrombus Localized to the LAA

Blackshear JL and Odell JA, *Ann Thorac Surg* 1996;61:755-759

Left atrial appendage:
the most lethal human attachment ?



Sinus rhythm **Atrial fibrillation**

Johnson WD, Ganjoo AK, Stone CD, et al. Eur J Cardiothorac Surg 2000;17:718–22.

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Atrial Fibrillation

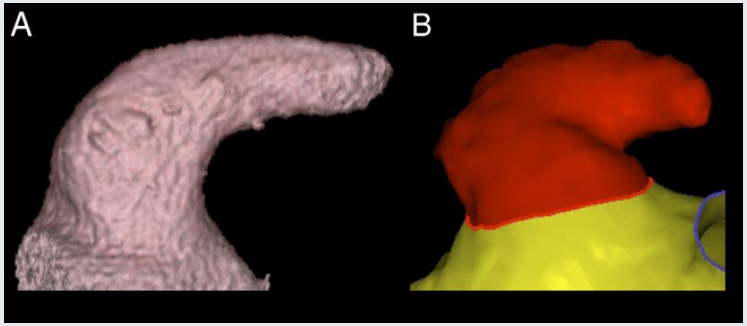
Does the Left Atrial Appendage Morphology Correlate With the Risk of Stroke in Patients With Atrial Fibrillation?

Results From a Multicenter Study

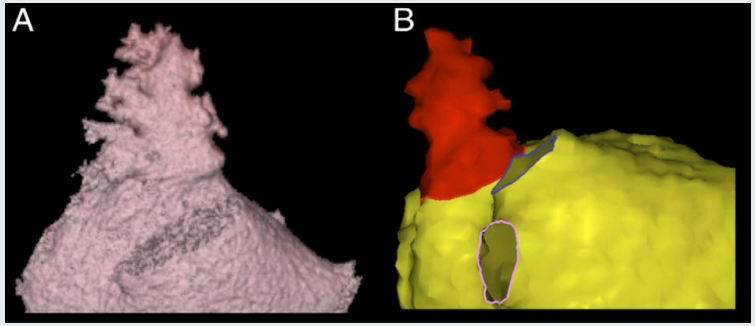
Luigi Di Biase, MD, PHD,*†‡ Pasquale Santangeli, MD,*‡ Matteo Anselmino, MD, PHD,§ Prasant Mohanty, MBBS, MPH,* Ilaria Salvetti, MD,§ Sebastiano Gili, MD,§ Rodney Horton, MD,* Javier E. Sanchez, MD,* Rong Bai, MD,* Sanghamitra Mohanty, MD,* Agnes Pump, MD,* Mauricio Cereceda Brantes, MD,* G. Joseph Gallinghouse, MD,* J. David Burkhardt, MD,* Federico Cesarani, MD,‖ Marco Scaglione, MD,¶ Andrea Natale, MD,*† Fiorenzo Gaita, MD§

Left Atrial Appendage Morphology

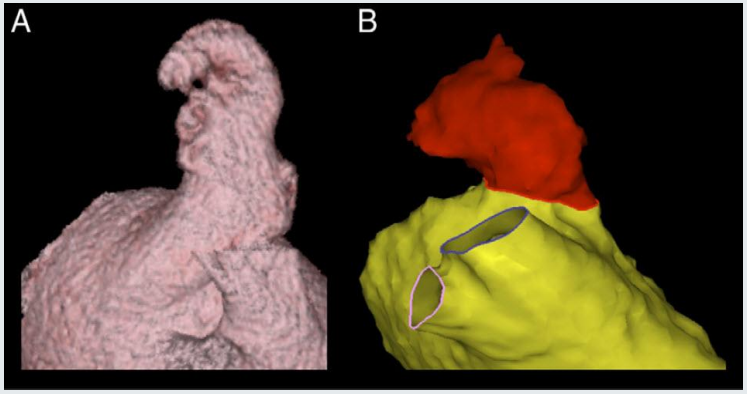
Analysis of CT and MRI from 932 patients with atrial fibrillation



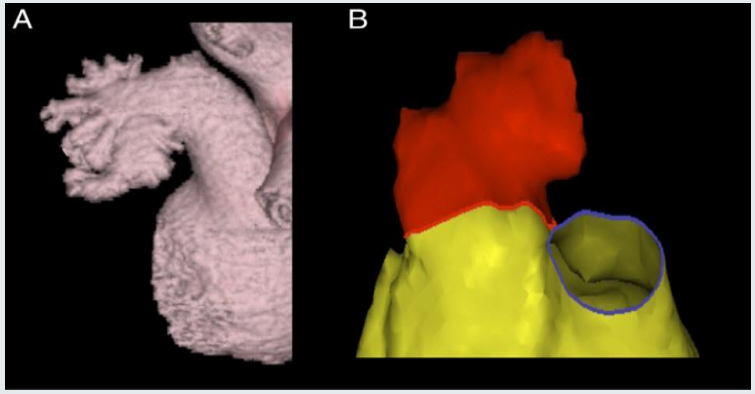
CT and MRI Scans of a Chicken Wing LAA Morphology (48%)



CT and MRI Scans of a Cactus LAA Morphology (30 %)



CT and MRI Scans of a Windsock LAA Morphology (19 %)

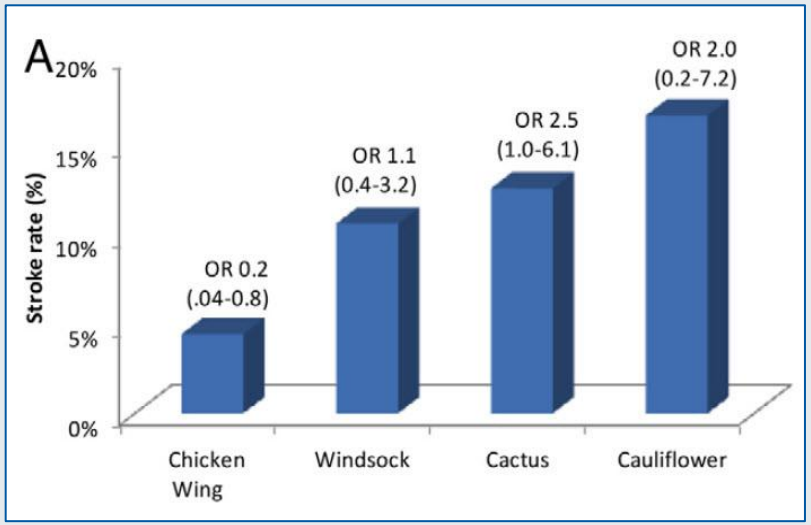


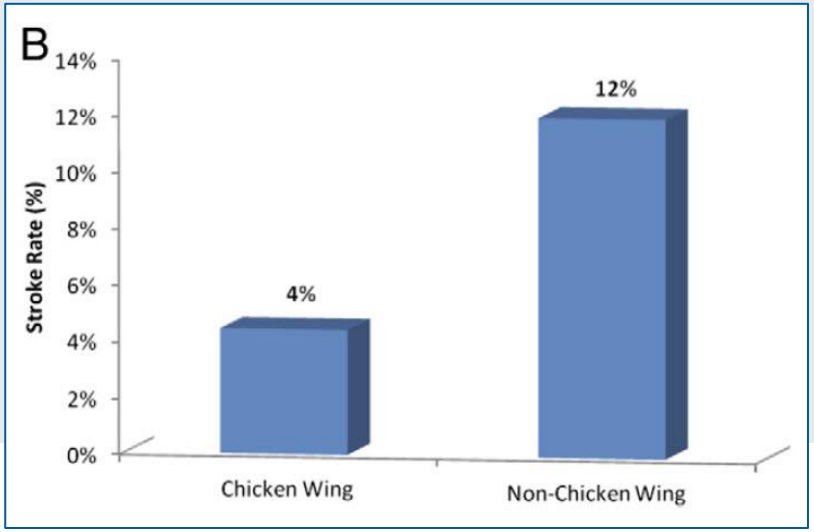
CT and MRI Scans of a Cauliflower LAA Morphology (3 %)

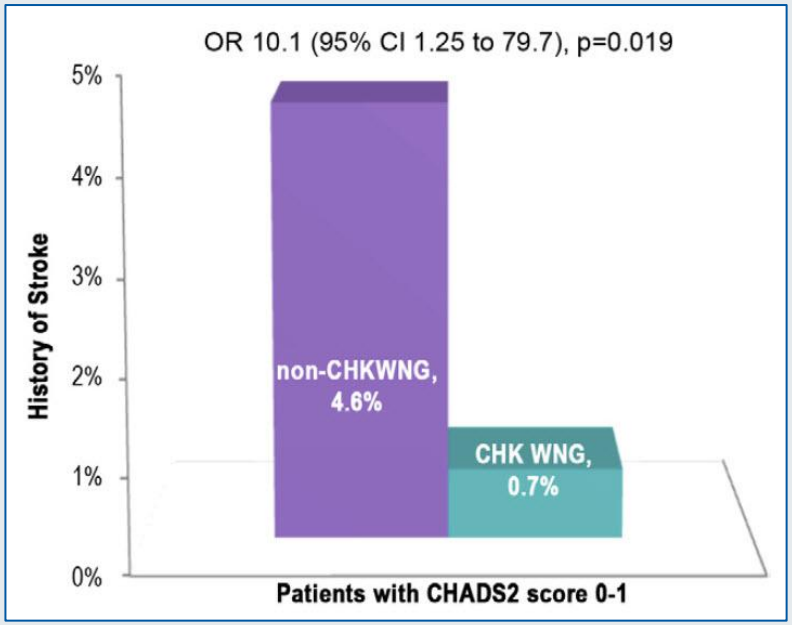
Di Biase L et al. *JACC* 2012; 60(6):531–8

Does LAA morphology relate to risk of stroke ?

Prevalence of Prior Stroke/TIA According to Different LAA Morphologies





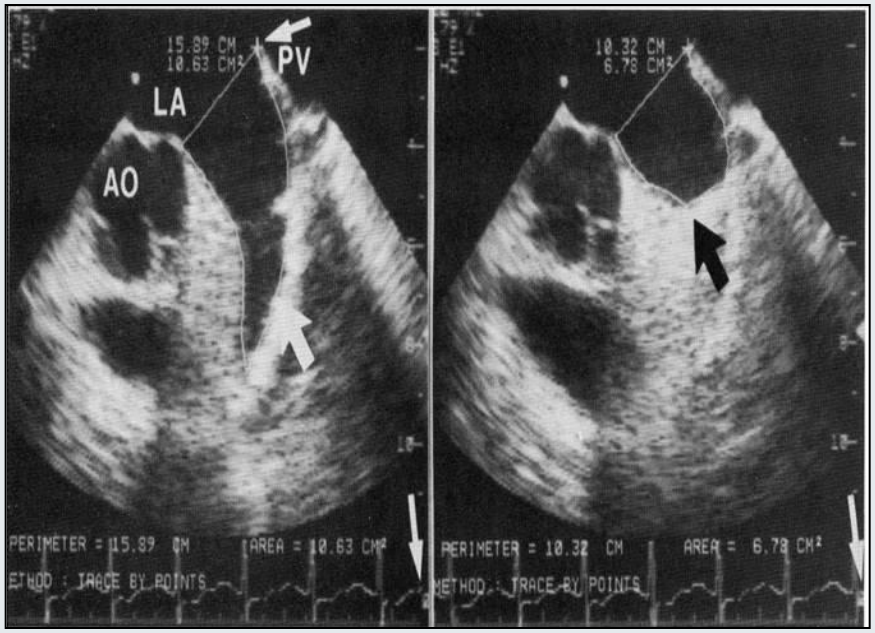


Chicken Wing Versus Non–Chicken Wing Morphologies

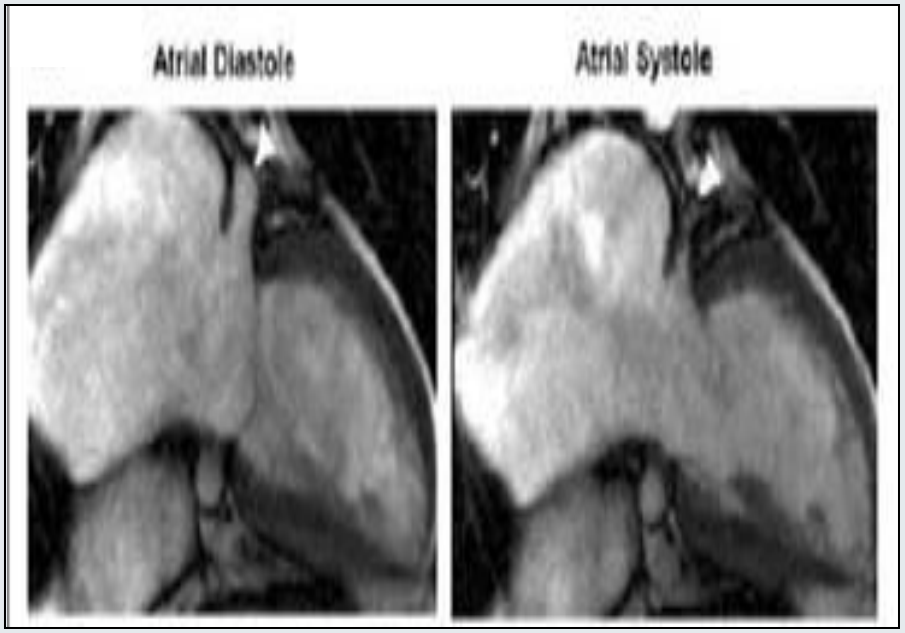
Di Biase L et al. *JACC* 2012; 60(6):531–8

Left atrial appendage function in sinus rhythm:

LAA in systole and diastole by TEE (left) and cardiac MRI (right)



Pollick C et al.; Circulation 1991



Holmes D et al.; Circulation 2009

LAA – prothrombotic mileu in atrial fibrillation

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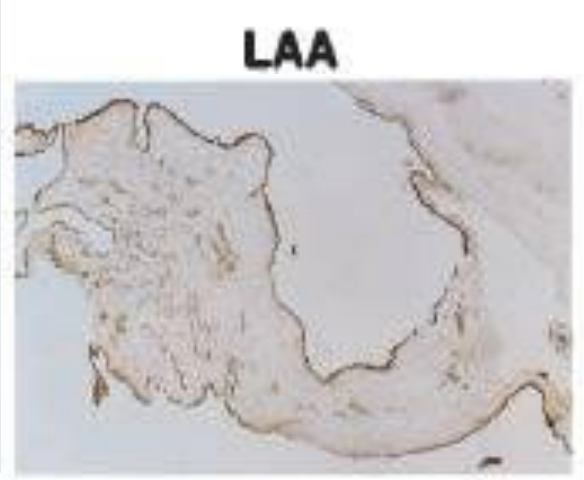
Thrombogenesis

Increased von Willebrand Factor in the Endocardium as a Local Predisposing Factor for Thrombogenesis in Overloaded Human Atrial Appendage

Mitsumasa Fukuchi, MD,* Jun Watanabe, MD,* Koji Kumagai, MD,* Yukio Katori, MD,†
Shigeo Baba, MD,* Koji Fukuda, MD,* Takuya Yagi, MD,* Atsushi Iguchi, MD,‡
Hitoshi Yokoyama, MD,‡ Masahito Miura, MD,* Yutaka Kagaya, MD,* Shigekazu Sato, MD,§
Koichi Tabayashi, MD,‡ Kunio Shirato, MD*
Sendai, Japan

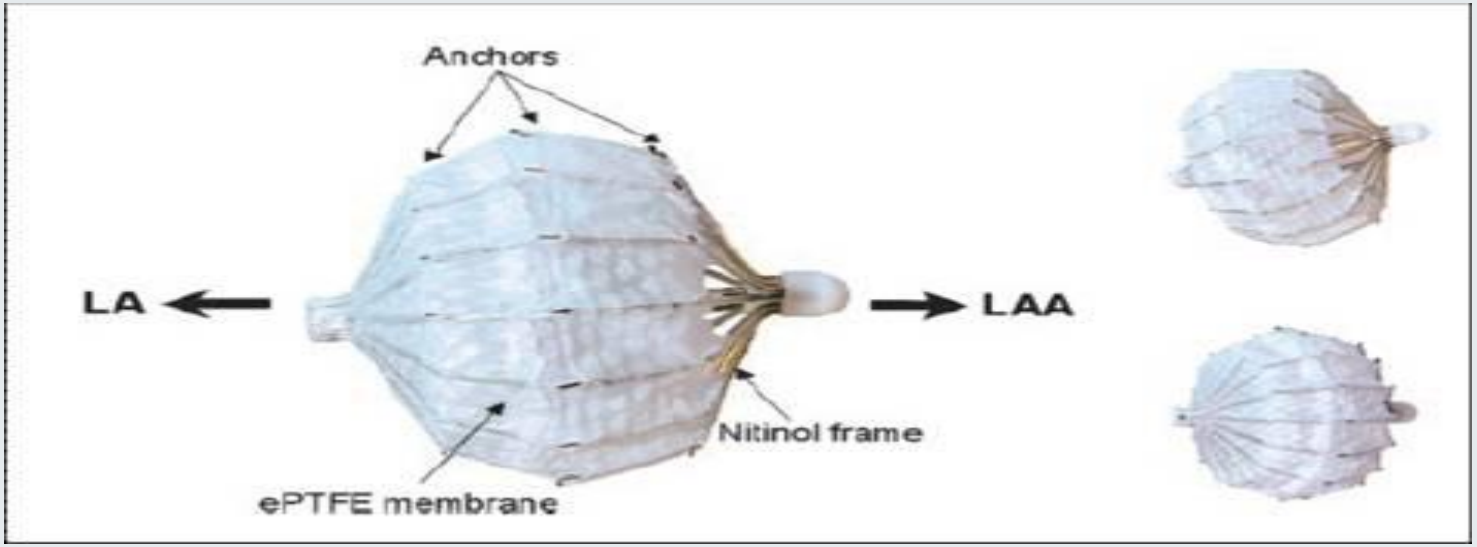
SR



A.fib.

vWF expression

Feasability of percutaneous left atrial appendage closure



Percutaneous Left Atrial Appendage Transcatheter Occlusion to Prevent Stroke in High-Risk Patients With Atrial Fibrillation

Early Clinical Experience

Horst Sievert, MD; Michael D. Lesh, MD; Thomas Trepels; Heyder Omran, MD; Antonio Bartorelli, MD; Paola Della Bella, MD; Toshiko Nakai, MD; Mark Reisman, MD; Carlo DiMario, MD; Peter Block, MD; Paul Kramer, MD; Dirk Fleschenberg; Ulrike Krumsdorf; Detlef Scherer, MD

Conclusions—Thus, transcatheter closure of the LAA is feasible in humans. This novel implant technology may be appropriate for patients with AF who are not suitable candidates for anticoagulation therapy. Further trials are needed to show the long-term safety and its efficacy in reducing stroke. (*Circulation*. 2002;105:1887-1889.)

