

Stroke Prevention in Atrial Fibrillation **Old Standards, New Developments, and** **the Future**

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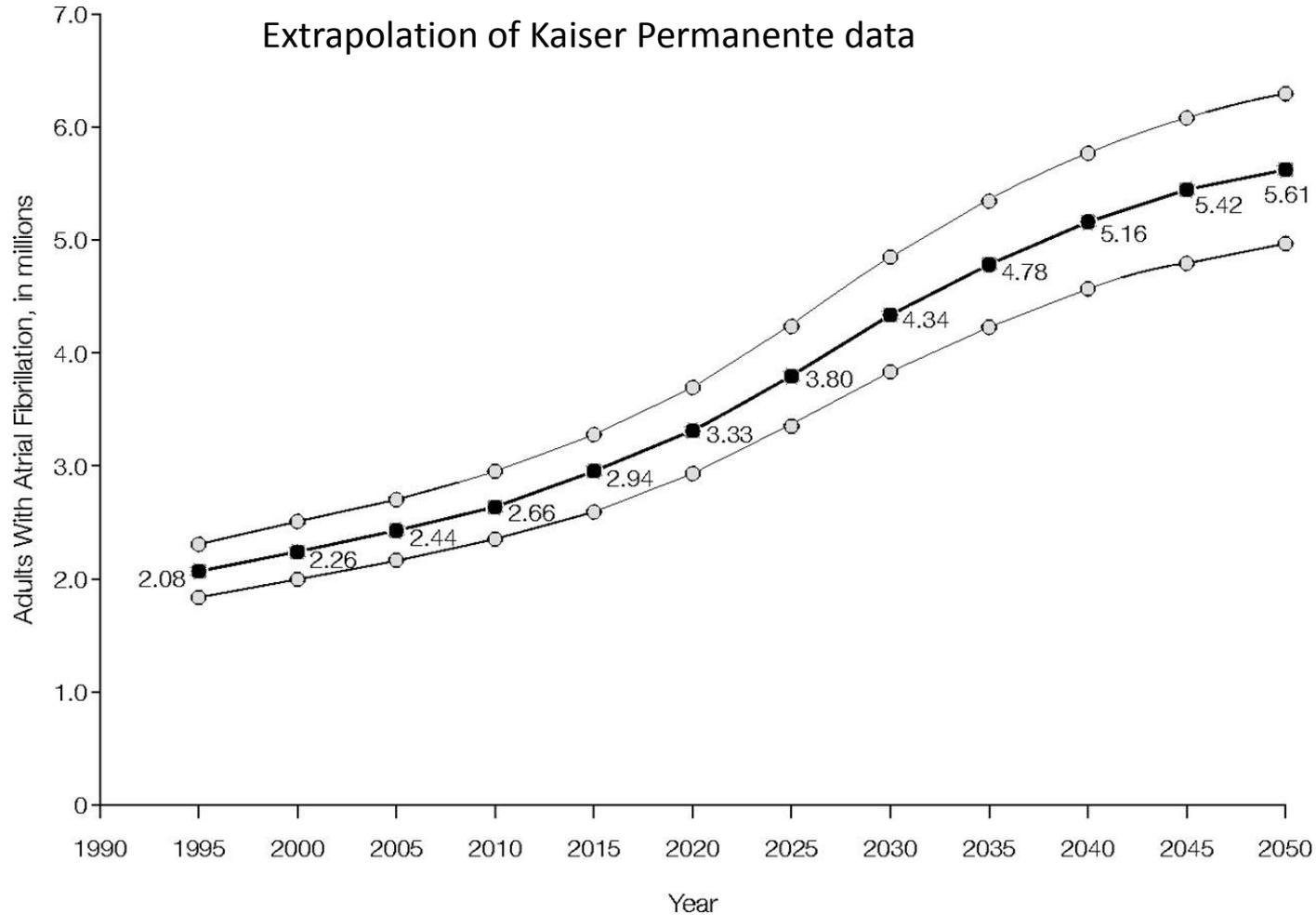
Disclosures

Consultant:

Abbott Vascular
Boston Scientific
St. Jude Medical

The AF Epidemic

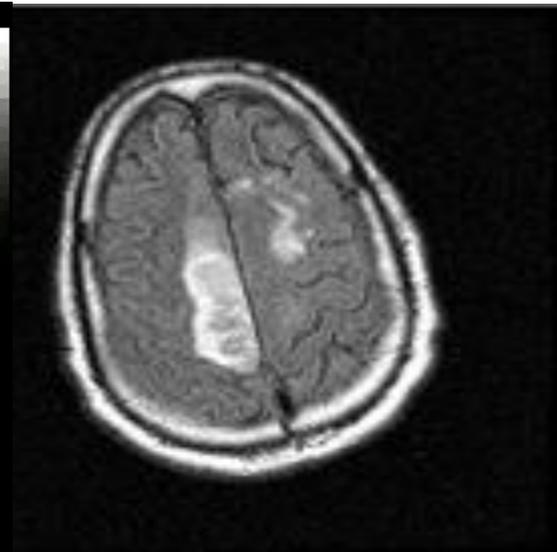
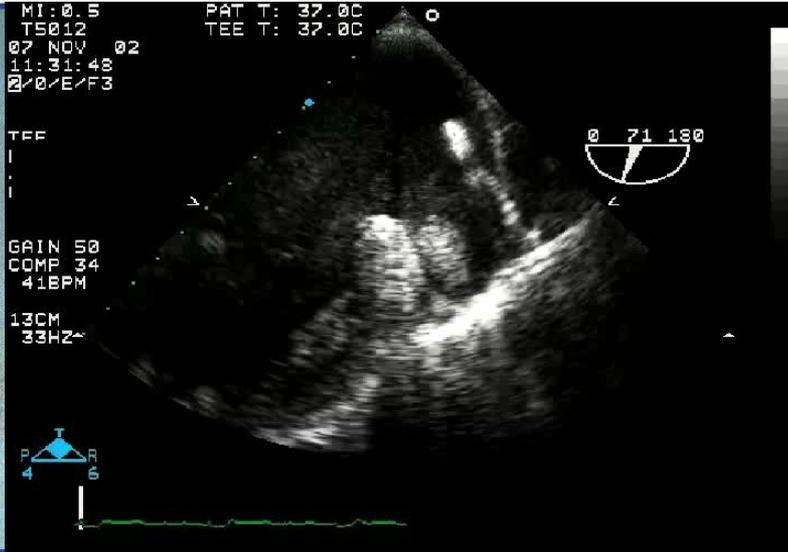
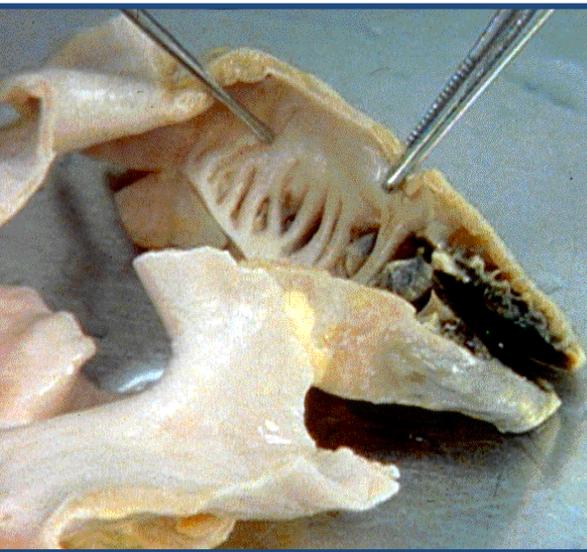
Projected Number of Adults with Atrial Fibrillation in the United States



Go, A. S. et al. JAMA 2001;285:2370-2375.

AF is a Major Cause of Stroke

LAA source of embolic stroke in 90%



Assessment of Thromboembolic Risk

CHA₂DS₂-VASc

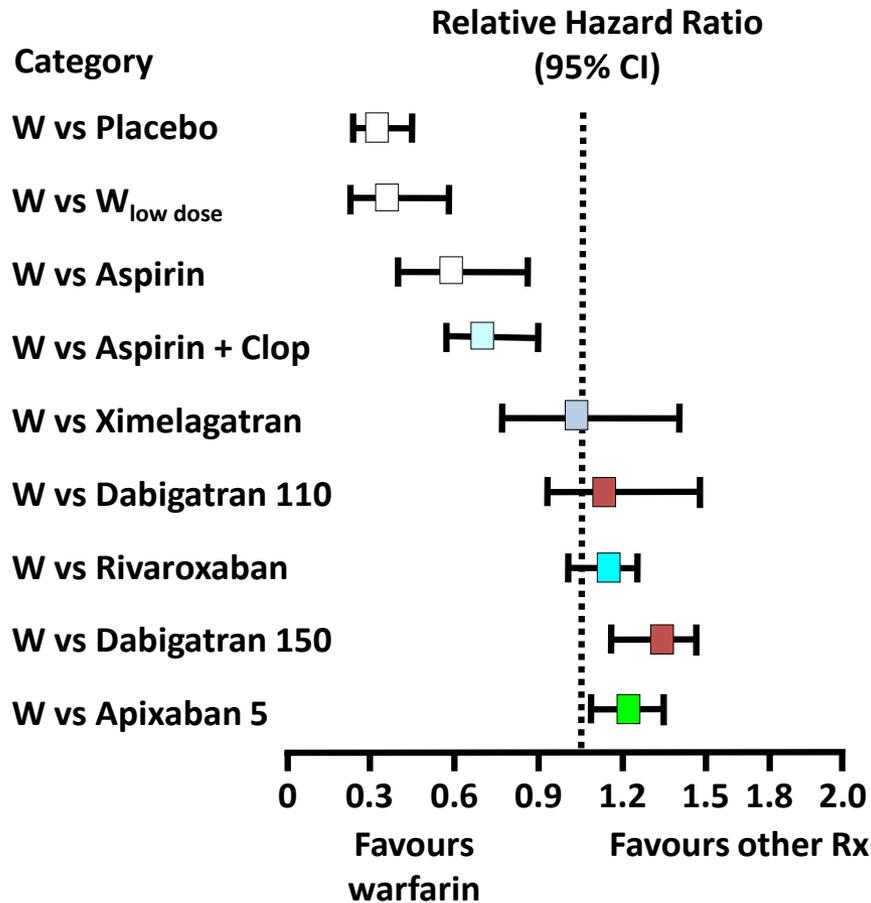
CHF/ LV dysfunction	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (CAD, AoD, PAD)	1
Age 65–74 years	1
Sex category (female)	1
Score 0–9	

Score	Annual stroke rate, %	
n	1,084 ¹	73,538 ²
0	0	0.78
1	1.3	2.01
2	2.2	3.71
3	3.2	5.92
4	4.0	9.27
5	6.7	15.26
6	9.8	19.74
7	9.6	21.50
8	6.7	22.38
9	15.2	23.64

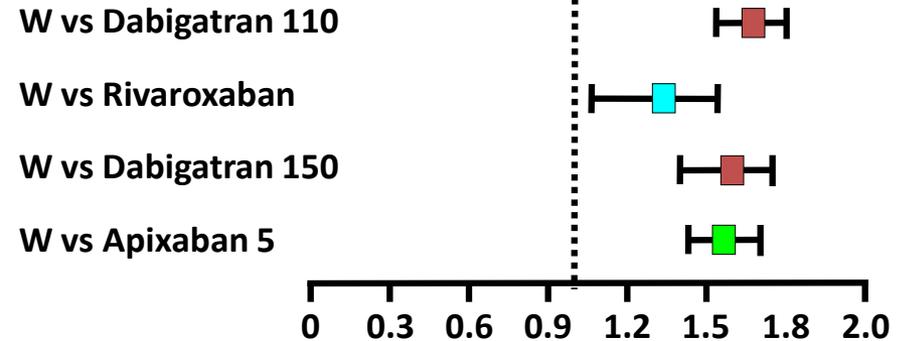
1. Lip GY, et al. *Chest* 2010;137(2):263–272
 2. Olesen JB, et al. *BMJ* 2011;342:d124