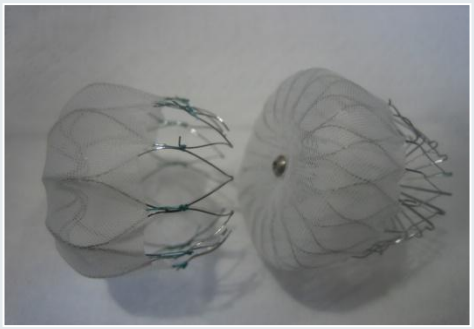
Currently available data on LAA closure with PLAATO device and stroke rate

Author (yr)	# Pat.	FU	Estimated annual stroke rate	Actual annual stroke rate
Block [2009]	64	5 years	6.6%	3.8%
Park [2009]	73	2 years	5.0%	0.0%
Ussia [2009]	20	40±10 month	6.4%	0.0%
De Meester [2008]	10	3±47 month	7.1%	0.0%
Ostermeyer [2005]	111	9.8 month	6.3%	2.2%

Devices for percutaneous left atrial appendage closure

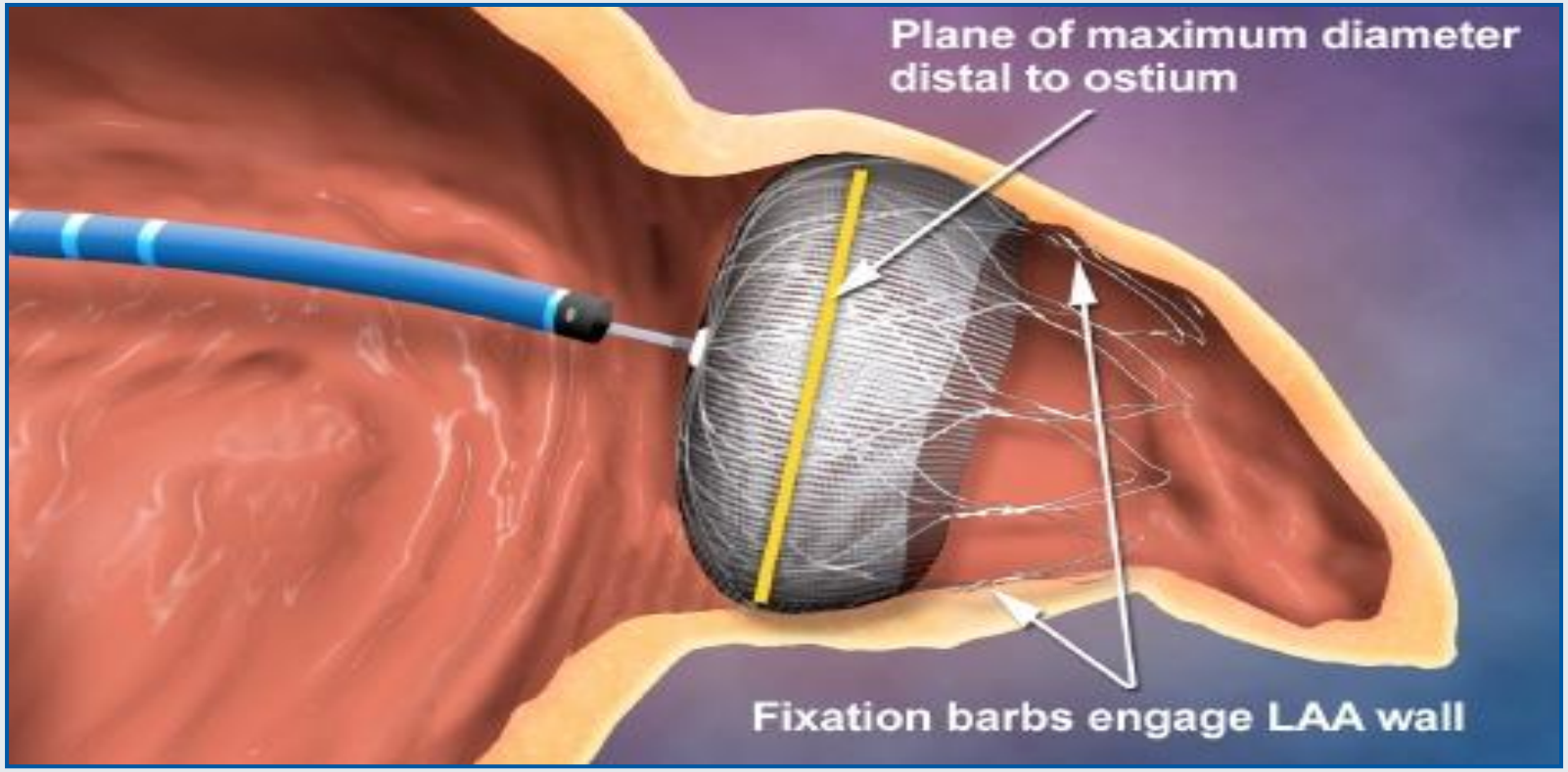
PLAATO

WATCHMAN



One body (anchoring and sealing)

WATCHMAN LAA Closure Device in situ

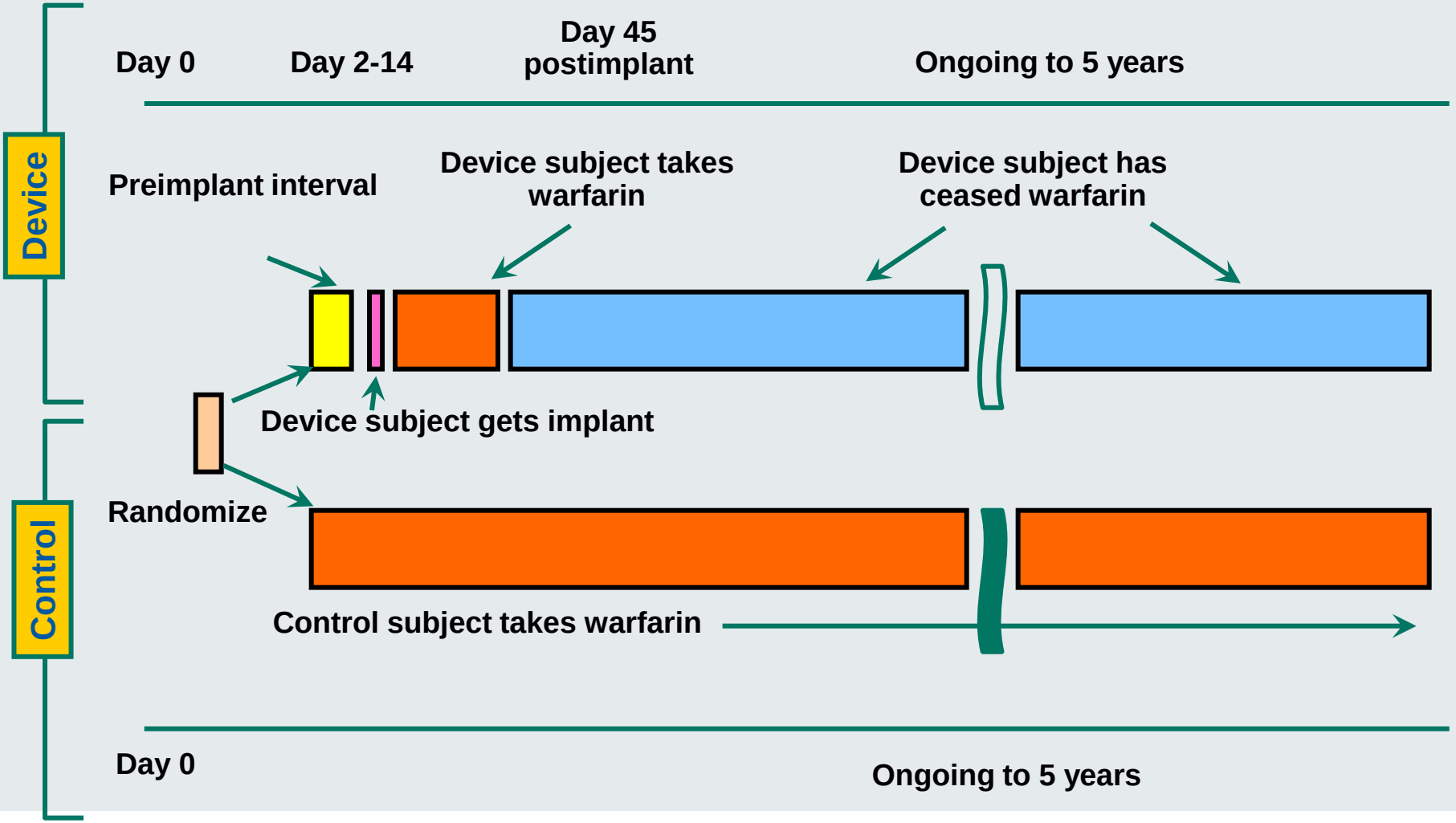


Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

*David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators**

Lancet 2009; 374: 534–42

PROTECT AF - Patient Study Timeline



Holmes DR, et al. *Lancet* 2009; 374:534-42

PROTECT AF Study - Key Inclusion/Exclusion Criteria

- Key Inclusion Criteria
  - Age 18 years or older
  - Documented non-valvular AF
  - Eligible for long-term warfarin therapy, and no other conditions that would require long-term warfarin therapy
  - Calculated CHADS2 score ≥ 1

- Key Exclusion Criteria
  - NYHA Class IV Congestive Heart Failure
  - ASD and/or atrial septal repair or closure device
  - Planned ablation procedure within 30 days of potential WATCHMAN Device implant
  - Symptomatic carotid disease
  - LVEF < 30%
  - TEE Criteria: Suspected or known intracardiac thrombus

Holmes DR, et al. *Lancet* 2009; 374:534-42

PROTECT AF Study - Primary Endpoint

Primary efficacy endpoint (combined)

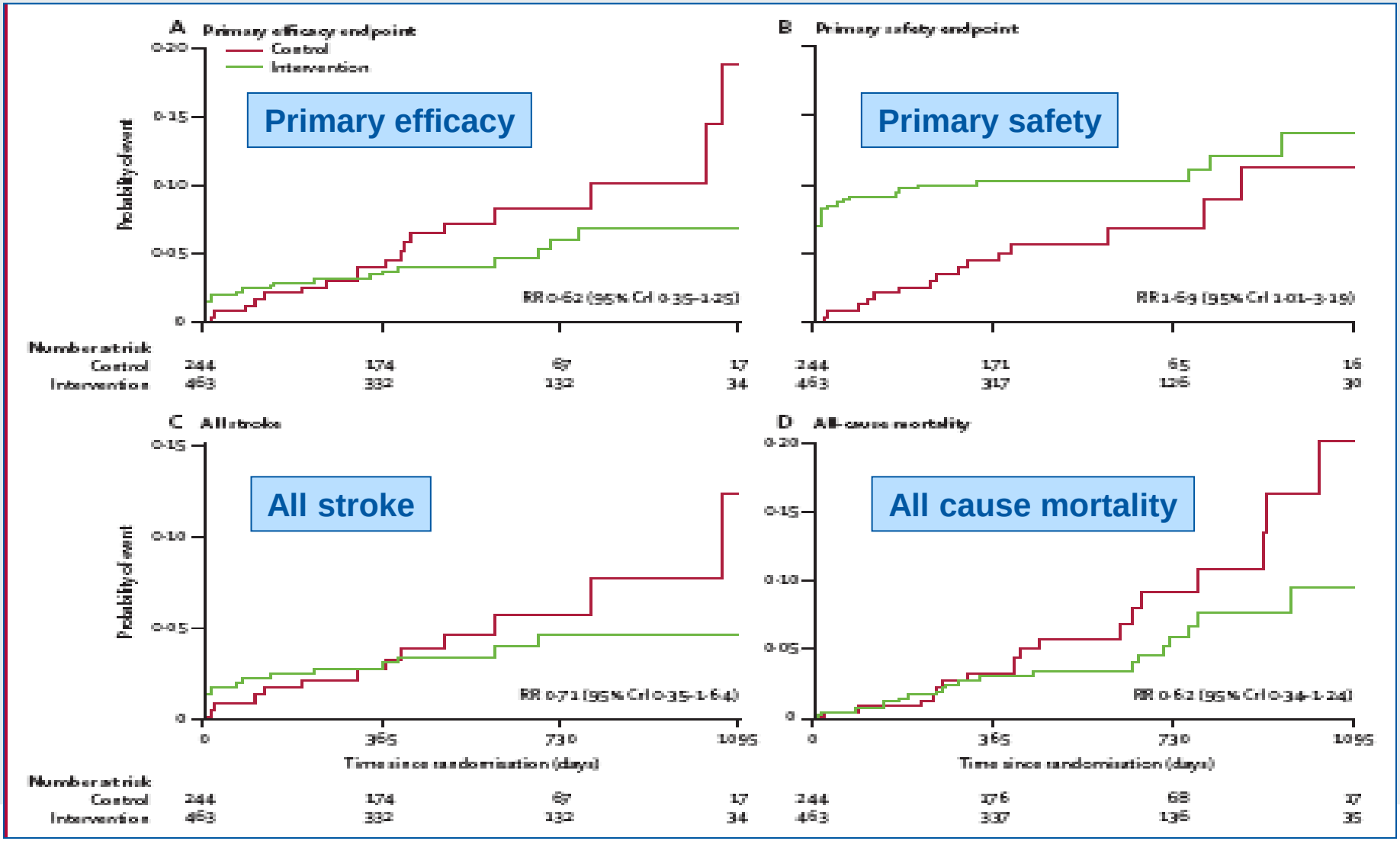
- ischemic stroke
- hemorrhagic stroke
- cardiovascular/unexplained death
- systemic embolism

Primary safety endpoint

- excessive bleeding
- procedure related complications (serious pericardial effusion, device embolization, procedure related stroke)

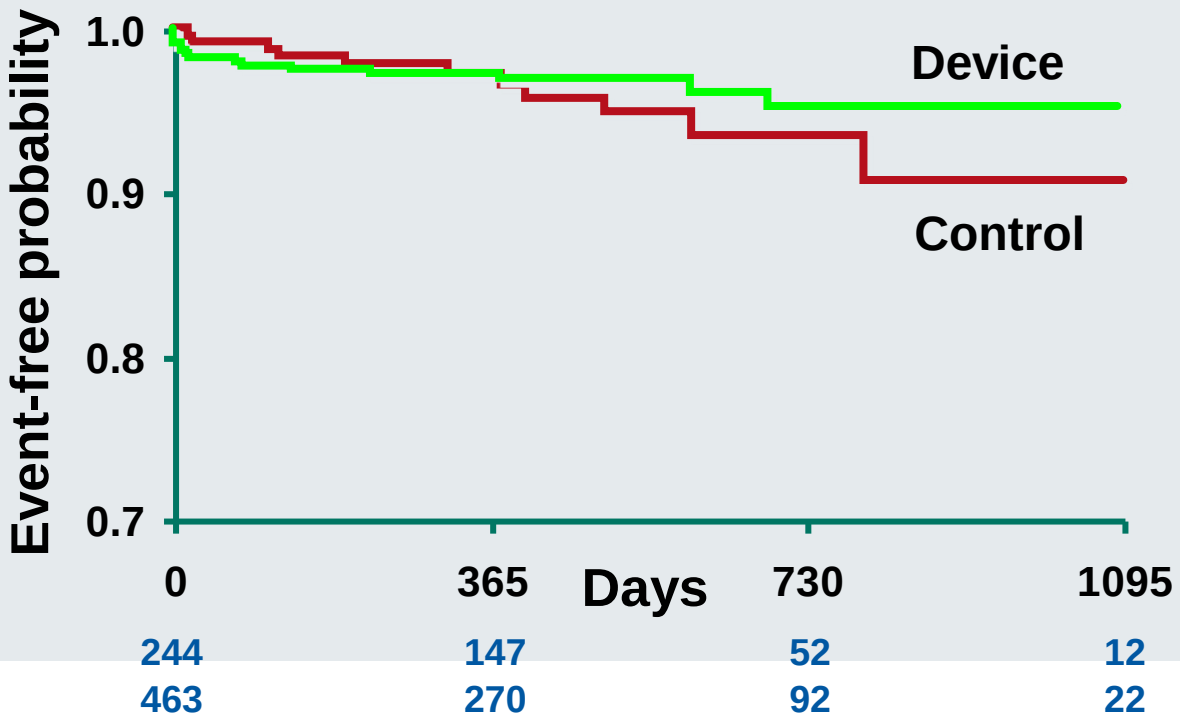
Holmes DR, et al. *Lancet* 2009; 374:534-42

PROTECT AF - Primary Endpoint



PROTECT AF - All Stroke

	Device			Control				Posterior probabilities	
Cohort	Events eve	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)	RR (95% CI)	Non-inferiority	Superiority
900 pt-yr	15	582.9	2.6 (1.5, 4.1)	11	318.1	3.5 (1.7, 5.7)	0.74 (0.36, 1.76)	0.998	0.731

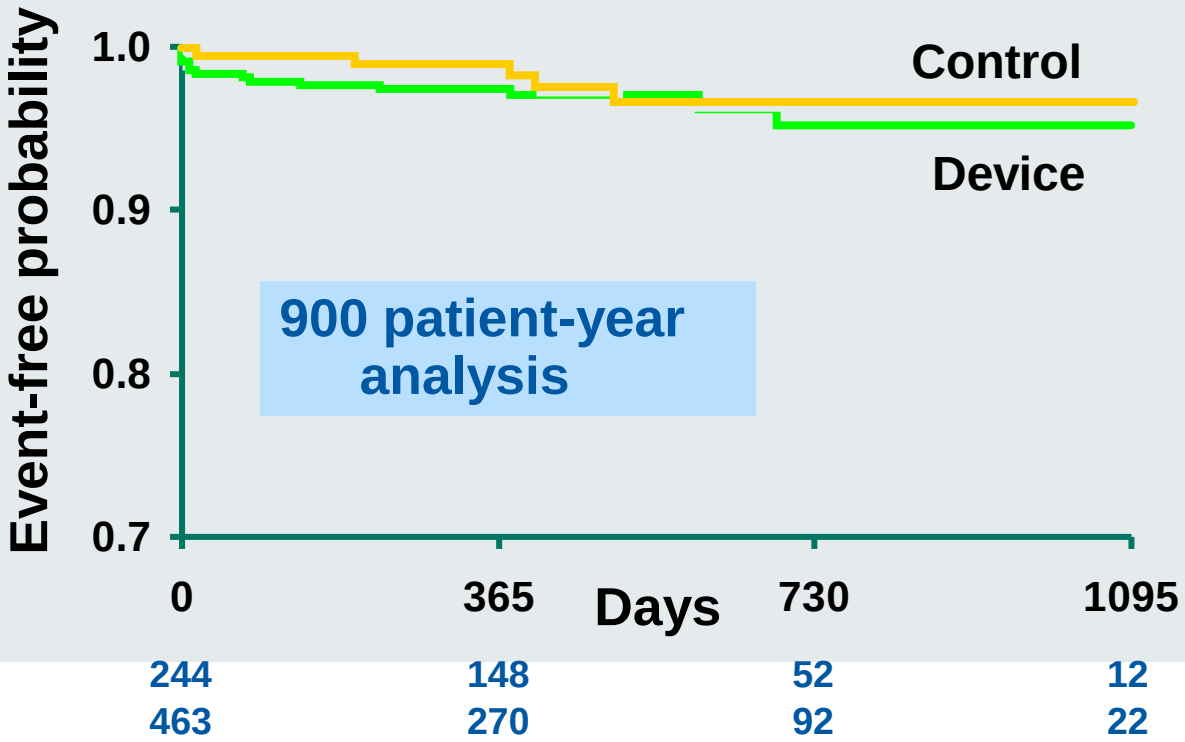


ITT cohort:
patients analyzed based on their randomly assigned group (regardless of treatment received)