Stroke Prevention: Pharmacologic Options

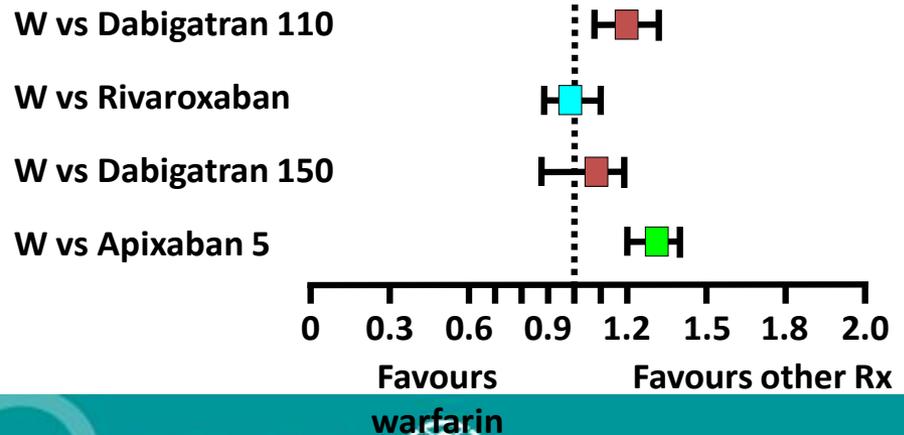
Stroke or systemic embolism



Intracranial haemorrhage

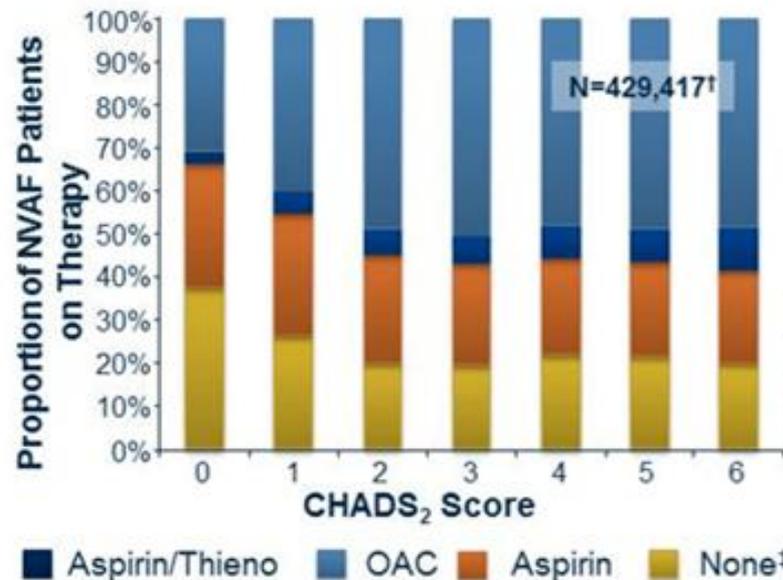


Major bleeding



ACC NCDR® PINNACLE-AF Registry*: Analysis of Utilization of Oral Anticoagulants in NVAF Patients at Risk for Stroke

Prevalence/Distribution of Antithrombotic Therapies Across CHADS₂ Scores of Real-World NVAF Outpatients (2008–2013)[†]



- Analysis evaluated patients from PINNACLE-AF Registry (2008 to 2013) to determine the proportion of NVAF outpatients treated with OAC, antiplatelet therapy, and no antithrombotic therapy, across CHADS₂ scores¹
- Of 429,417[†] patients, 44.9% were treated with OACs, 25.9% were treated with aspirin, 5.5% were treated with combination aspirin/thienopyridine, and 23.8% were not treated with any antithrombotic therapy¹

Limitations of PINNACLE-AF Registry^{2,3}

- PINNACLE-AF is an observational dataset
- PINNACLE-AF utilizes retrospective data collection
- Majority of participants in PINNACLE-AF are cardiologists

The ACC does not endorse the use of any specific oral anticoagulant

* BMS and Pfizer are founding sponsors of the PINNACLE-AF Registry.

† Outpatients with AF enrolled in the ACC NCDR-PINNACLE Registry between 2008 and 2013.

‡ No antithrombotic therapy.

OAC=oral anticoagulant; Thieno=thienopyridine.

1. Hsu JC et al. Presented at the 35th Annual Scientific Sessions of the Heart Rhythm Society; May 7–10, 2014; San Francisco, CA.

2. NCDR® PINNACLE Registry®. www.ncdr.com/webncdr/pinnacle. Accessed July 25, 2014.

3. PINNACLE Registry® Brochure. ACC Foundation. 2012.

Bleeding Risk Prediction with Oral AC

HAS-BLED 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

Score	Bleeds per 100 pt-yrs
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70

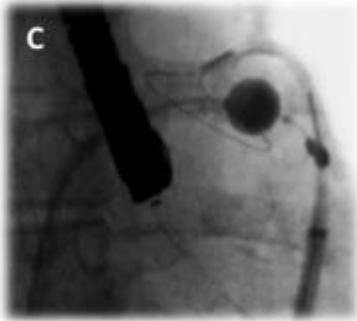
New Oral AC Drugs vs. Warfarin

Study	Treatment	Major Bleeding	Hemorrhagic Stroke
RE-LY ¹	Dabigatran (110 mg)	2.71%	0.12%
	Dabigatran (150 mg)	3.11%	0.10%
	Warfarin	3.36%	0.38%
ROCKET-AF ²	Rivaroxaban	3.6%	0.5%
	Warfarin	3.4%	0.7%
ARISTOTLE ³	Apixaban	2.13%	0.24%
	Warfarin	3.09%	0.47%

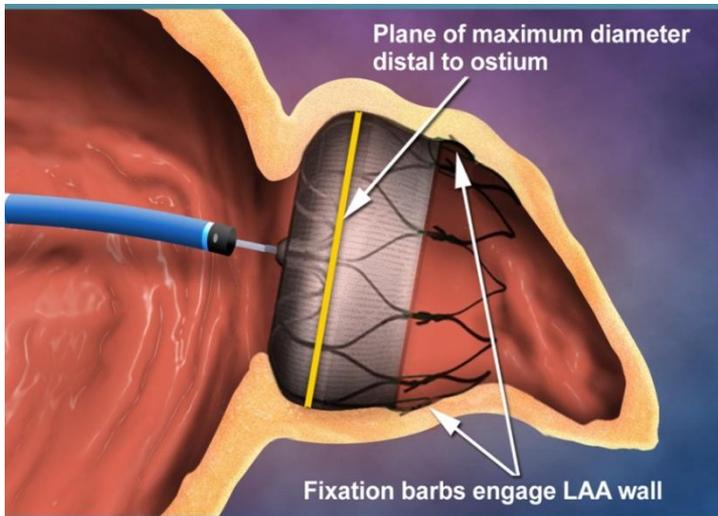
Non Pharmacologic Options for Stroke Prevention

Surgical LAA Closure

- **Performed as part of cardiac surgery**
- **Excision or suture exclusion**
- **Limitations**
 - **No randomized data showing benefit**
 - **Stump remnant**
 - **Cleveland Clinic experience**
 - **Only 73% excision and 23% exclusion adequate**
 - **40% with inadequate result had thrombus by TEE**