Holmes DR, et al. *Lancet* 2009; 374:534-42

PROTECT AF - Ischemic Stroke

	Device			Control				Posterior probabilities	
Cohort	Events (no.)	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)	RR (95% CI)	Non-inferiority	Superiority
900 pt-yr	14	582.9	2.4 (1.3, 3.9)	5	318.9	1.6 (0.5, 3.1)	1.53 (0.64, 5.43)	0.617	0.150

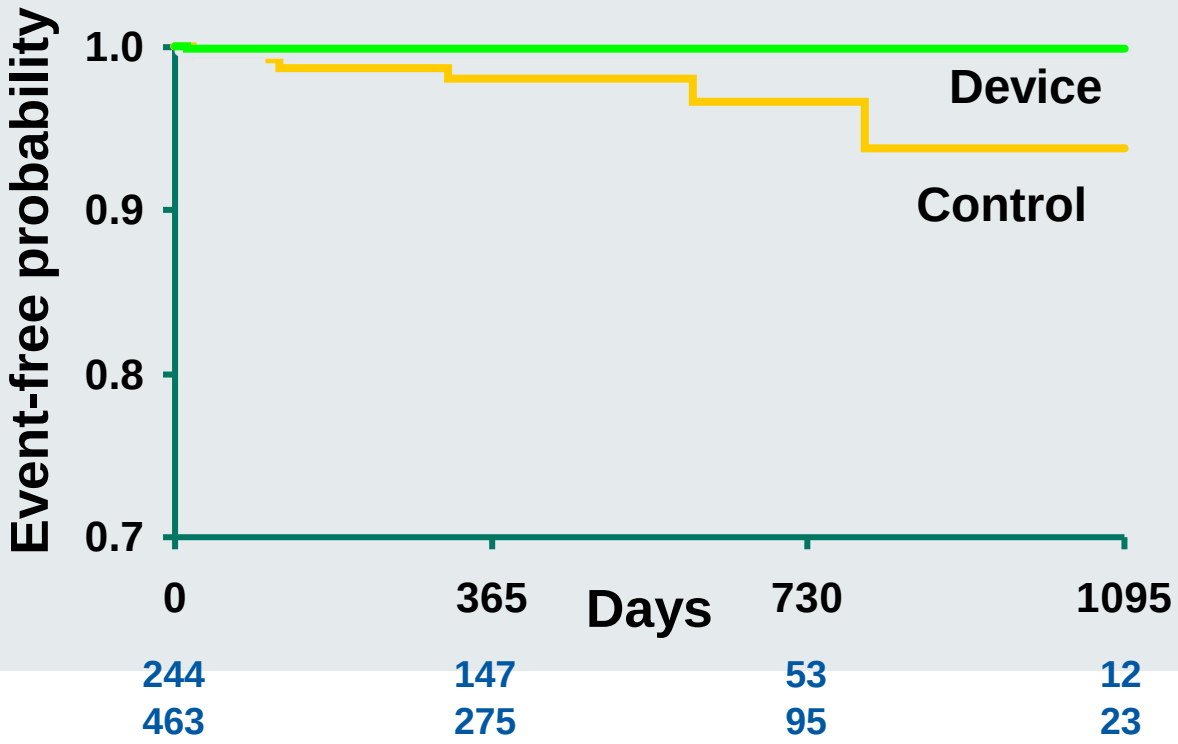


ITT cohort:
patients analyzed based on their randomly assigned group (regardless of treatment received)

Holmes DR, et al. *Lancet* 2009; 374:534-42

PROTECT AF - Hemorrhagic Stroke

	Device			Control				Posterior probabilities	
Cohort	Events (no.) (0.0, 0.9)	Total pt-yr	Rate (95% CI)	Events (no.) (0.5, 3.9)	Total pt-yr (0.00, 0.80)	Rate (95% CI)	RR (95% CI)	Non-inferiority	Superiority
900 pt-yr	1	593.6	0.2 (0.0, 0.6)	6	319.4	1.9 (0.7, 3.7)	0.09 (0.00, 0.45)	>0.999	0.998



ITT cohort:
patients analyzed based on their randomly assigned group (regardless of treatment received)

Holmes DR, et al. *Lancet* 2009; 374:534-42

Pericardial Effusions by Experience

- Pericardial effusions – most common safety issue
- Throughout PROTECT AF Trial, procedural modifications and training enhancements were implemented

Site implant group	Any		Serious	
	No.	%	No.	%
Early patients (1-3)	13/154	8.4	10/154	6.5
Late patients (≥4)	27/388	7.0	17/388	4.4
Total	**40/542**	**7.2**	**27/542**	**5.0**

- Continued ACCESS Registry

Improved safety with experience: Continued Access Registry

Safety of Percutaneous Left Atrial Appendage Closure

Results From the Watchman Left Atrial Appendage System for Embolic Protection in Patients With AF (PROTECT AF) Clinical Trial and the Continued Access Registry

Vivek Y. Reddy, MD; David Holmes, MD; Shephal K. Doshi, MD; Petr Neuzil, MD, PhD; Saibal Kar, MD

Table 3. Safety Event Rates at Sites Participating in Both PROTECT AF and CAP

	PROTECT AF	CAP	*P*
Procedure time, mean±SD, min	56±27	50±21	<0.001
Implant success, n/total (%)	335/367 (91.3)	437/460 (95.0)	0.033
Procedure/device-related safety adverse event within 7 d, n/total (%)	24/367 (6.5)	17/460 (3.7)	0.061
Serious pericardial effusion within 7 d, n/total (%)	15/367 (4.1)	10/460 (2.2)	0.110
Procedure-related stroke, n/total (%)	2/367 (0.5)	0/460 (0.0)	0.113

PREVAIL Trial to be reported soon

Circulation 2011 ;123(4):417-24

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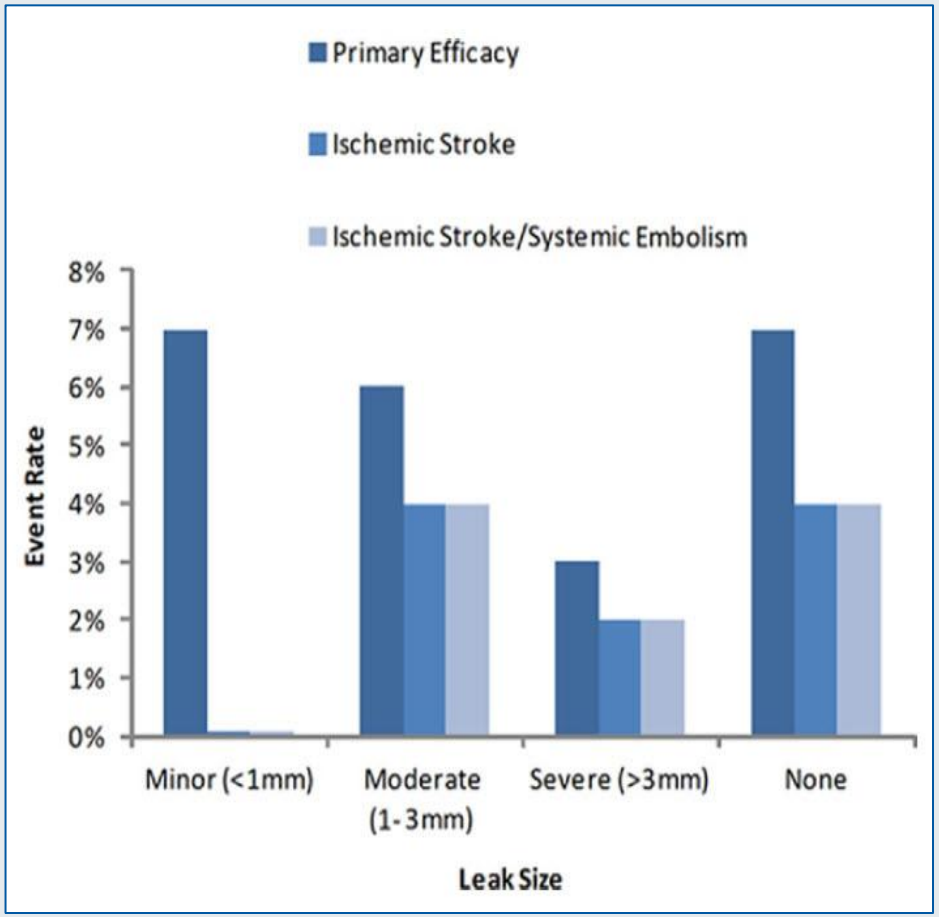
Heart Rhythm Disorders

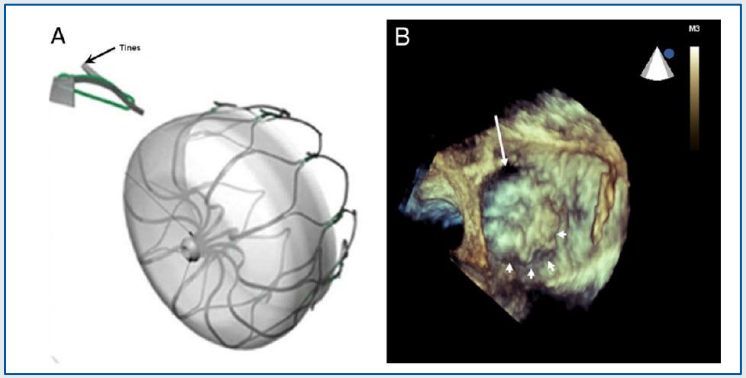
The Clinical Impact of Incomplete Left Atrial Appendage Closure With the Watchman Device in Patients With Atrial Fibrillation

A PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) Substudy

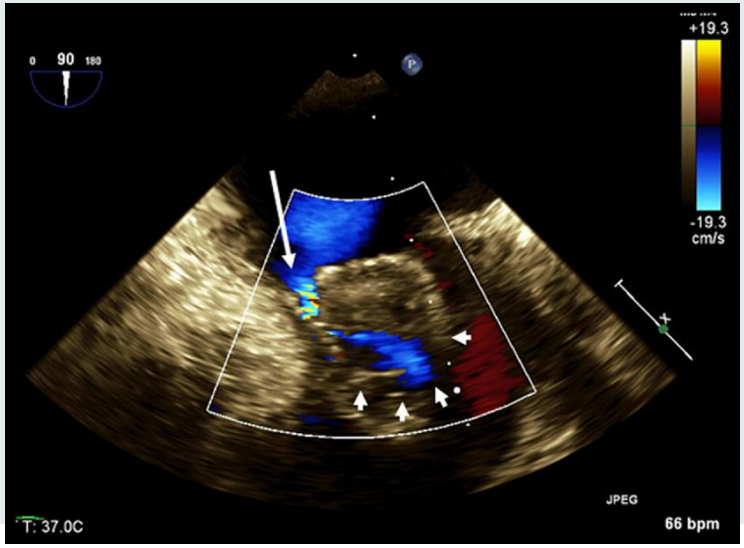
Juan F. Viles-Gonzalez, MD,* Saibal Kar, MD,† Pamela Douglas, MD,‡ Srinivas Dukkipati, MD,* Ted Feldman, MD,§ Rodney Horton, MD,‖ David Holmes, MD,¶ Vivek Y. Reddy, MD*

Primary Efficacy Endpoint Rates by Leak Severity





LAA Ostium by 3-Dimensional TEE and Watchman Device



Peri-Device Leak by TEE Imaging

Viles-Gonzalez et al. *JACC* 2012;59(10):923–9

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

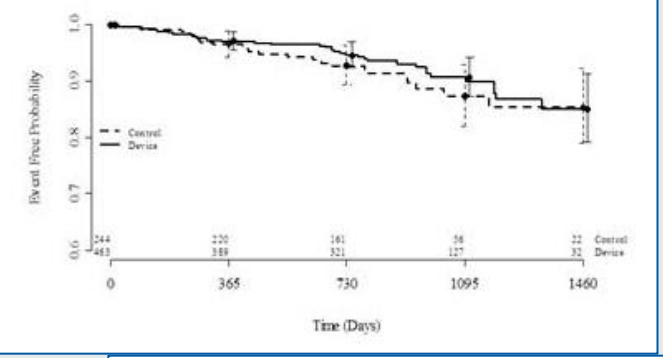
Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients with Atrial Fibrillation: 2.3 Year Follow-Up of the PROTECT AF Trial

Vivek Y. Reddy, Shephal K. Doshi, Horst Siever, Maurice Buchbinder, Petr Neuzil, Kenneth Huber, Jonathan L. Halperin and David Holmes

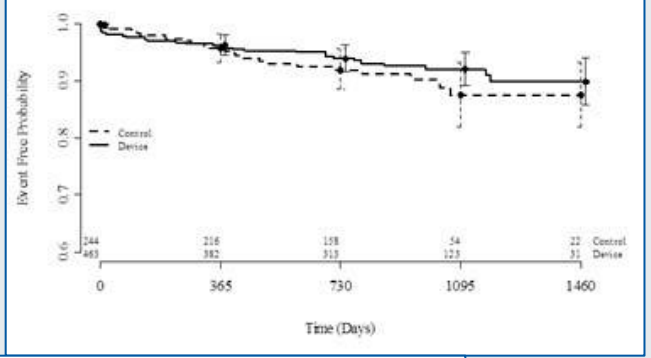
Circulation. published online January 16, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

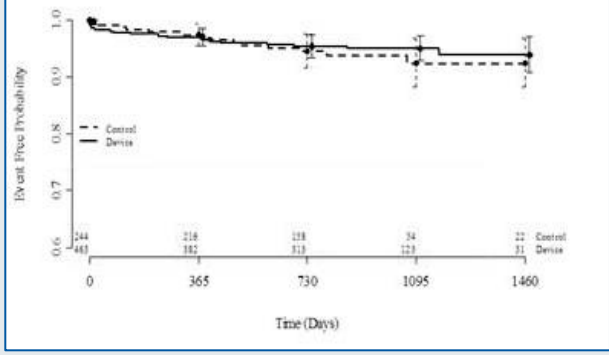
All-Cause Mortality



Primary Efficacy



Stroke



	LAA Closure Group Events (per 100 pt-yrs)	Warfarin Group Events (per 100 pt-yrs)	Relative Risk (95% CI)
ITT	1.5 (16 / 1047.1)	3.7 (21 / 563.9)	0.41 (0.22, 0.82)
Post-procedure	1.3 (13 / 1037.0)	3.7 (21 / 563.9)	0.34 (0.17, 0.70)
Per-protocol	1.2 (12 / 1011.6)	3.6 (20 / 563.3)	0.33 (0.16, 0.71)
Terminal Therapy	1.3 (9 / 713.1)	3.6 (20 / 563.3)	0.36 (0.16, 0.79)

Functional impact endpoint is either an MRS Increase ≥ 2 or Death.

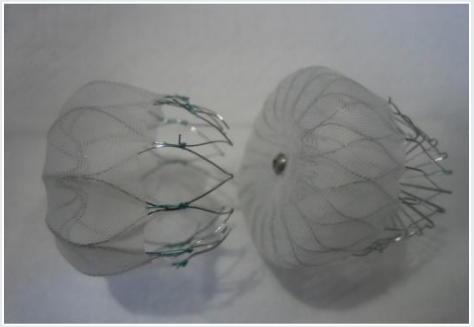
Functional Impact of Clinical Events: Significant Disability or Death

Reddy VY et al. *Circulation.* published online January 16, 2013

Devices for percutaneous left atrial appendage closure

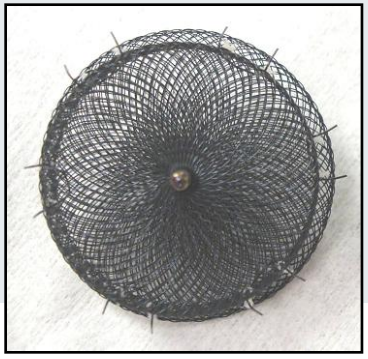
PLAATO

WATCHMAN



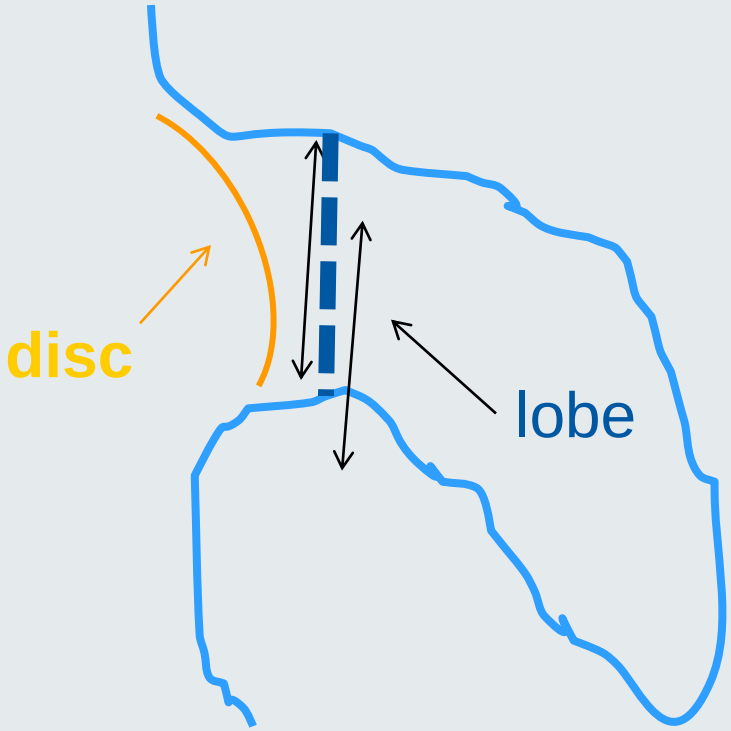
One body (anchoring and sealing)

Amplatzer Cardiac Plug (ACP)