Percutaneous LAA Occlusion

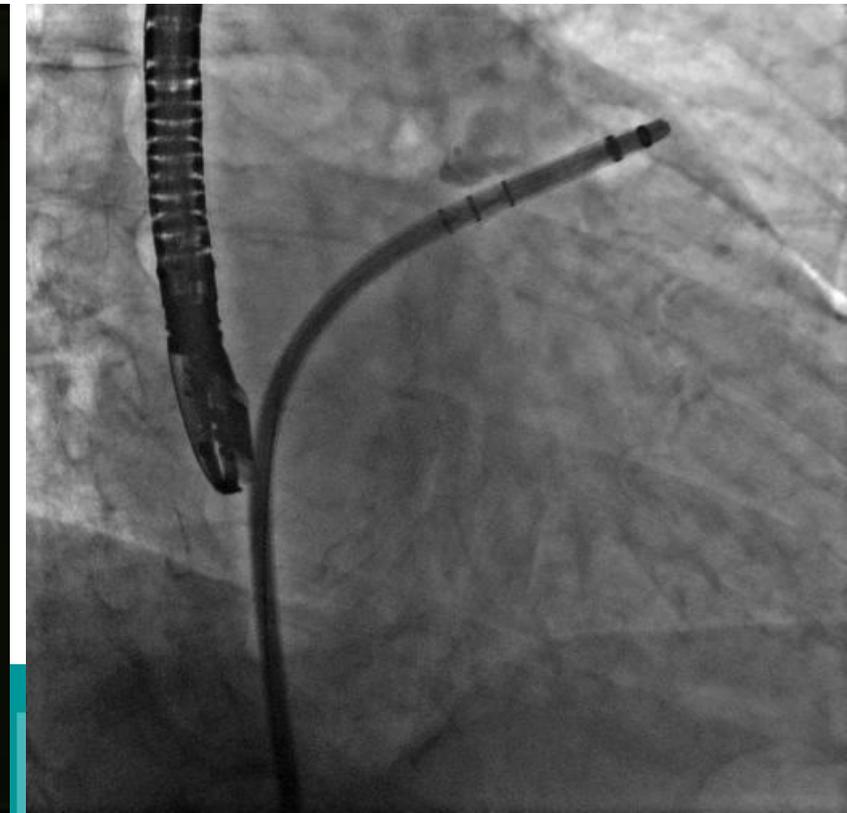
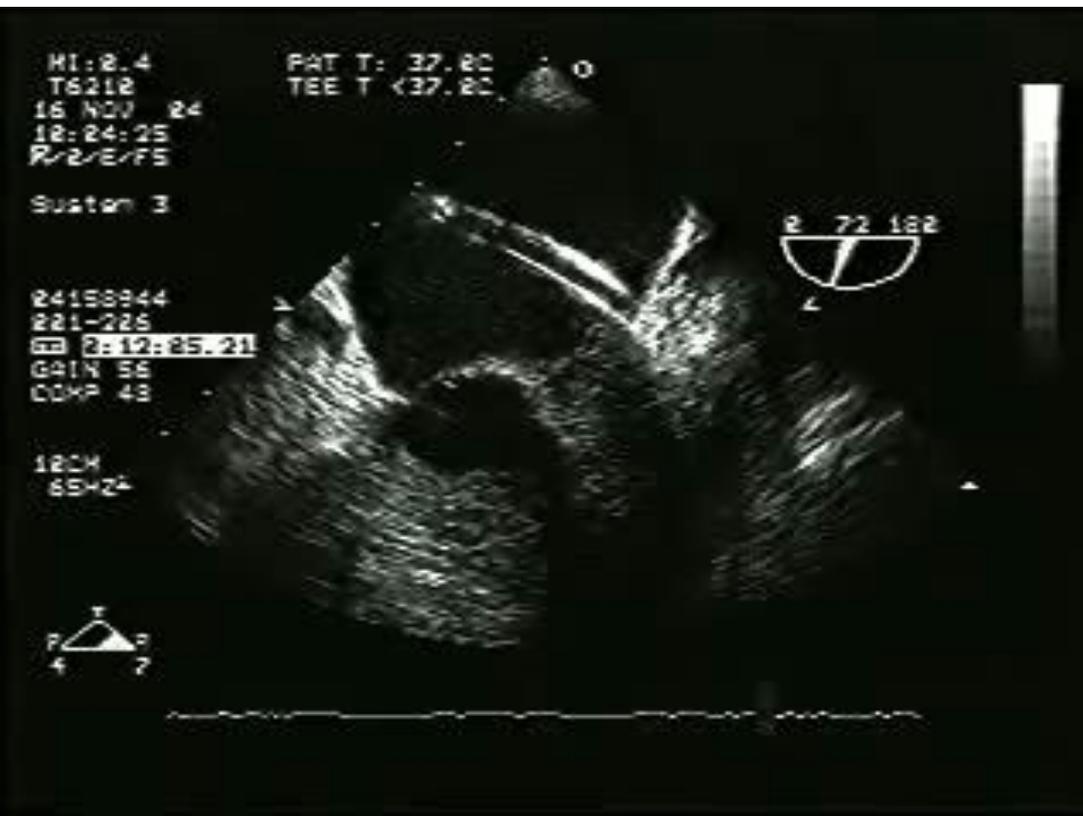