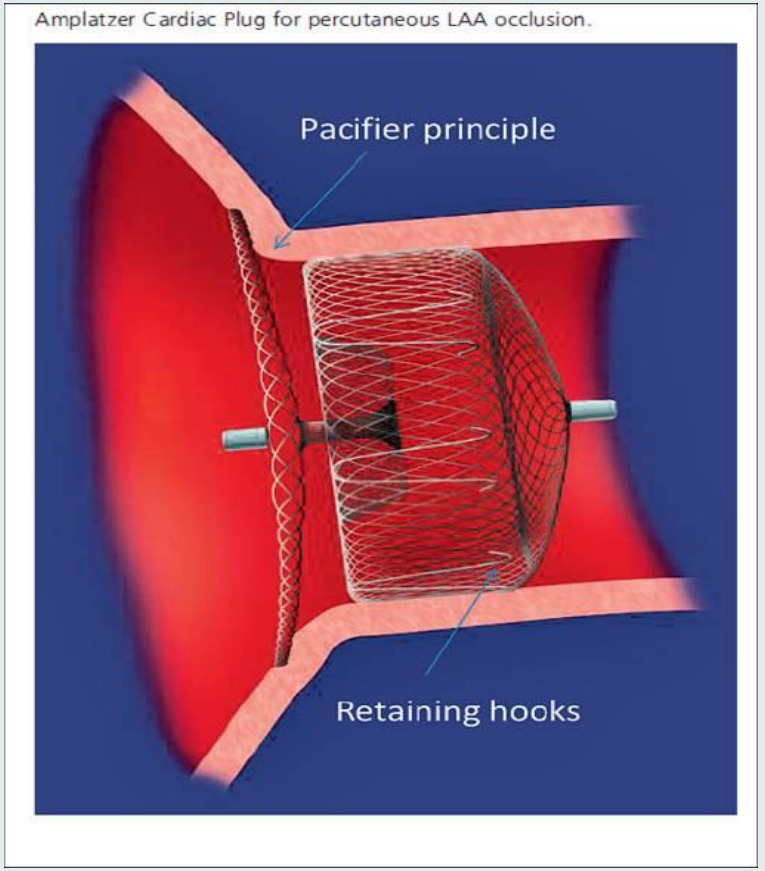


Two bodies (anchoring and disc for sealing)

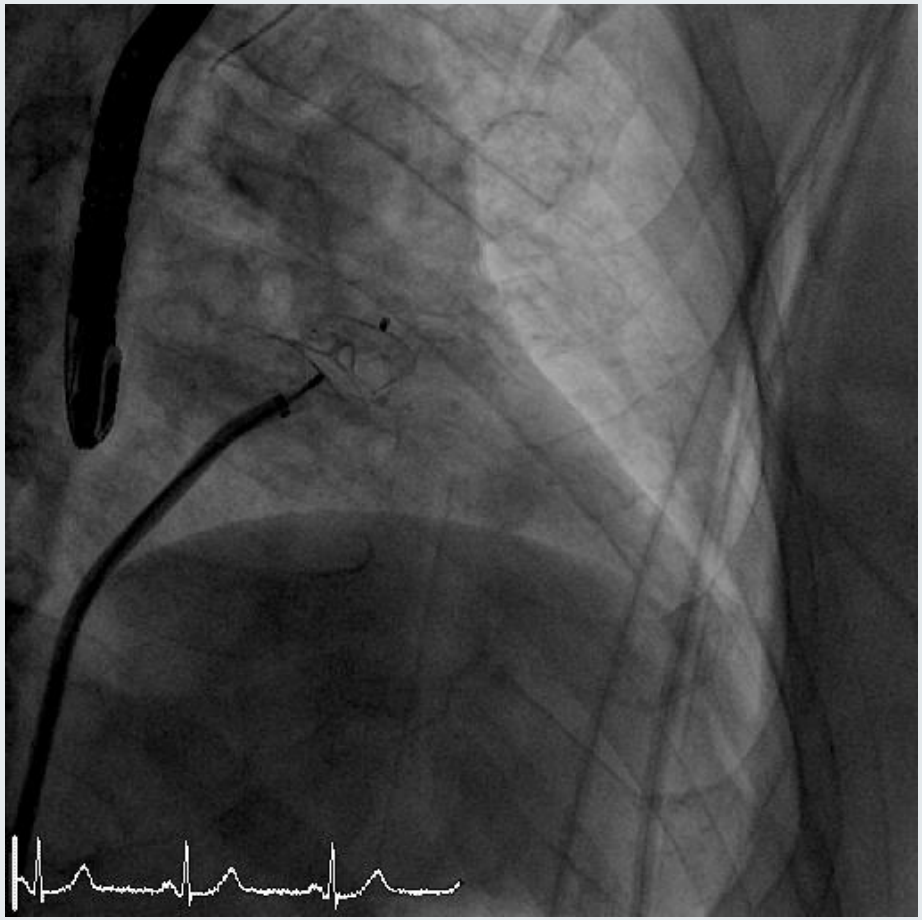
Atrial Appendix Closure Device
Amplatzer Cardiac Plug (ACP)



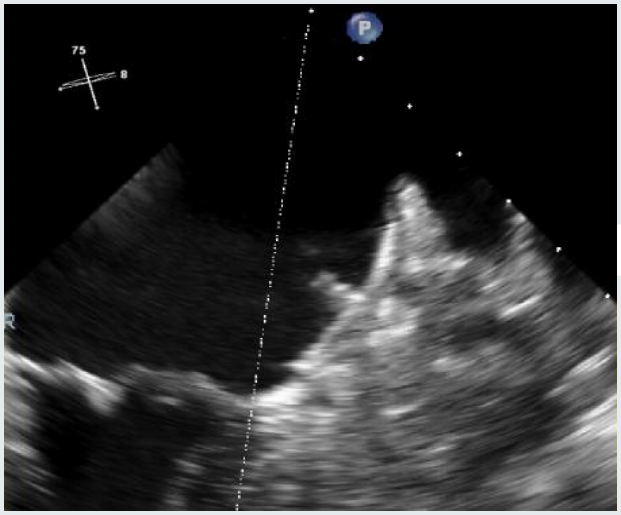
Lobe landing zone

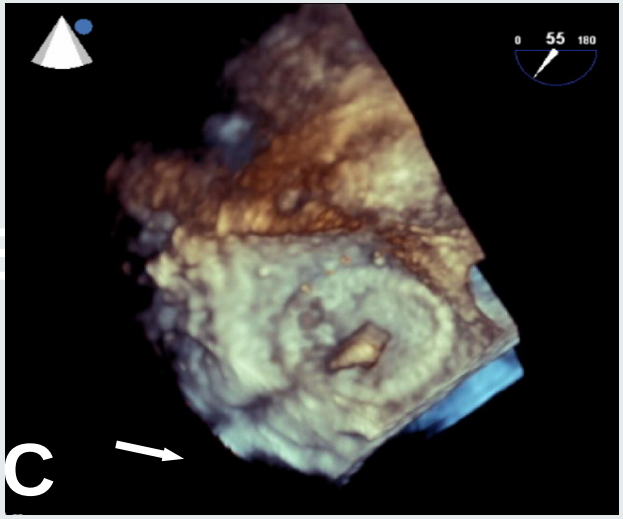


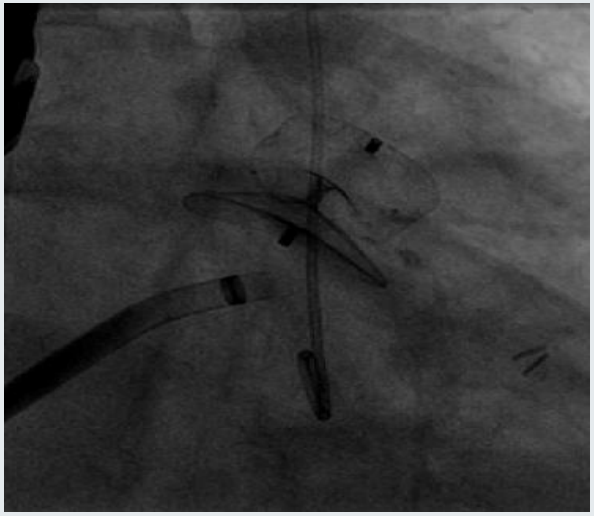
Angiography of LAA and implantation of the LAA occluder *(ACP Device)*



LAA occlusion with the ACP device

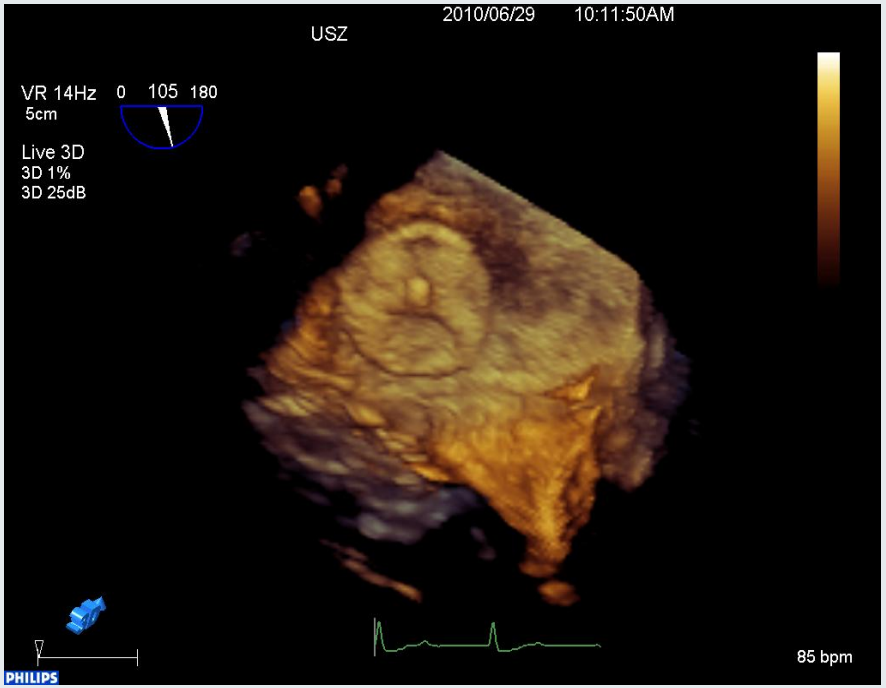






Landmesser U et al. *Eur Heart J* 2012
Jaguszewski et al. Submitted

3D Echo of LAA before and after the occlusion (using ACP)



ACP trial

- recruiting patients: estimated 3000 patients
- Aim: non-inferiority for efficacy and superiority for safety

European Heart Journal (2012) **33**, 2719–2747
doi:10.1093/eurheartj/ehs253

ESC GUIDELINES

2012 focused update of the ESC Guidelines for the management of atrial fibrillation

An update of the 2010 ESC Guidelines for the management of atrial fibrillation

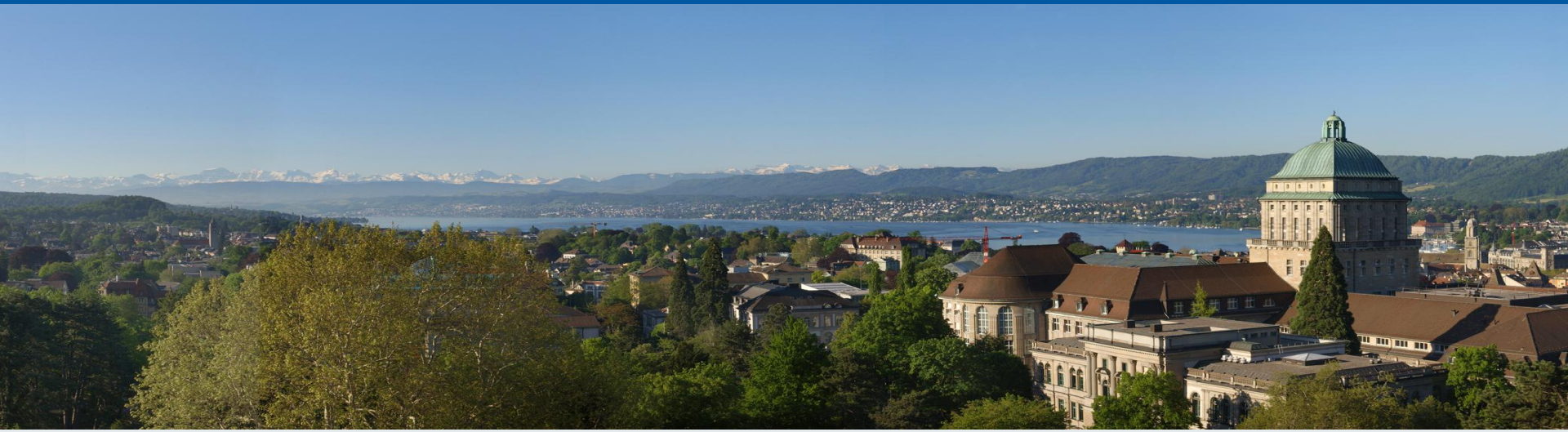
Developed with the special contribution of the European Heart Rhythm Association

Summary and Conclusions

1. In addition to novel anticoagulants, *non-pharmacological approaches* are being developed for prevention of strokes in patients with A.fibrillation

2. The PROTECT-AF study has supported the concept that LAA closure can prevent strokes in patients with A.fib. - the safety of this approach is improving. PREVAIL and ACP trials are ongoing.

3. In particular, in patients with A.fib. and contra-indications for anticoagulation and a relevant cerebro-ischemic risk, LAA closure representa a possible treatment option.

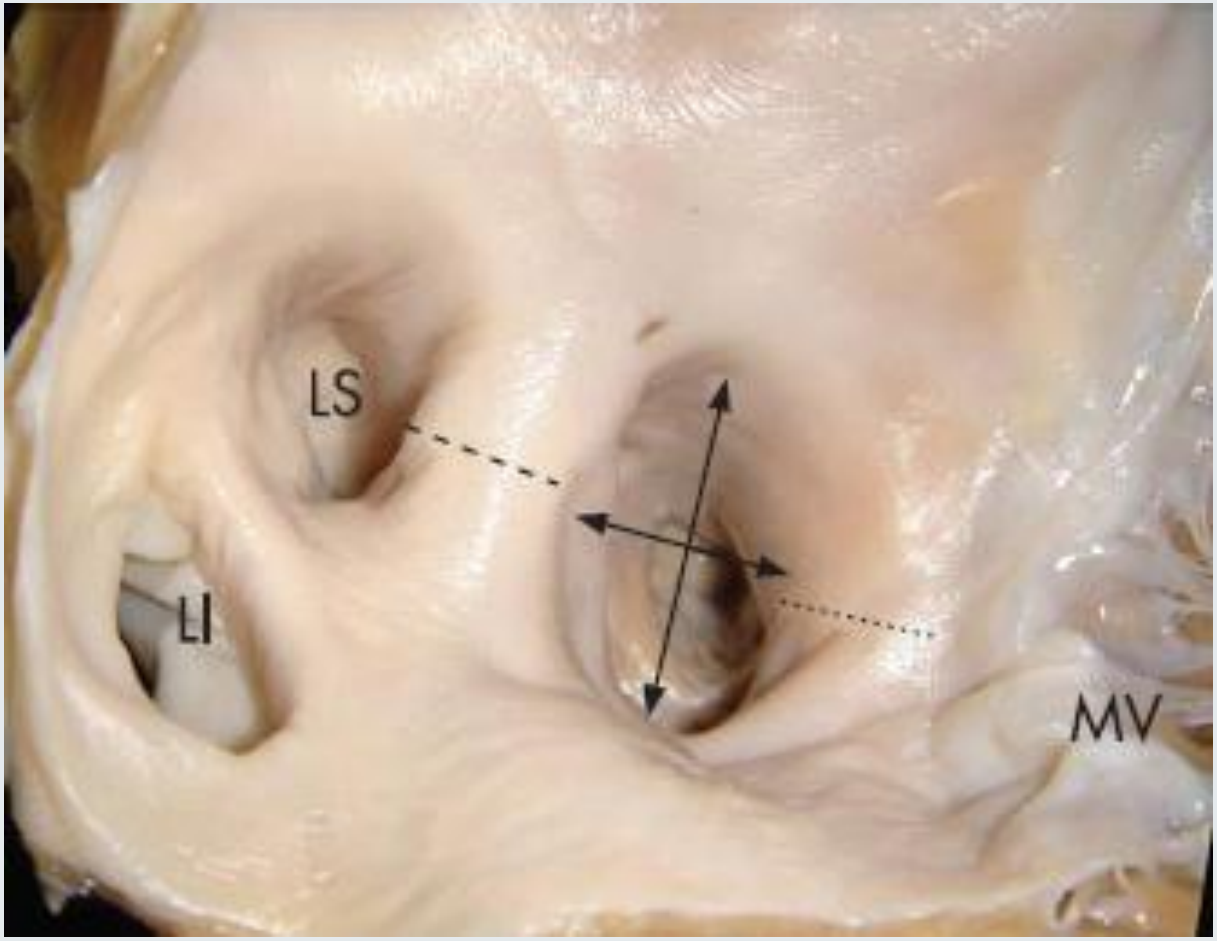


Thank you

UniversityHospital Zurich

University of Zurich[UZH]

LAA – anatomical considerations



JACC Vol. 23, No. 3
March 1, 1994:599–607

Assessment of Left Atrial Appendage Function by Biplane Transesophageal Echocardiography in Patients With Nonrheumatic Atrial Fibrillation: Identification of a Subgroup of Patients at Increased Embolic Risk

ANDREAS MÜGGE, MD, FACC, HENNING KÜHN, PETER NIKUTTA, MD, JOCHEN GROTE, MD, J. ANTONIO G. LOPEZ, MD, FACC, WERNER G. DANIEL, MD, FACC
Hannover, Germany

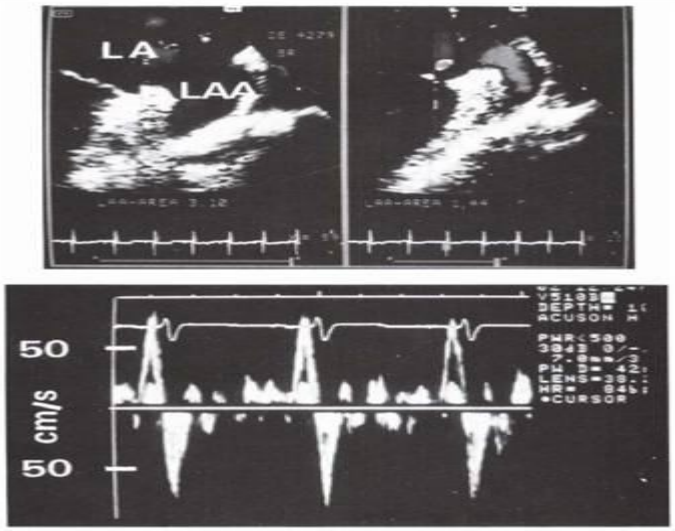


Figure 2. Demonstration of the left atrial appendage (LAA) by transesophageal echocardiography (vertical view) in a patient with sinus rhythm. **Top,** The maximal **(left panel,** 3.10 cm) and minimal **(right panel,** 1.44 cm) areas of the left atrial appendage cavity during one cardiac cycle (54% area change). **Bottom,** Pulsed Doppler signal measured at the outlet of the appendage. Note the biphasic flow patterns with filling and emptying velocities >50 cm/s. LA = left atrium.