Watchman Procedure

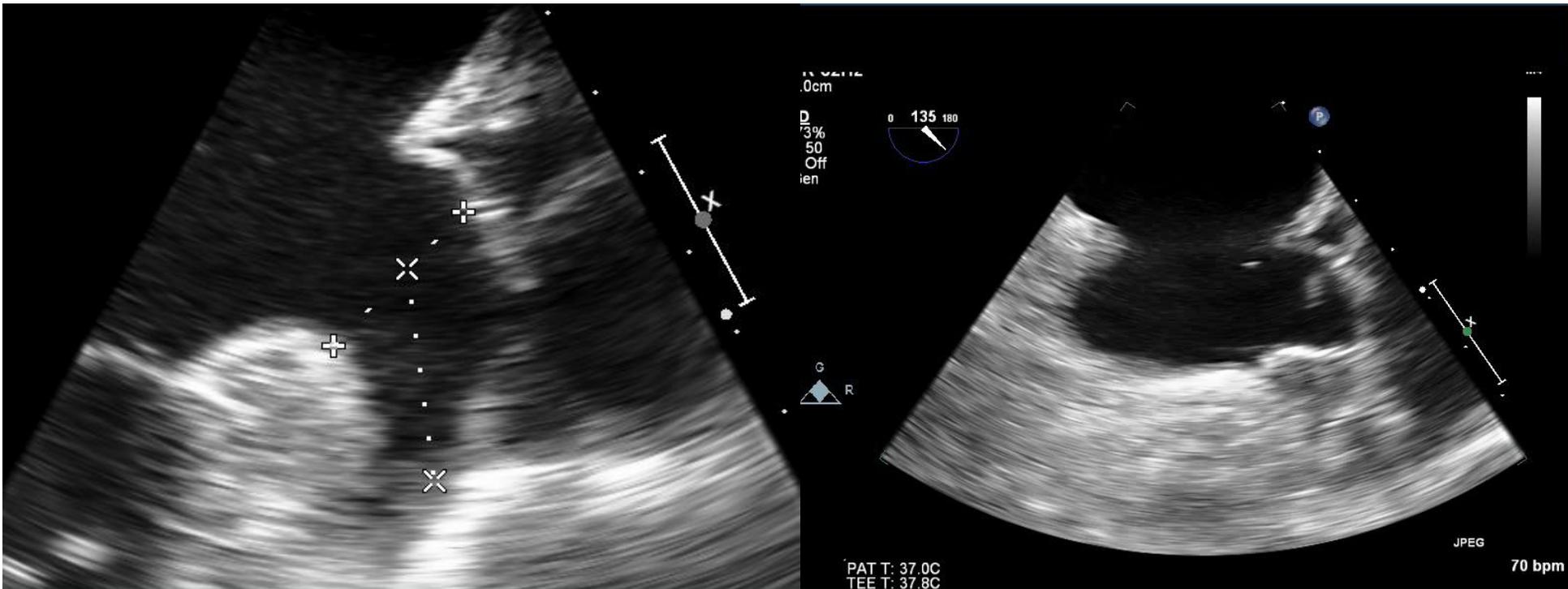
Femoral venous access

Trans-septal sheath

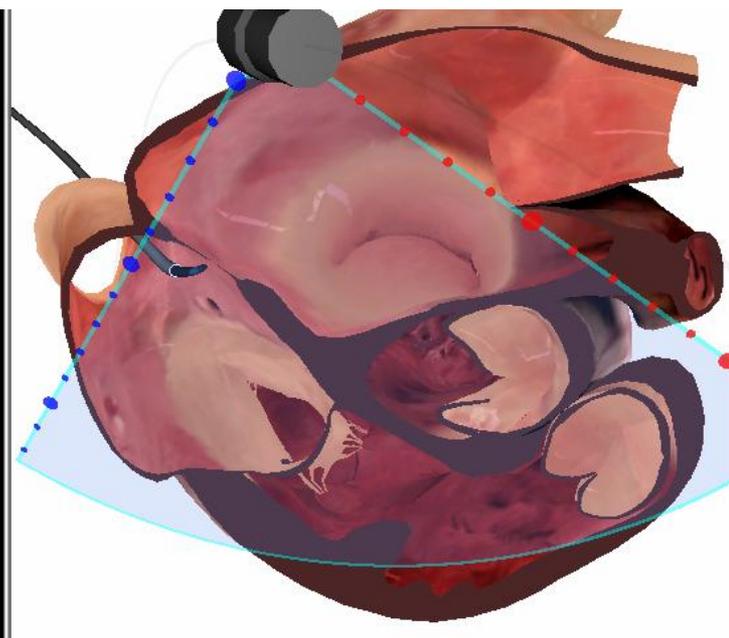
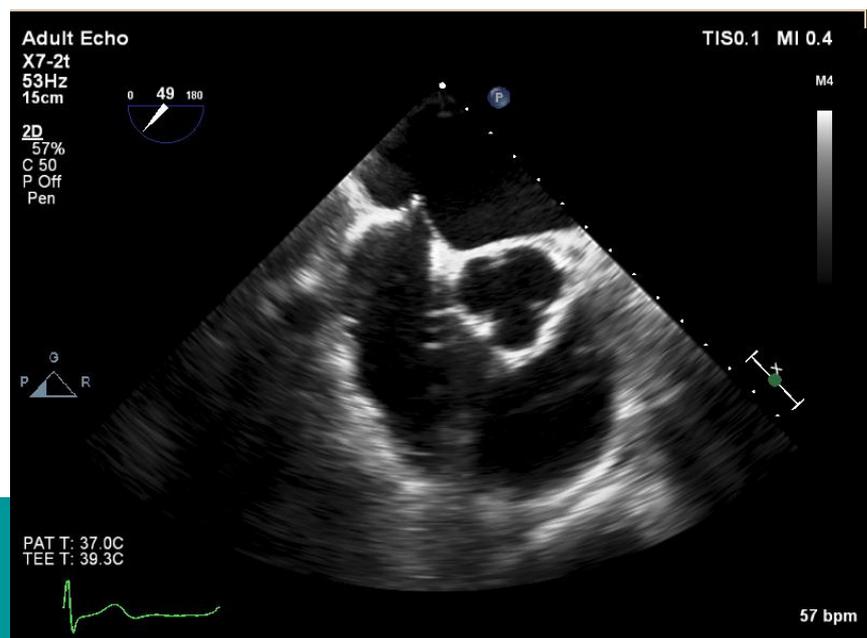
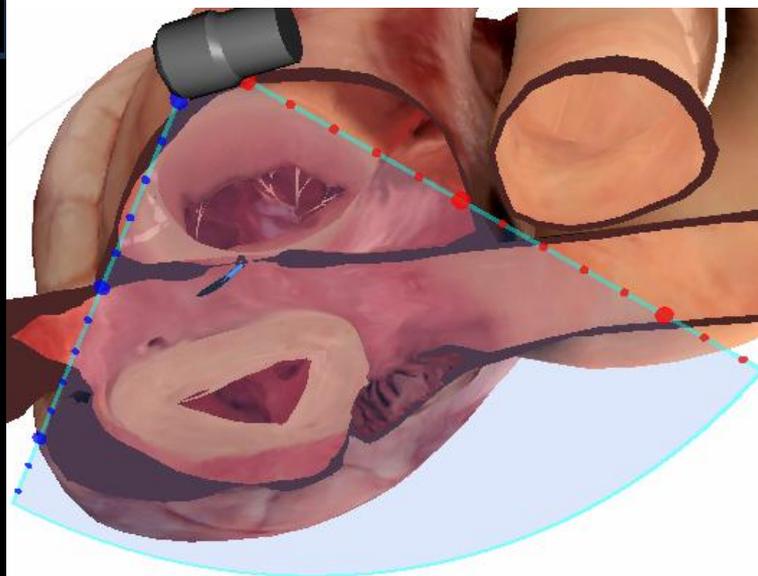
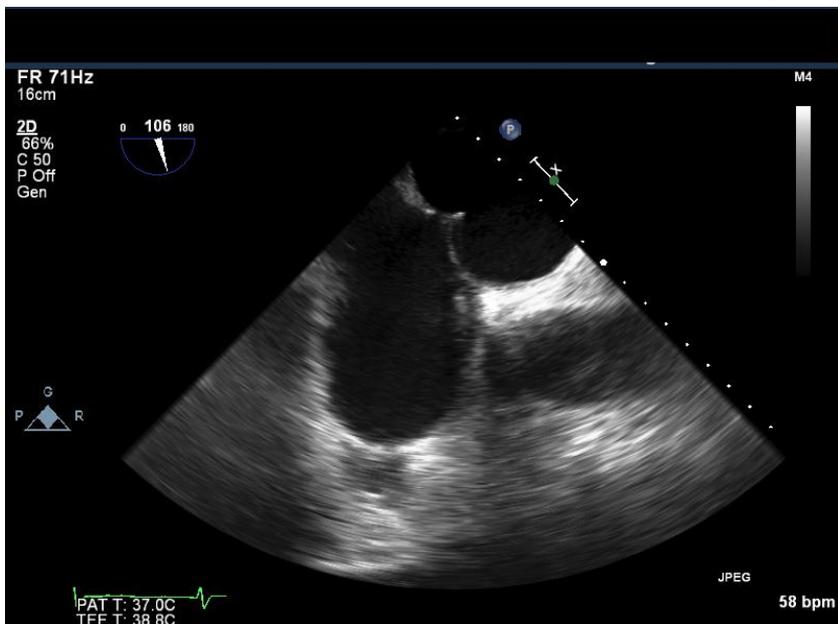
TEE and flourosopic guidance



LAA is a highly variable structure
Must be measure accurately with TEE to assess
suitability for closure

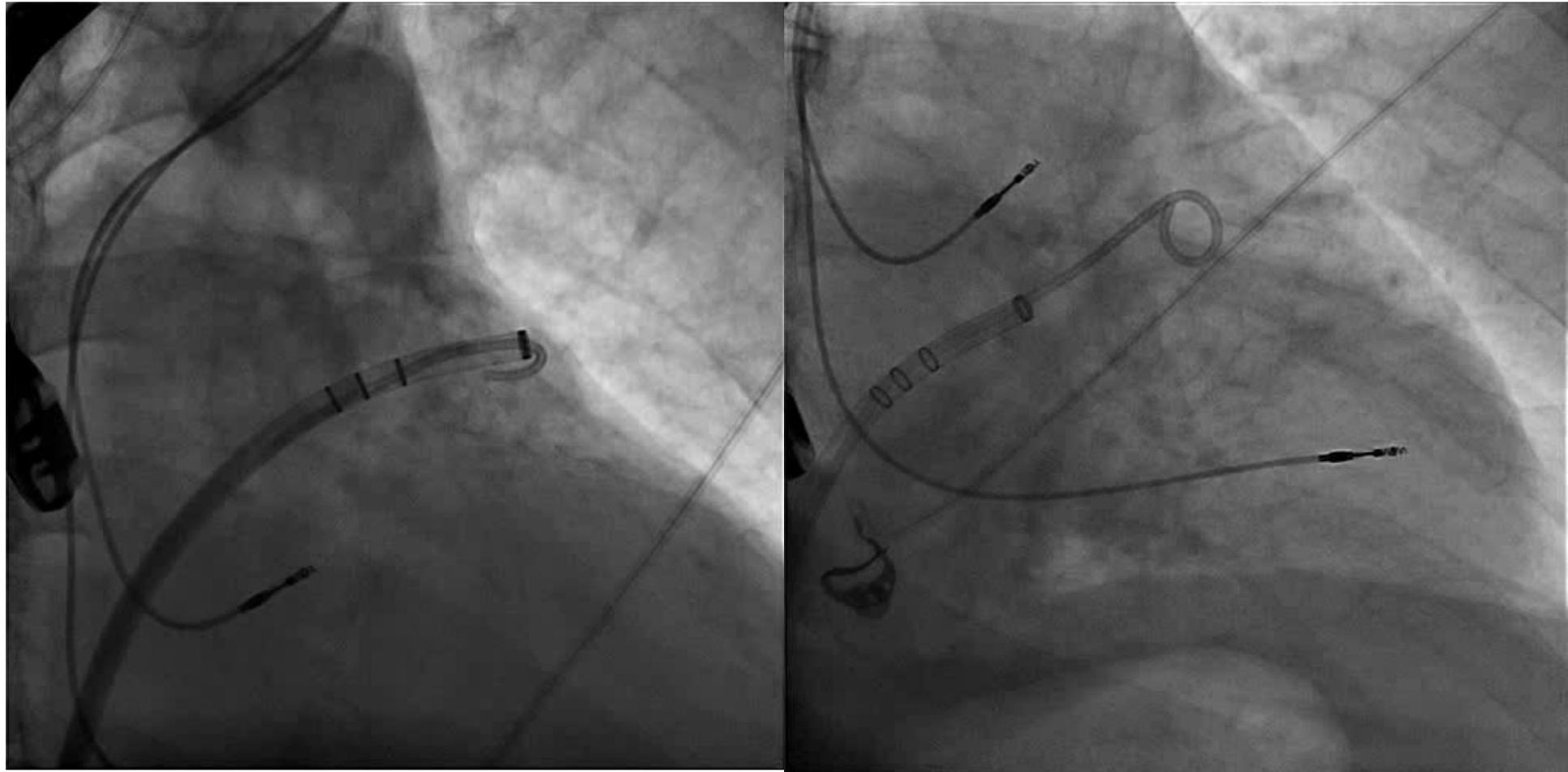


TEE Guided Trans-septal: Bicaval and SAX-B

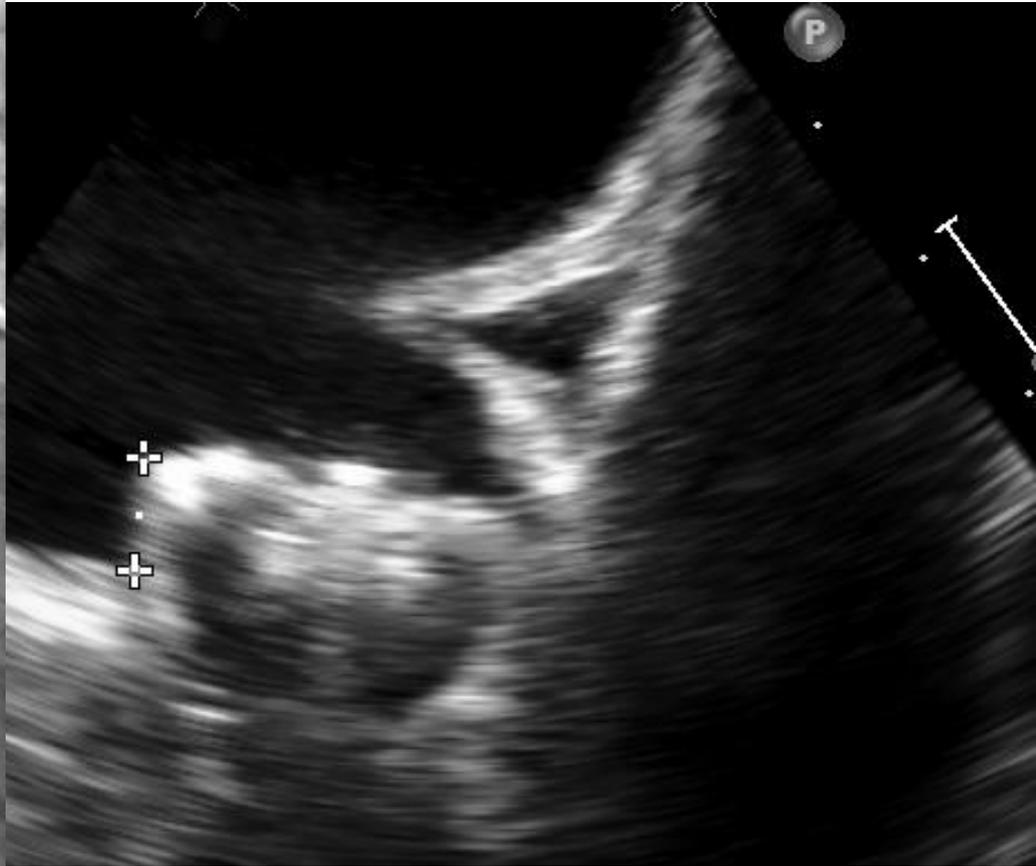
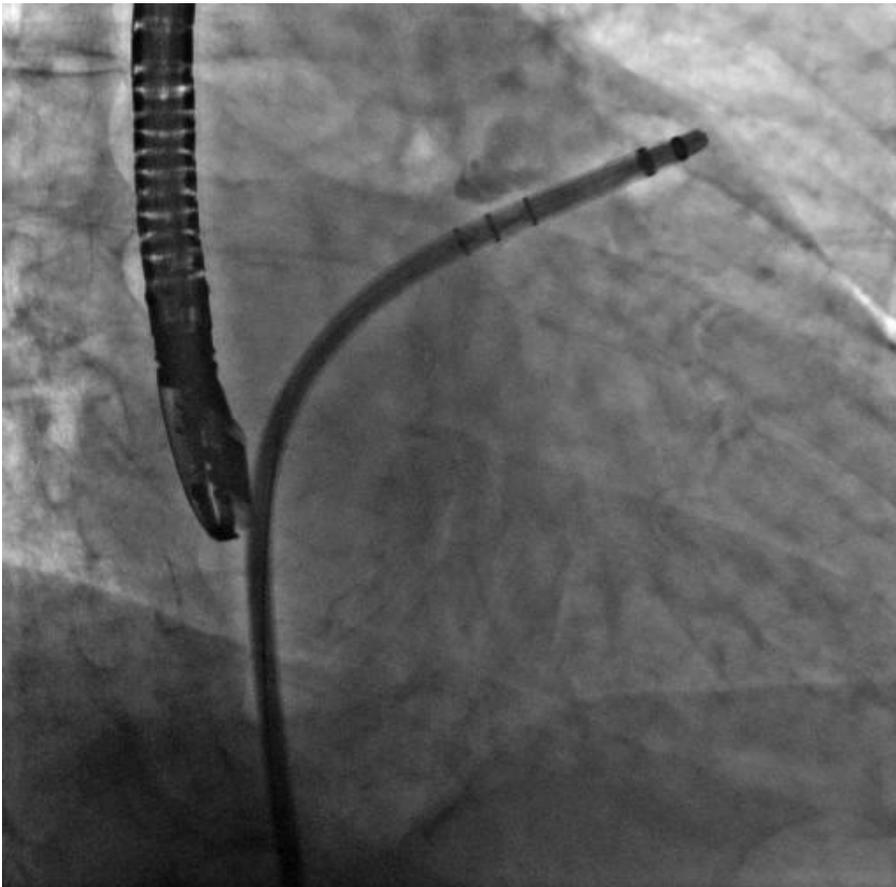