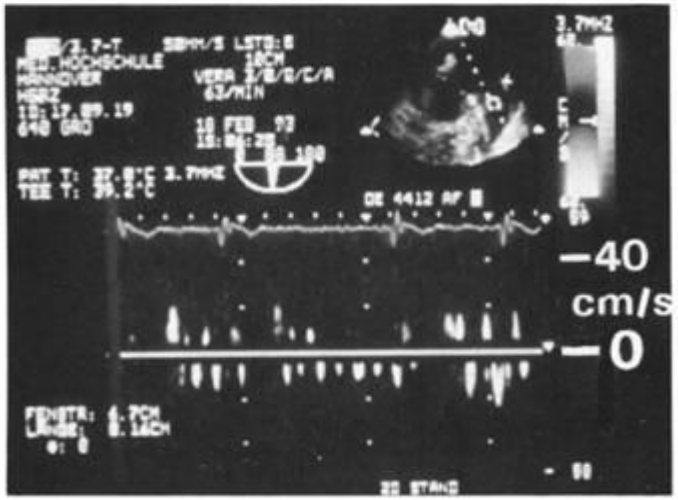
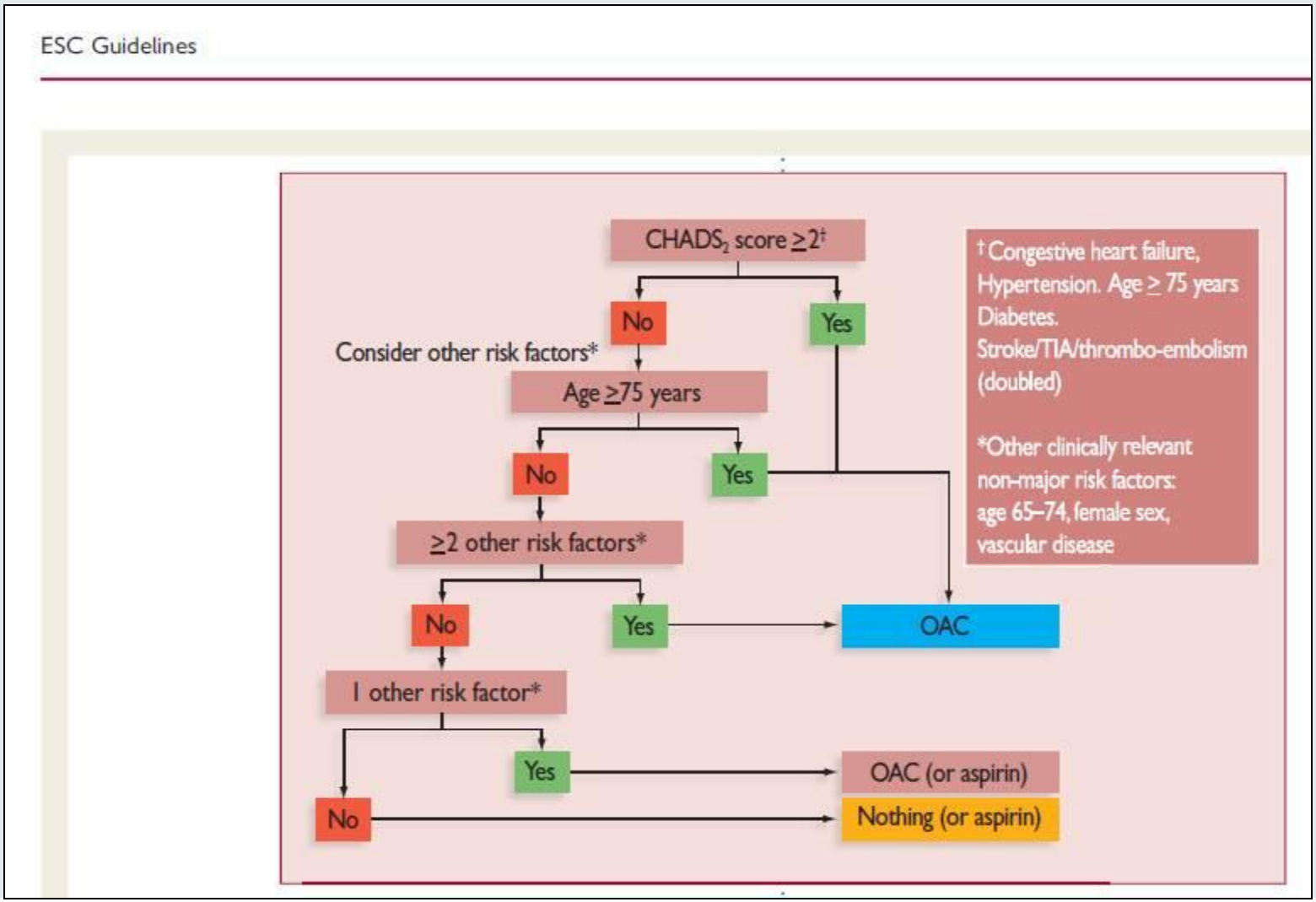


Figure 5. Pulsed Doppler spectrum measured at the outlet of the left atrial appendage in a patient with chronic nonrheumatic atrial fibrillation. Note that there is near negligible flow measurable in this patient.

Vorhofflimmern - Antikoagulation



Eur Heart J 2010

Stroke risk in patients with nonvalvular atrial fibrillation

CHADS2 risk criteria	Score
Prior stroke or TIA	2
Age .75 y	1
Hypertension	1
Diabetes mellitus	1
Heart failure	1

Patients (N = 1733)	Adjusted stroke rate (%/y) (95% CI)	CHADS2-score
120	1.9 (1.2 to 3.0)	0
463	2.8 (2.0 to 3.8)	1
523	4.0 (3.1 to 5.1)	2
337	5.9 (4.6 to 7.3)	3
220	8.5 (6.3 to 11.1)	4
65	12.5 (8.2 to 17.5)	5
5	18.2 (10.5 to 27.4)	6

ESC Guideline 2010 – HAS-BLED Bleeding Risk Score

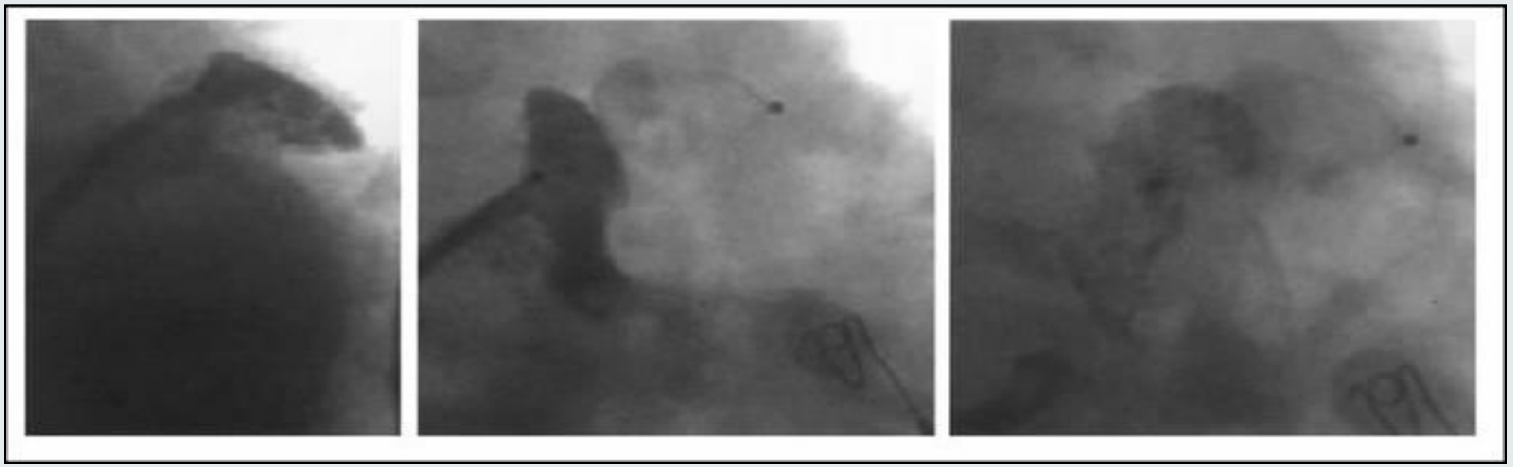
Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

[a]'Hypertension' is defined as systolic blood pressure >160 mmHg. 'Abnormal kidney function' is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥200 μmol/L. 'Abnormal liver function' is defined as chronic hepatic disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin >2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3 x upper limit normal, etc.). 'Bleeding' refers to previous bleeding history and/or predisposition to bleeding, e.g. bleeding diathesis, anaemia, etc. 'Labile INRs' refers to unstable/high INRs or poor time in therapeutic range (e.g. <60%). Drugs/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse, etc.
INR = international normalized ratio. Adapted from Pisters *et al.*[60]

Eur Heart J 2010

Amplatzer atrial septal occluder to occlude LAA



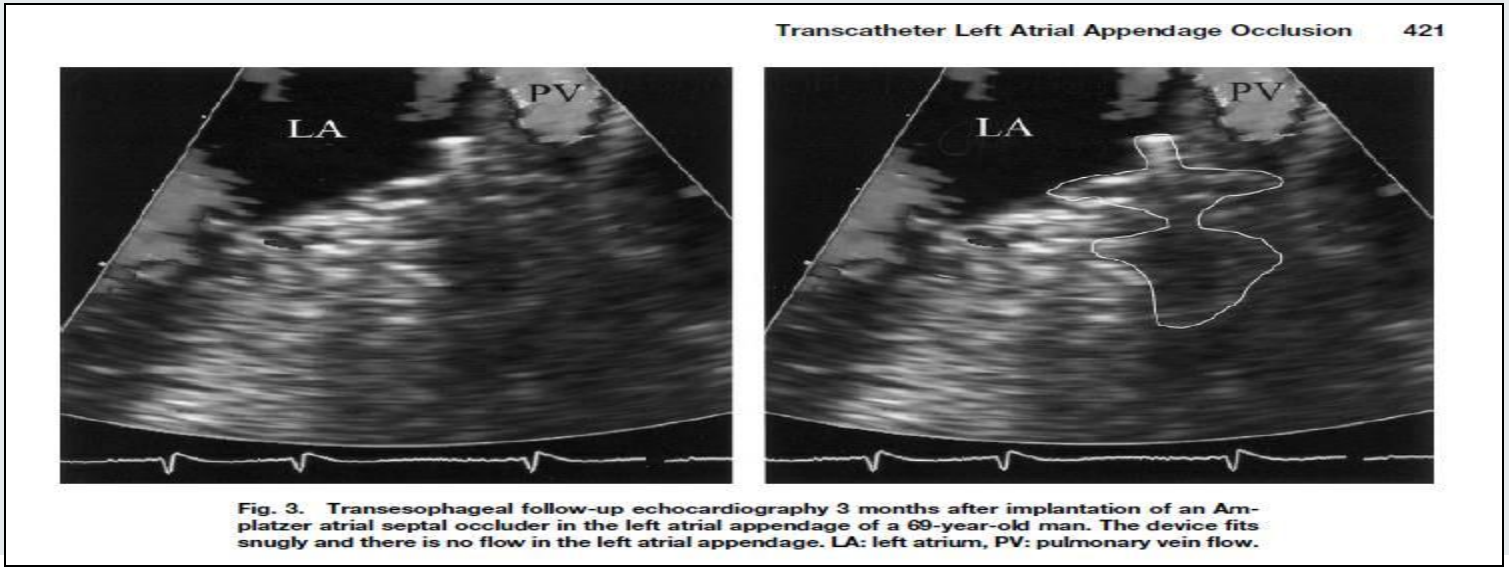


Fig. 3. Transesophageal follow-up echocardiography 3 months after implantation of an Amplatzer atrial septal occluder in the left atrial appendage of a 69-year-old man. The device fits snugly and there is no flow in the left atrial appendage. LA: left atrium, PV: pulmonary vein flow.

Meier B et al. *Catheter Cardiovasc Interv*. 2003; 60:417-22

Left atrial appendage flow velocity and spontaneous echo contrast/thrombus

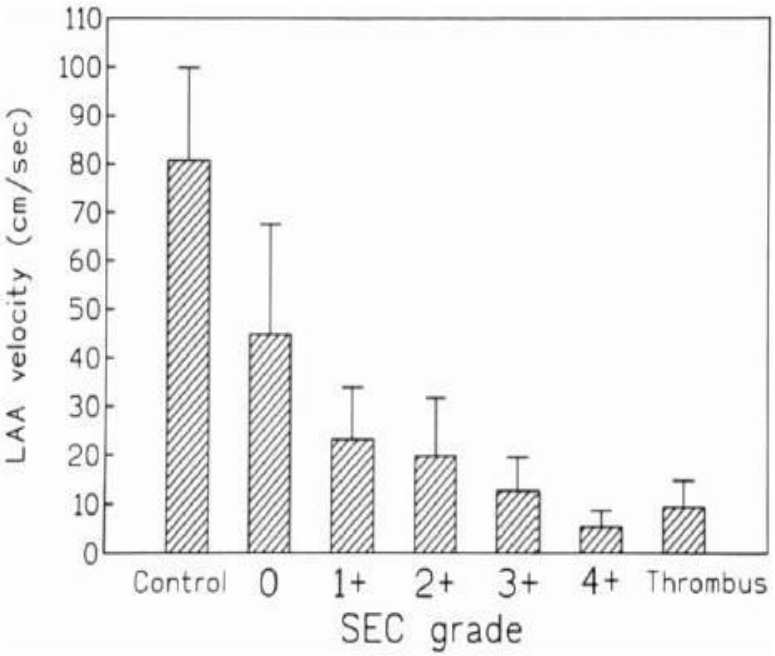


Figure 2. Mean left atrial appendage (LAA) Doppler velocity in control patients and in subgroups of patients with increasing grades of severity of left atrial spontaneous echo contrast (SEC) and left atrial thrombus.

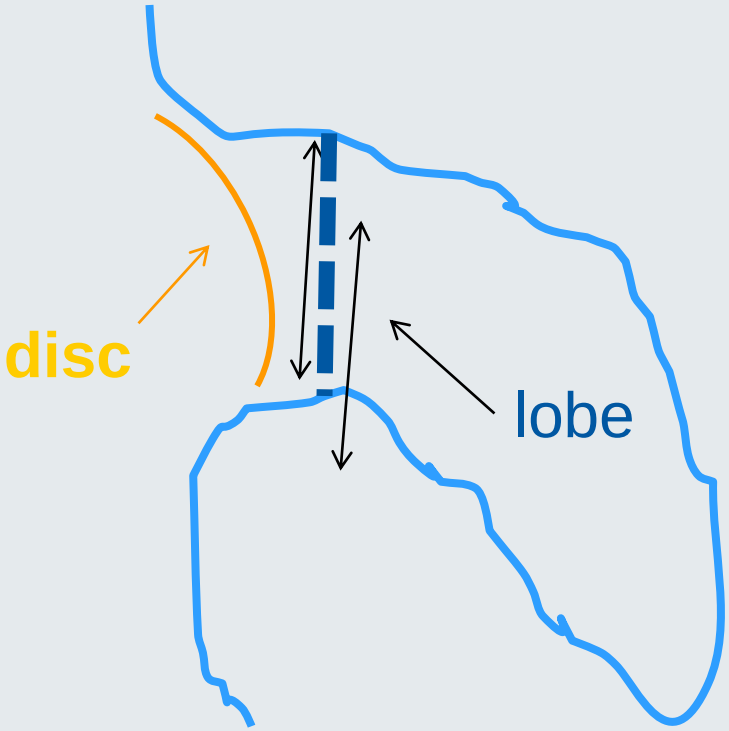
Table 3. Clinical and Echocardiographic Characteristics of Patients With and Without Left Atrial Thrombus

	Left Atrial Thrombus		
	No (n = 125)	Yes (n = 15)	p Value
LAA vel (cm/s)	32 ± 21	9 ± 6	<0.001
LA SEC	64 (51%)	14 (93%)	0.005
MS/MVR	23 (18%)	8 (53%)	0.006
Paroxysmal AF	50 (40%)	0 (0%)	0.006
LAA shear rate (s^{-1})	51 ± 95	99 ± 77	0.027
Chronic AF	67 (54%)	13 (87%)	0.033
Ist episode AF	8 (7%)	2 (13%)	NS
Mitral regurgitation	35 (28%)	5 (33%)	NS
LA area (cm^2)	25 ± 15	28 ± 10	NS
LV FS <28%	21 (17%)	1 (7%)	NS
Age (yr)	64 ± 12	66 ± 10	NS
Anticoagulation (H/C)	66 (53%)	12 (80%)	NS
Aspirin therapy	32 (26%)	2 (13%)	NS

Values presented are mean value ± SD or number (%) of patients. Abbreviations as in Tables 1 and 2.

Fatkin D et al.; JACC *1994;* 23:961-9

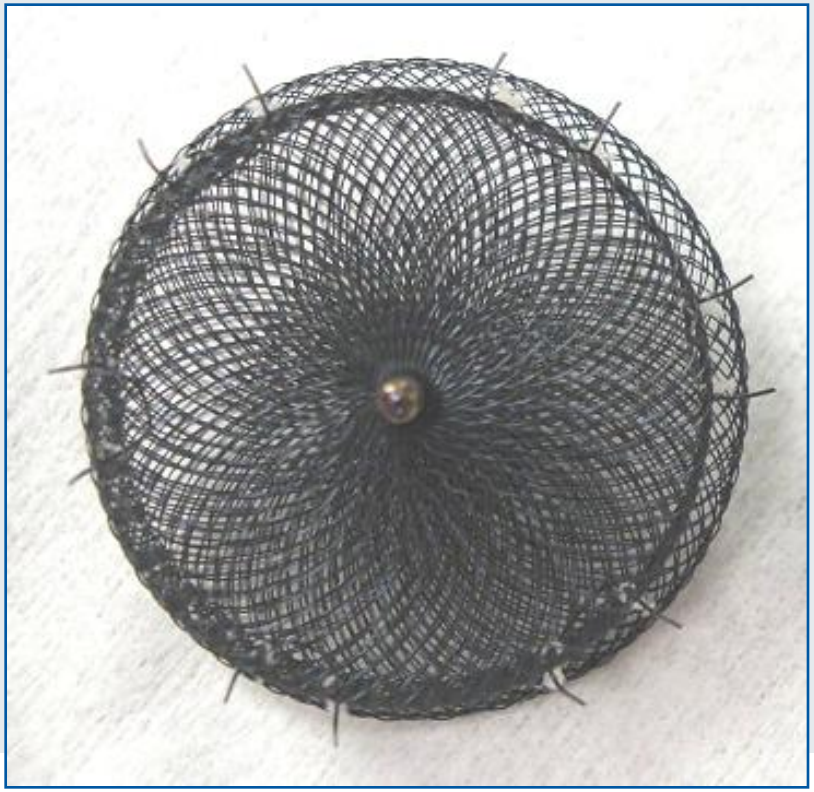
Correct sizing depends only on accurate measurement of lobe landing zone



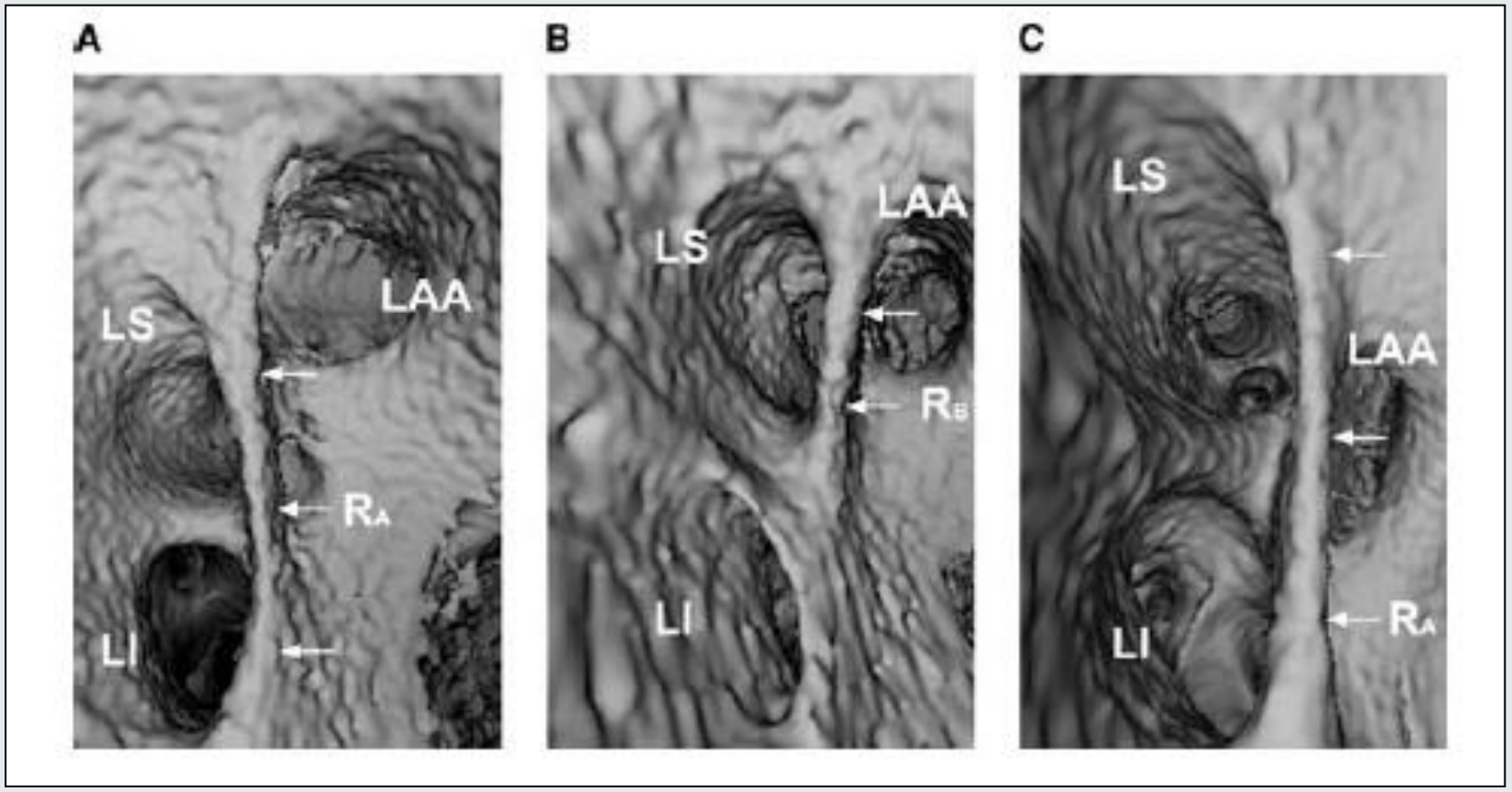
Lobe landing zone

A C P

Amplatzer Cardiac Plug



Virtual endoscopic view of the left superior (LS) and left inferior (LI) PVs and LAA



Wongcharoen W et al. J Cardiovasc Electrohpysiol 2006;17:951-956.

PROTECT AF

	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

*Defined as the need for percutaneous or surgical drainage. †Major bleeding is defined as a bleeding event that required at least 2 units of packed red blood cells or surgery to correct. ‡Of the seven haemorrhagic strokes, six resulted in death (intervention group, n=1; control group, n=5). §An oesophageal tear and a procedure-related arrhythmia.

Table 3: Adverse events

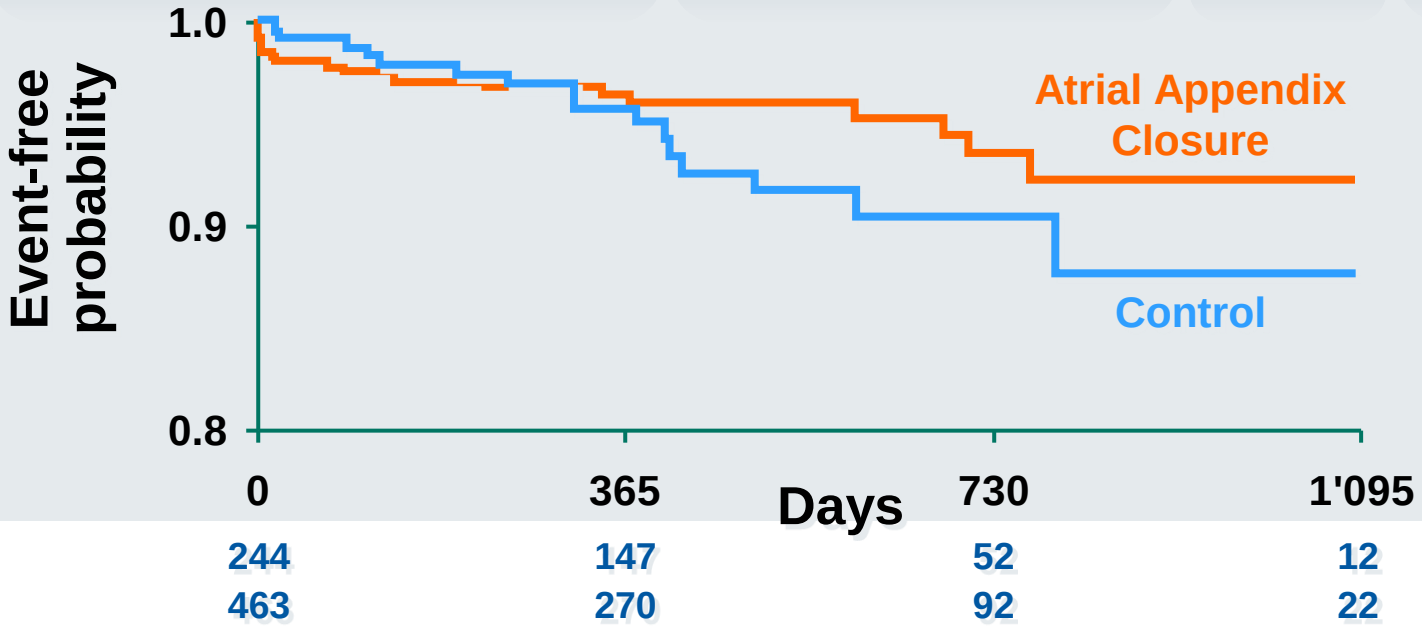
Holmes DR, et al. for the PROTECT AF Investigators. LANCET 2009;374:534-42.

Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators*

Lancet 2009; 374: 534–42

	Device			Control					
Cohort	Events (no.)	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)	Rel. Risk (95% CI)	Non-inferiority	Superiority
900 pt-yr	20	582.3	3.4 (2.1, 5.2)	16	318.0	5.0 (2.8, 7.6)	0.68 (0.37, 1.41)	0.998	0.837

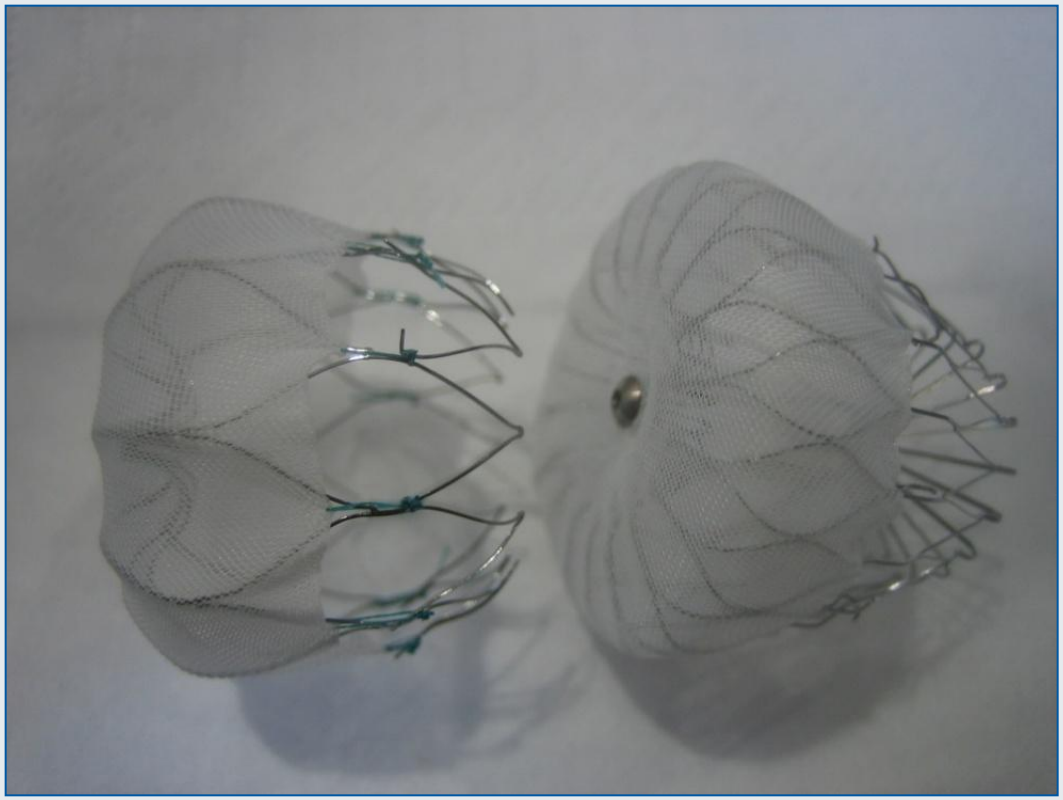


ITT Cohort:
Non-inferiority criteria met

Differences between PLAATO/WATCHMAN and ACP in terms of function

- PLAATO/WATCHMAN have one body which is responsible for anchoring as well as for sealing.
- ACP has two bodies, the puck for anchoring and the disc for sealing.

WATCHMAN

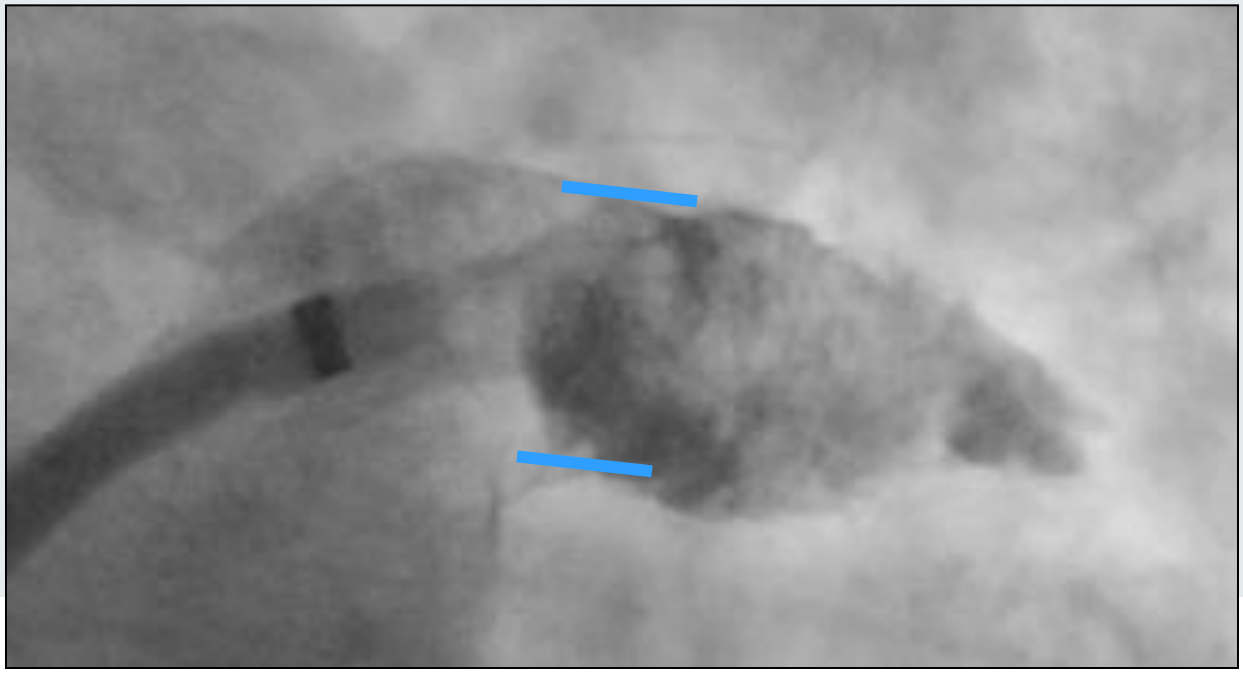


Baseline Risk Factors			
	WATCHMAN N= 463	Control N= 244	P-value
CHADS Score			
1	158/463 (34.1)	66/244 (27.0)	0.3662
2	157/463 (33.9)	88/244 (36.1)	
3	88/463 (19.0)	51/244 (20.9)	
4	37/463 (8.0)	24/244 (9.8)	
5	19/463 (4.1)	10/244 (4.1)	
6	4/463 (0.9)	5/244 (2.0)	
AF Pattern			
Paroxysmal	200/463 (43.2)	99/244 (40.6)	0.7623
Persistent	97/463 (21.0)	50/244 (20.5)	
Permanent	160/463 (34.6)	93/244 (38.1)	
Unknown	6/463 (1.3)	2/244 (0.8)	
LVEF %	57.3 ± 9.7 460 (30.0, 82.0)	56.7 ± 10.1 239 (30.0, 86.0)	0.4246

Reading the lobe landing zone

- parallel landing runway of 10mm length desired

- for secure ACP lobe enchoring the distal part of the landing zone should be trabeculated (contrast trap)



ACP Implant Sizing

1. Read the desired lobe landing zone.
2. Measure the landing zone at this position.
3. Estimate the space behind the landing zone.

Small space:
Landing zone + 3 mm

Lobe deployment
at the landing zone

Big space:
Landing zone + 5 mm

Sandwich technique

Recommendations for transcatheter LAA-occlusion

- Extended LAA imaging (TEE, CT, MRI) prior implantation (LAA morphology, thrombus detection)
- Avoiding high transseptal puncture
- All 3 implants appropriate for long, cylindric LAA body
- Tapered LAA-body with big entrance cross-section diameter and short LAA-body length bares an increased risk of device embolization and LAA-perforation. This is true in particular for ocluders of PLAATO- and WATCHMAN-type.

Recommended requirements to start transcatheter LAA-occlusion

- Experience in the transseptal puncture technique
- Experienced, hand-in-hand assistence
- Experienced TEE-guidance
- Experience in the pericardial puncture technique
- Simulator training
- At least three proctor guided implantations

Warfarin Discontinuation

87% of implanted subjects were able to cease warfarin at 45 days and the rate further increased at later time points

Visit	Watchman N/Total (%)
45 day	349/401 (87.0)
6 month	347/375 (92.5)
12 month	261/280 (93.2)
24 month	95/101 (94.1)

Reasons for remaining on warfarin therapy after 45-days:

- Observation of flow in the LAA (n = 30)
- Physician Order (n = 13)
- Other (n = 9)

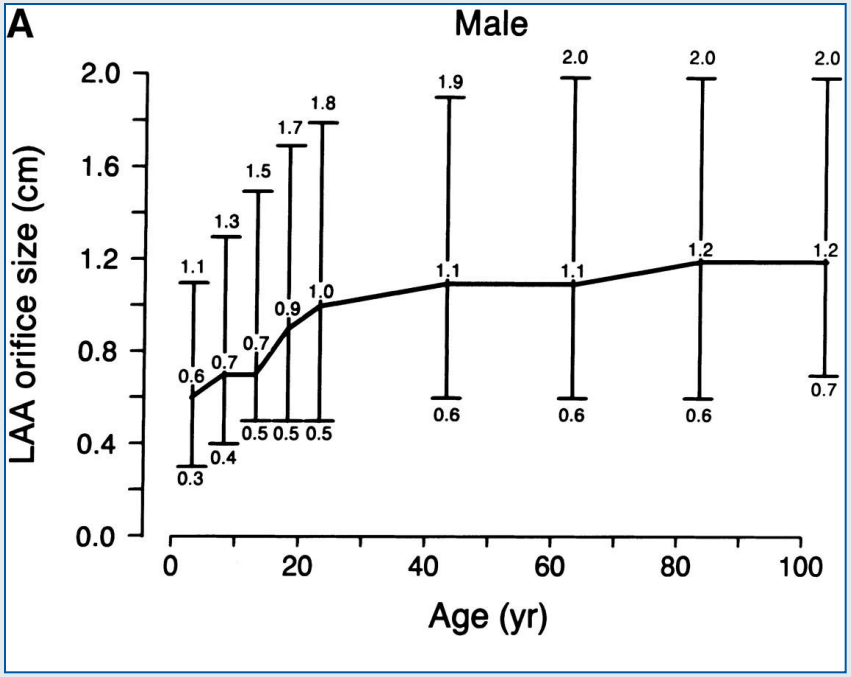
Abklärung und mögliche Indikationen

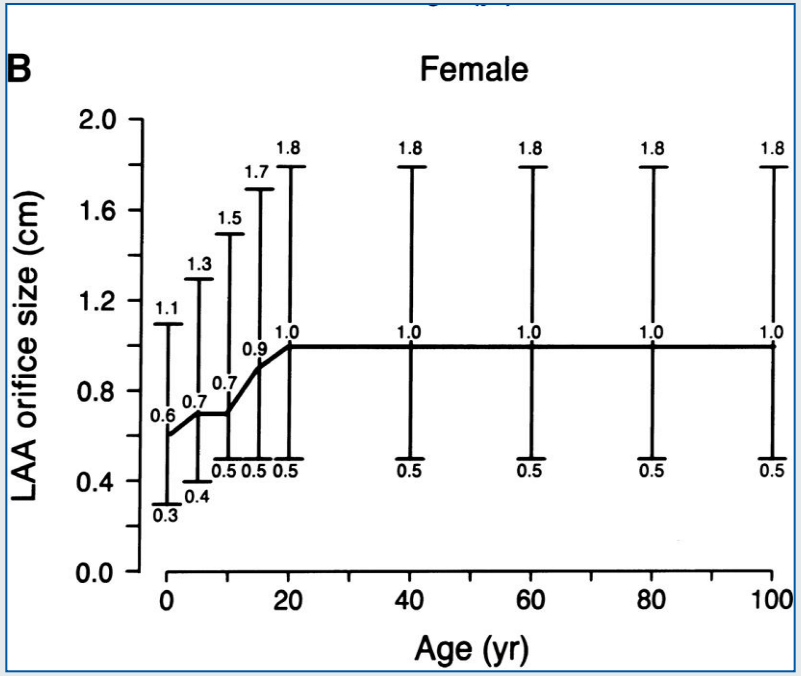
Abklärung: TEE (Ausschluss von Thromben)