LAA is a Complex Variable Structure

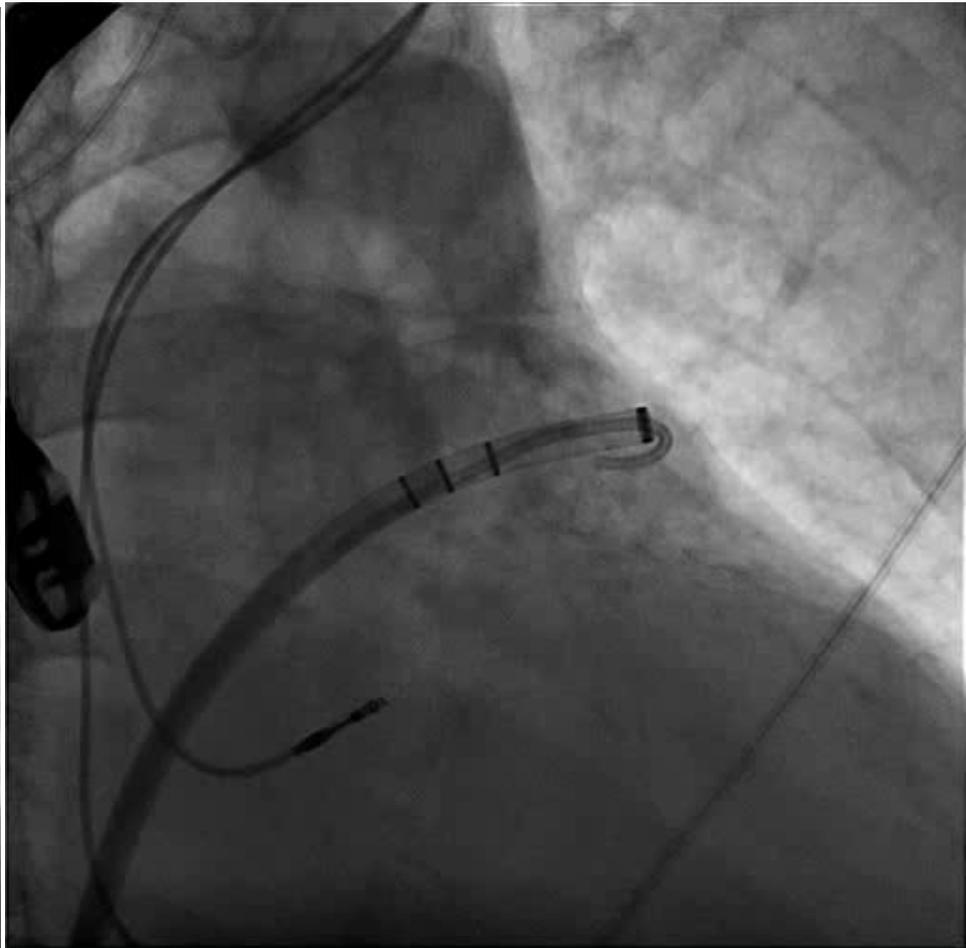
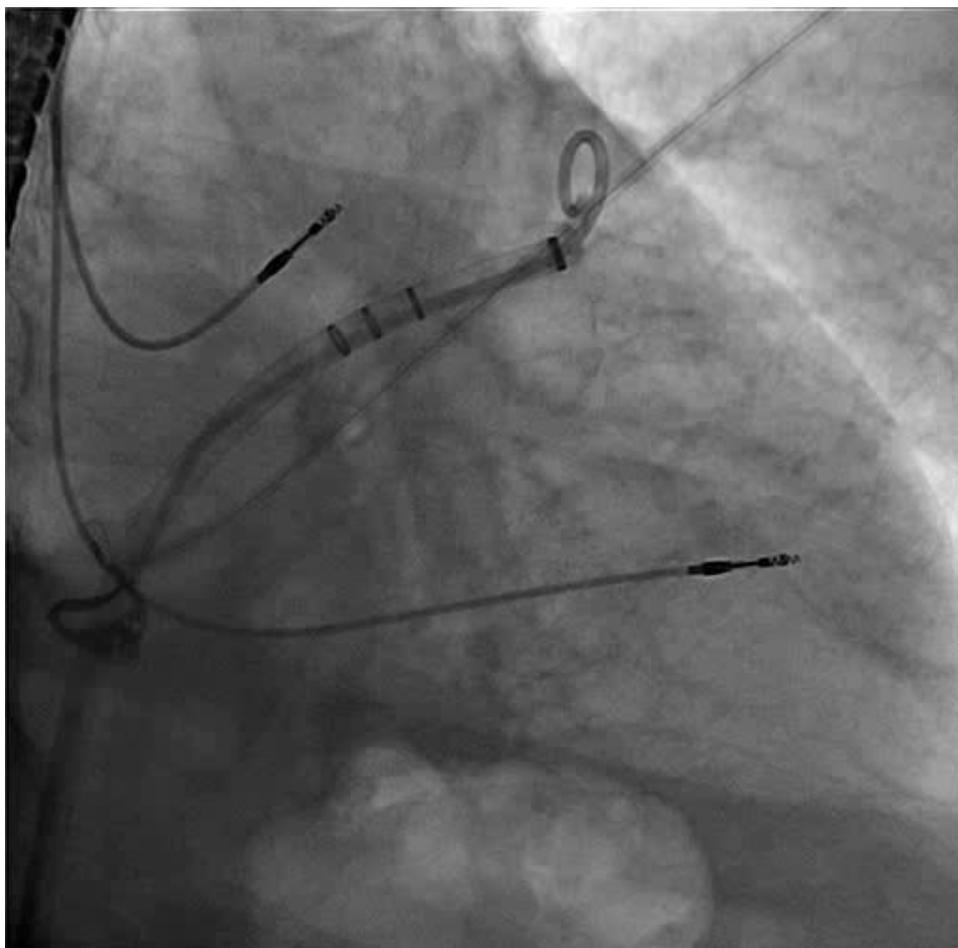
Sheath is inserted into a LAA lobe