Indikation:

- Patienten mit CHADS Score (≥2) und erhöhtem Blutungsrisiko unter oraler Antikoagulation

Orifice size of left atrial appendage (LAA) as a function of age for A, male subjects, and B, female subjects

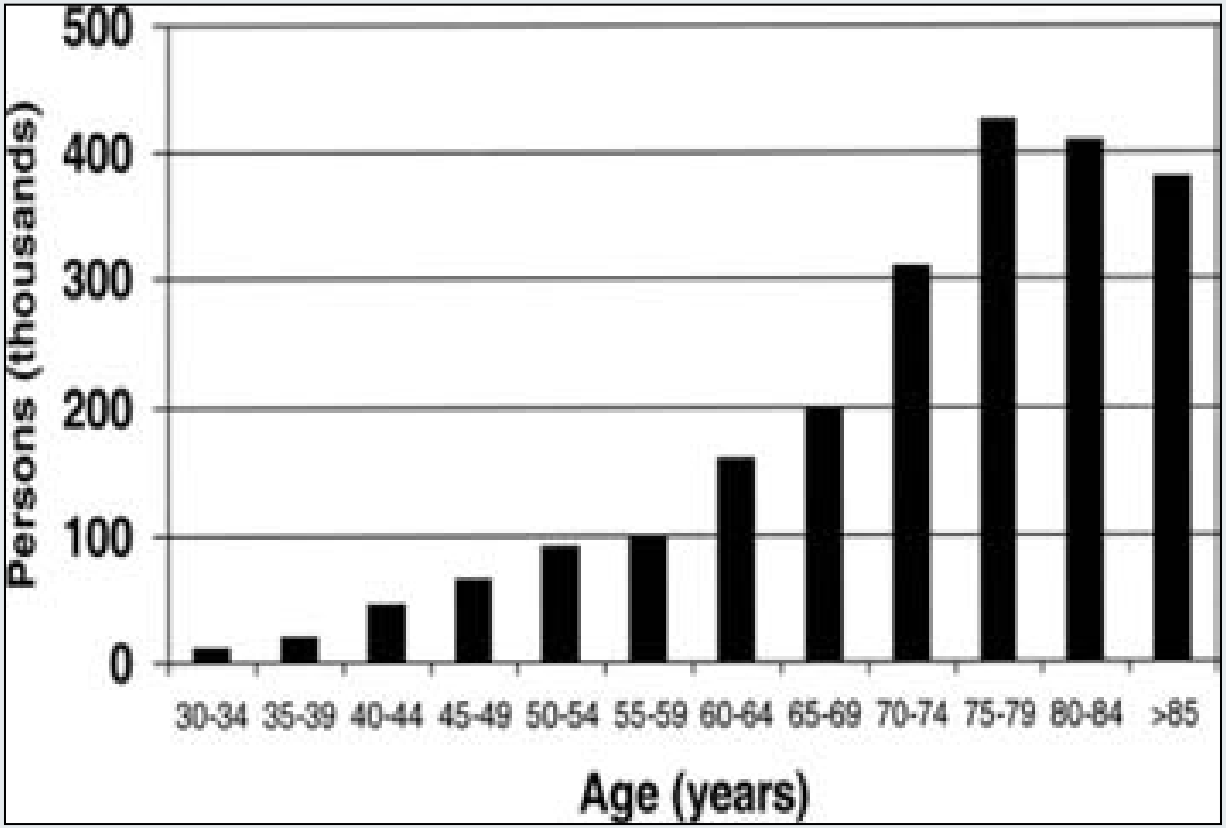




Veinot, J. P. et al. Circulation 1997;96:3112-3115

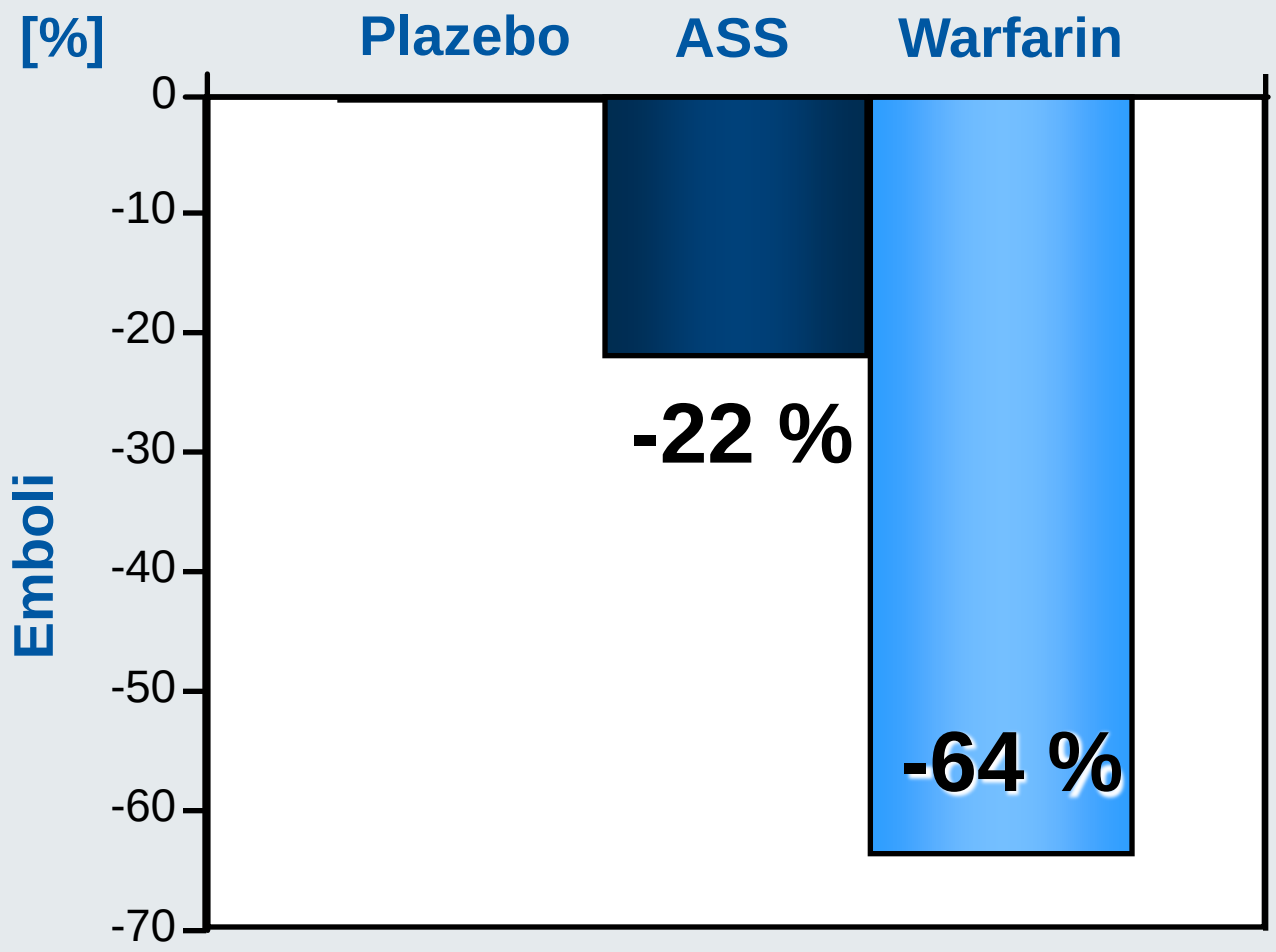
Age Dependent Prevalence of Atrial Fibrillation

0.4% - 1% in the general population
8% in individuals of 80 yrs and older



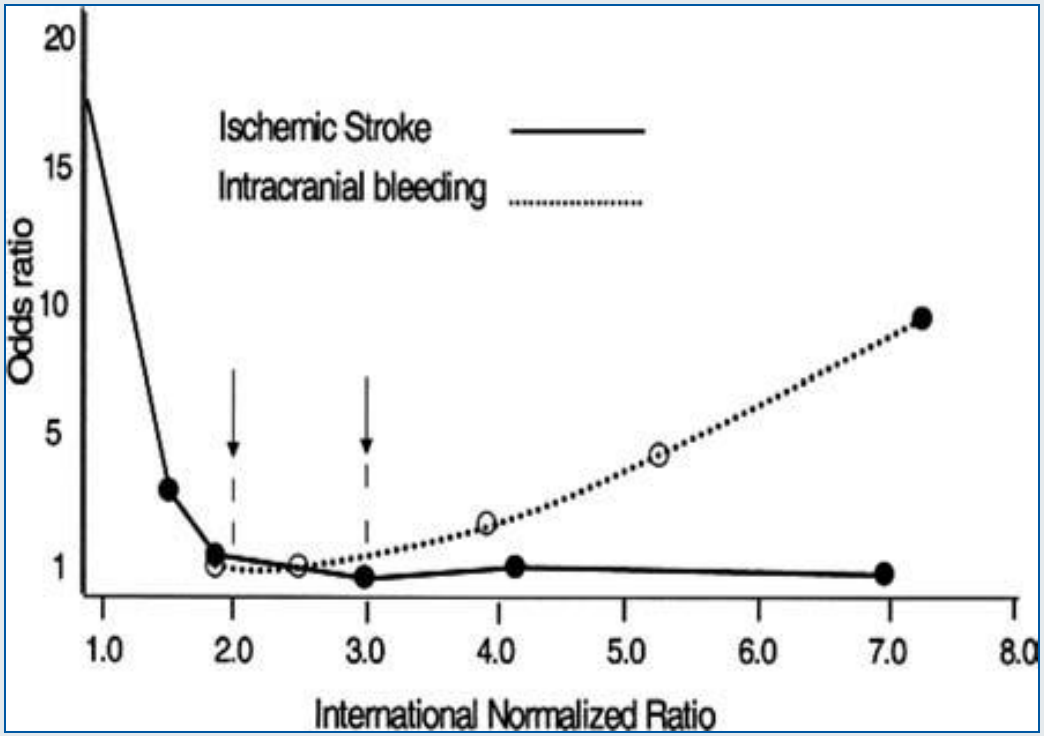
ACC/AHA/ESC 2006 Guidelines. Europace 2006;8:651-745.

Risk Reduction by ASS / Warfarin



Hart RG et al. *Ann Intern Med* 1999;131:492-501

Adapted odds ratios for ischemic stroke and intracranial bleeding in dependence of anticoagulation intensity



ACC/AHA/ESC 2006 Guidelines. Europace 2006;8:651-745.

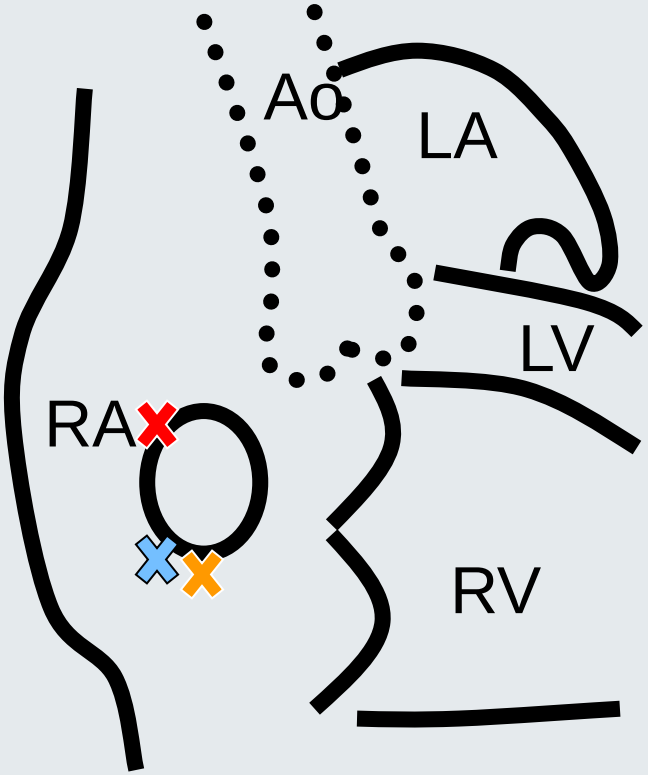
2x intracranial hemorrhage rate when INR > 3.0 !

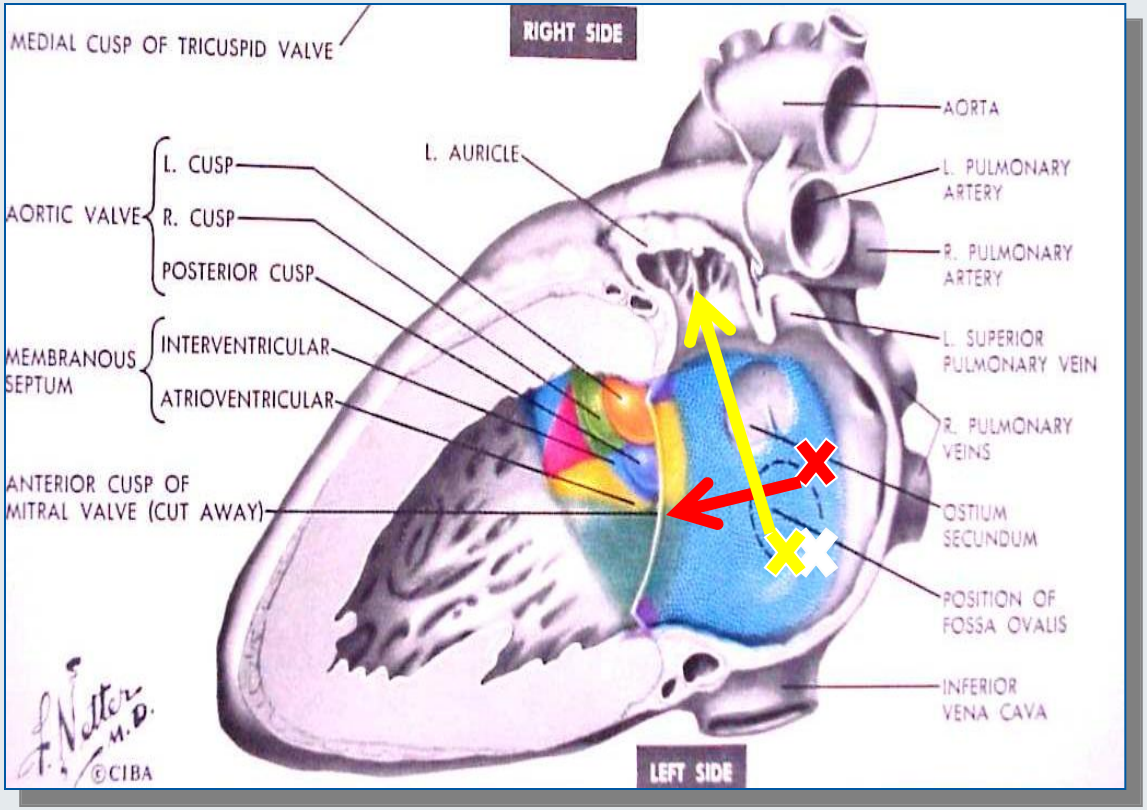
70% increase in stroke rate when INR < 2.0 !

Feld S. http://stanleyfeldmdmace.typepad.com/repairing_the_healthcare_/2008/03/safety-net-hosp.html.

Transseptal puncture

- Ablation for AFib
- Mitral valve intervention



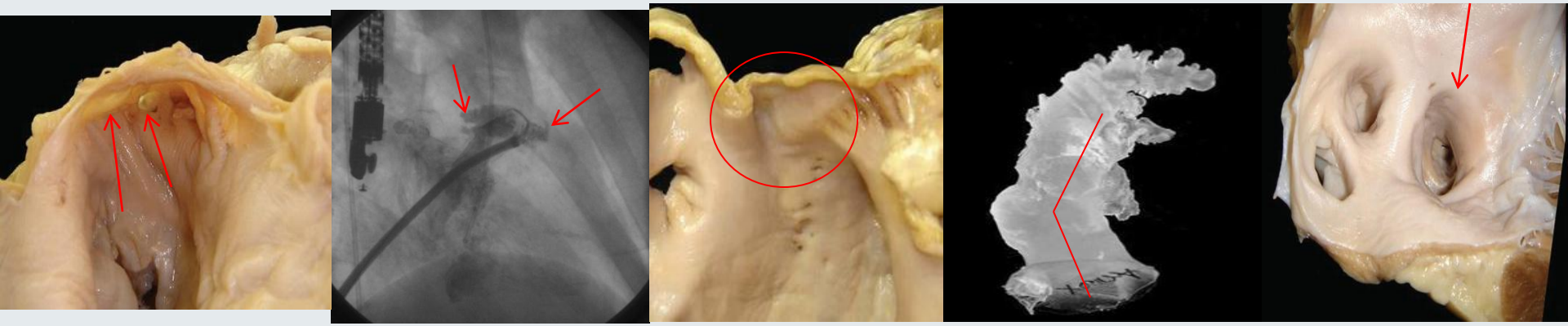


- LAA occlusion

LAA Anatomy

1. wall often thin
2. multiple lobes often
3. entrance mostly not trabeculated
4. neck mostly angulated
5. entrance always ovale

1. 2. 3. 4. 5.



Su P et al.
Heart 2008;94:1166-70

Park J-W et al.
Asklepios Hospital Hamburg Harburg, Germany

Patienten-Aufklärung

Patienteninformation

Einverständniserklärung zum Katheterverschluss des linken Vorhofohrs bei Vorhofflimmern

Ich wurde über den bei mir vorgesehenen Eingriff informiert und bin damit einverstanden.

Ich wurde über den Zweck, die Erfolgschancen und das Risiko sowie andere Behandlungsmöglichkeiten informiert. Ich weiss, dass während der Durchführung der Katheterbehandlung meine Ärztin/mein Arzt je nach Situation zusätzliche Massnahmen treffen muss, um das bestmögliche Resultat zu erreichen. Dies kann insbesondere den Einsatz einer Ultraschalluntersuchung durch die Speiseröhre (transösophageale Echokardiographie) oder einer Ultraschalluntersuchung im Herzen (intrakardiale Ultraschalluntersuchung) notwendig machen. Ich weiss, dass in wenigen Fällen die Schirmplatzierung nicht durchgeführt werden kann und eine notfallmässige oder geplante operative Behandlung angeschlossen werden muss. Ich bin darüber orientiert, dass sich in seltenen Fällen der Schirm kurz nach dem Einsetzen lösen kann und dann mittels Katheter oder mittels Operation aus dem Herzen oder einem Blutgefäss herausgeholt werden muss. Ich weiss, dass die Behandlung für ein halbes Jahr die Behandlung mit blutgerinnungshemmenden Medikamenten nötig macht. Andere ernsthafte Komplikationen sind eine Luftembolie in die Arterien oder eine Verletzung der Herzwand oder von Blutgefässen. Diese treten insgesamt sehr selten (< 1%) auf. Ich weiss, dass es nach der Schirmimplantation vorübergehend zu Störungen des Herzrhythmus kommen kann, die medikamentös behandelt werden müssen.

Ich bin orientiert worden, dass in wenigen Fällen das Vorhofohr nicht vollständig verschlossen werden kann, was unter Umständen eine zweite Behandlung nötig macht.

Ich wurde auch auf die allgemeinen Risiken einer Herzkatheteruntersuchung aufmerksam gemacht. Ich weiss, dass Blutungen z. B. an der Einstichstelle und Störungen des Herzrhythmus auftreten können und behandelt werden müssen. Andere ernste Komplikationen (schwere Allergie auf die verwendeten Medikamente, Durchblutungsstörungen der Arterien und Gerinnselbildung in den Arterien, Blutung in den Herzbeutel, Nierenfunktionsstörungen, Schlaganfälle usw.) treten bei weniger als 1% der Patienten auf.

Da ein kleines Risiko einer bakteriellen Infektion besteht, werde ich ein Antibiotikum erhalten und während einiger Monate bei Zahn- oder sonstigen Eingriffen oder fiebrigen Erkrankungen Antibiotika zur Vorbeugung einnehmen müssen.

Ich habe die mir gegebenen Informationen verstanden. Meine Fragen wurden alle befriedigend beantwortet.

-Perikarderguss (1-2 %)
- Device-Embolisation (< 1 %)

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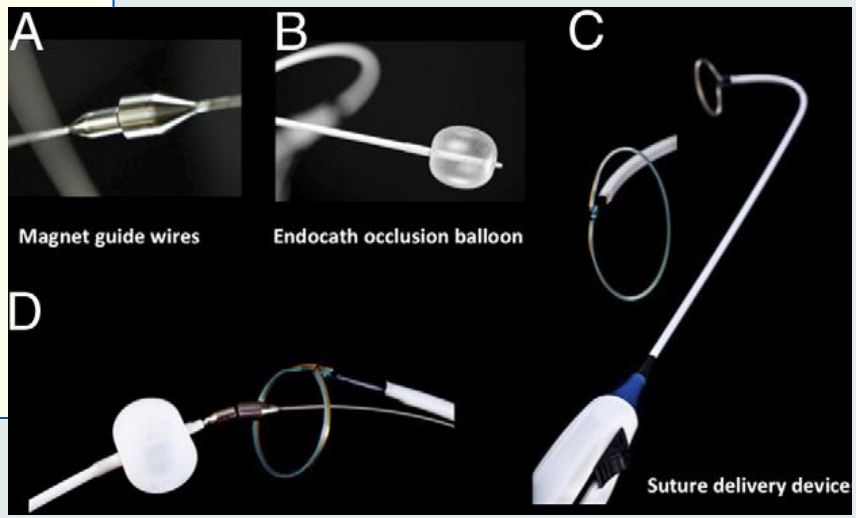
Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation

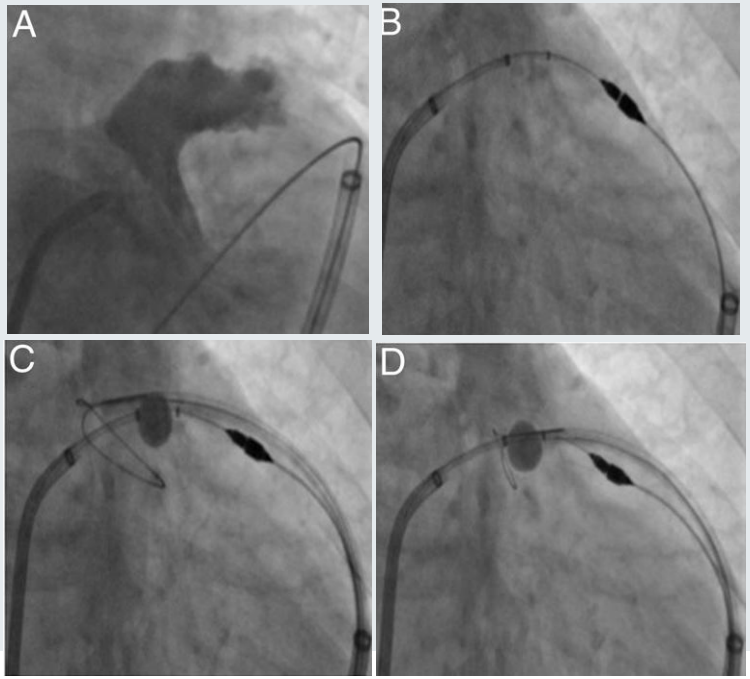
Initial Clinical Experience

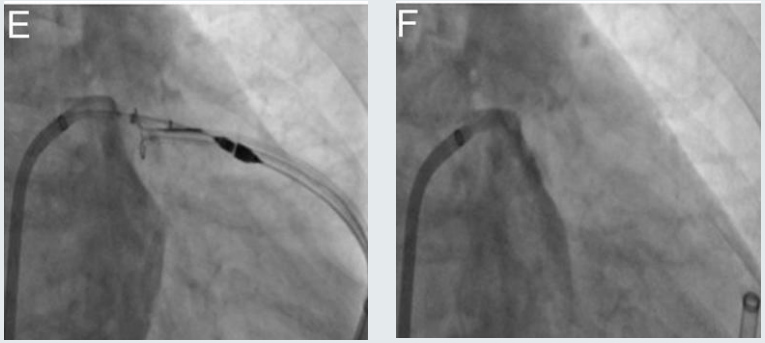
Krzysztof Bartus, MD, PHD,* Frederick T. Han, MD,† Jacek Bednarek, MD, PHD,‡ Jacek Myc, MD, PHD,* Boguslaw Kapelak, MD, PHD,* Jerzy Sadowski, MD, PHD,* Jacek Lelakowski, MD, PHD,‡ Stanislaw Bartus, MD, PHD,* Steven J. Yakubov, MD,§ Randall J. Lee, MD, PHD†‖¶

Krakow, Poland; San Francisco, California, and Columbus, Ohio



Components for the Percutaneous LAA Ligation Procedure





Fluoroscopic Guidance to Assist in the Closure of the LAA

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients with Atrial Fibrillation: 2.3 Year Follow-Up of the PROTECT AF Trial

Vivek Y. Reddy, Shephal K. Doshi, Horst Siever, Maurice Buchbinder, Petr Neuzil, Kenneth Huber, Jonathan L. Halperin and David Holmes

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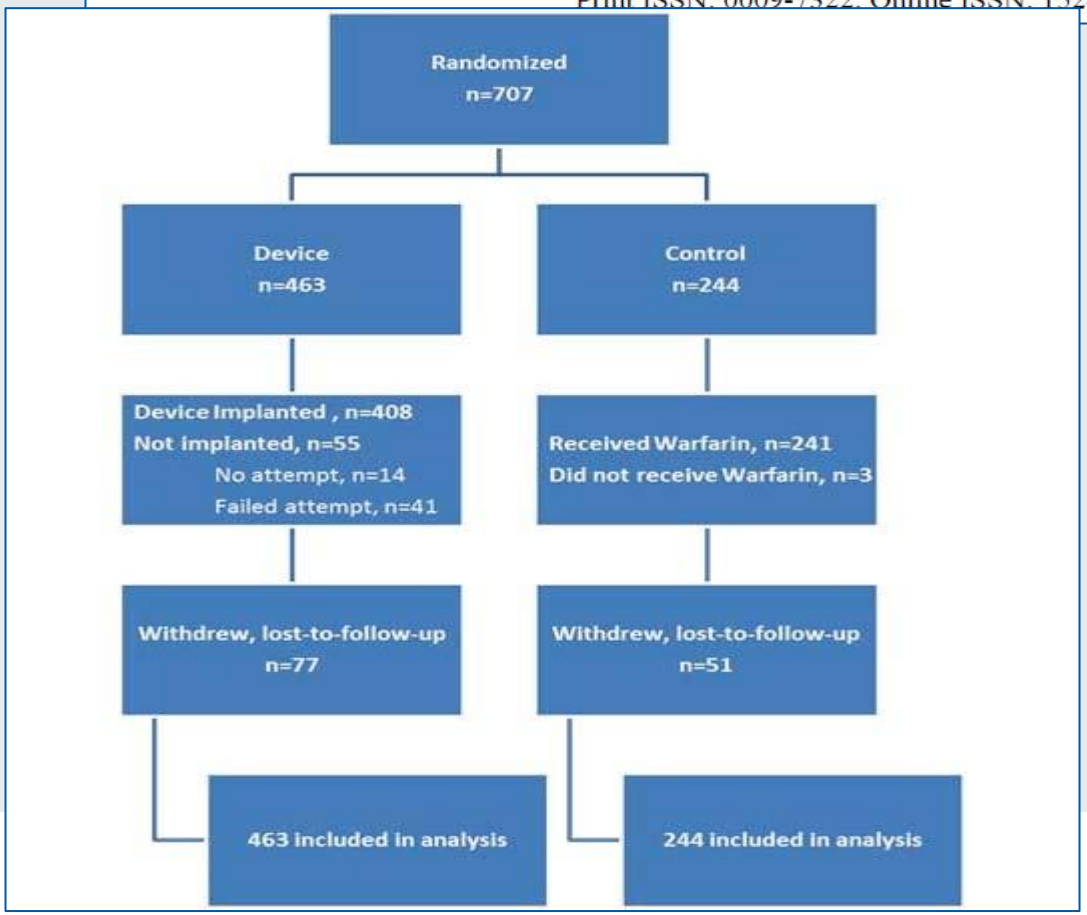


Trial Patient Profile.

Circulation: Cardiovascular Interventions

American Heart Association.

Catheter-Based Left Atrial Appendage (LAA) Ligation for the Prevention of Embolic Events Arising From the LAA

Initial Experience in a Canine Model

Randall J. Lee, MD, PhD; Krzysztof Bartus, MD; Steven J. Yakubov, MD

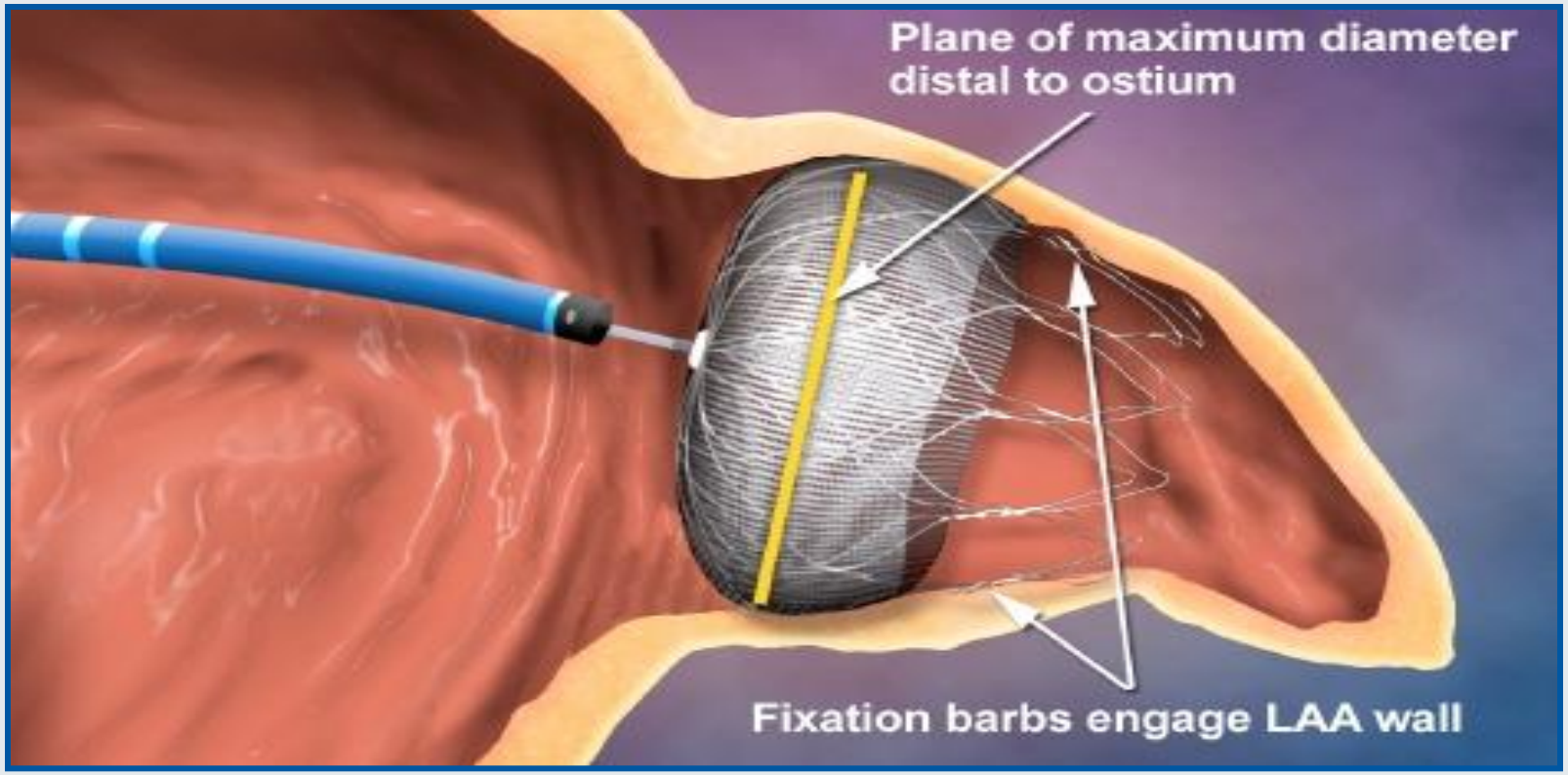
UniversitätsSpital
Zürich

PROTECT AF - Patient Demographics

Baseline Demographics			
Characteristic	**WATCHMAN N= 463**	**Control N= 244**	**P-value**
Age (years)	**71.7 ± 8.8** **463 (46.0, 95.0)**	**72.7 ± 9.2** **244 (41.0, 95.0)**	**0.1800**
Height (inches)	**68.2 ± 4.2** **462 (54.0, 82.0)**	**68.4 ± 4.2** **244 (59.0, 78.0)**	**0.6067**
Weight (lbs)	**195.3 ± 44.4** **463 (85.0, 376.0)**	**194.6 ± 43.1** **244 (105.0, 312.0)**	**0.8339**
Gender **Female** **Male**	 **137/463 (29.6)** **326/463 (70.4)**	 **73/244 (29.9)** **171/244 (70.1)**	**0.9276**

Holmes DR, et al. *Lancet* 2009; 374:534-42

WATCHMAN LAA Closure Device in situ



PREVAIL Trial is recruiting

Hemodynamics in AFib

AFib is associated with a decreased blood flow velocity in the left atrium.

In particular in the LAA, blood flow velocity frequently decreases to stasis, increasing the probability of thrombus formation in the LAA.

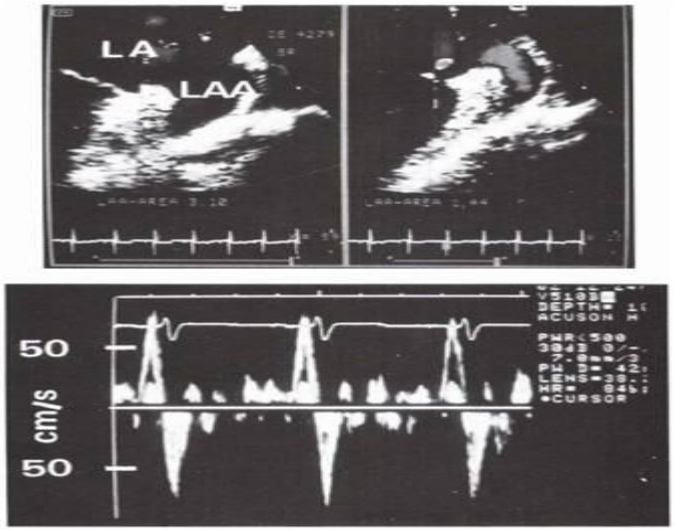


Figure 2. Demonstration of the left atrial appendage (LAA) by transesophageal echocardiography (vertical view) in a patient with sinus rhythm. **Top,** The maximal **(left panel,** 3.10 cm) and minimal **(right panel,** 1.44 cm) areas of the left atrial appendage cavity during one cardiac cycle (54% area change). **Bottom,** Pulsed Doppler signal measured at the outlet of the appendage. Note the biphasic flow patterns with filling and emptying velocities >50 cm/s. LA = left atrium.

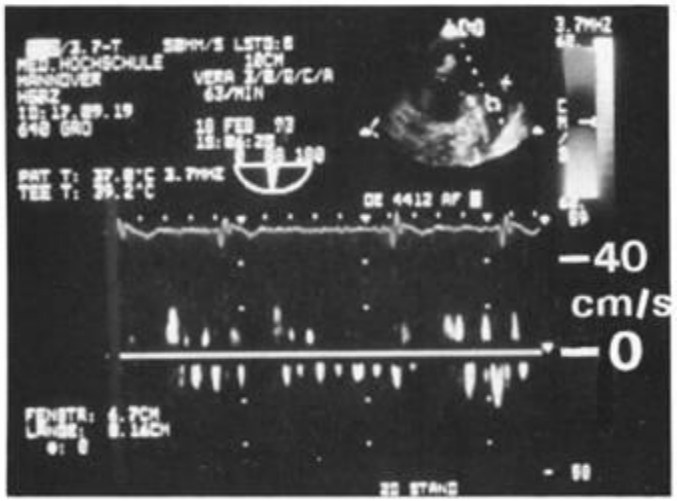


Figure 5. Pulsed Doppler spectrum measured at the outlet of the left atrial appendage in a patient with chronic nonrheumatic atrial fibrillation. Note that there is near negligible flow measurable in this patient.

Mügge A et al.; *JACC* 1994

PROTECT AF - Clinical Trial Design


WATCHMAN System

- Prospective, randomized study of WATCHMAN LAA Device vs. Long-term Warfarin Therapy in patients with non-valvular atrial fibrillation
- 2:1 allocation ratio device to control
- 707 eligible Patients enrolled
  - Device Group (463)
  - Control Group (244)
- 59 Enrolling Centers (U.S. & Europe)

Holmes DR, et al. *Lancet* 2009; 374:534-42