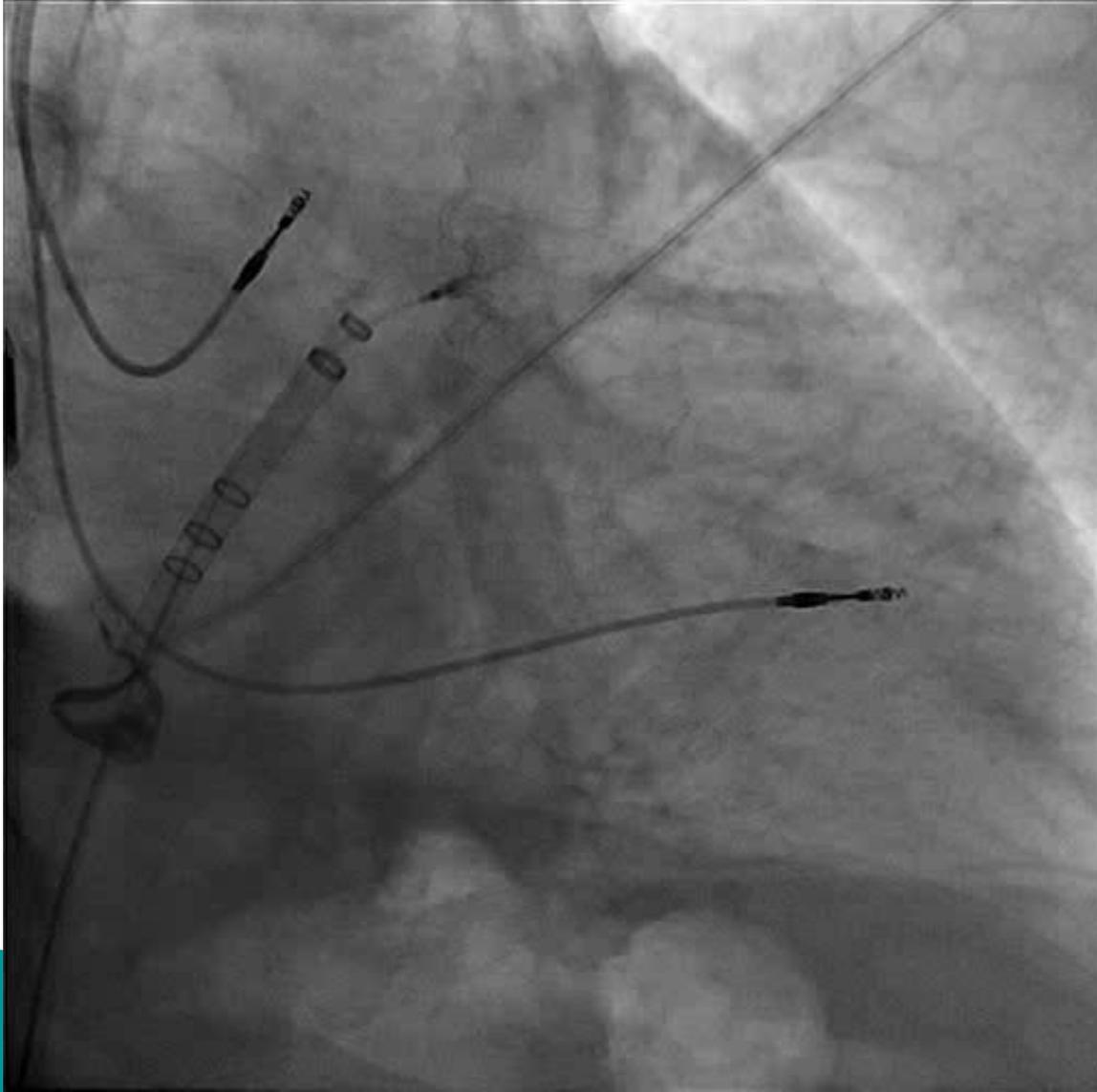
**Guide positioned by markers and device is deployed
deployment suboptimal – High shoulder suggests poor anchoring**



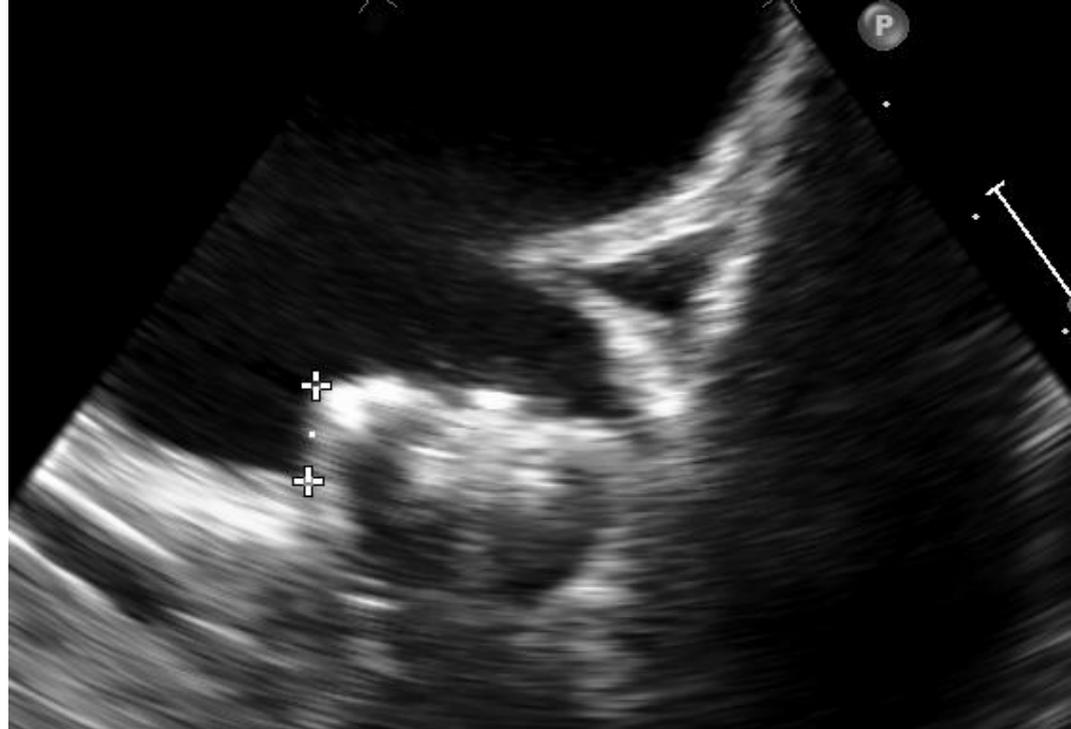
**A more superior lobe is selected and guice is positioned
Compare new position (left) with first position (right)**



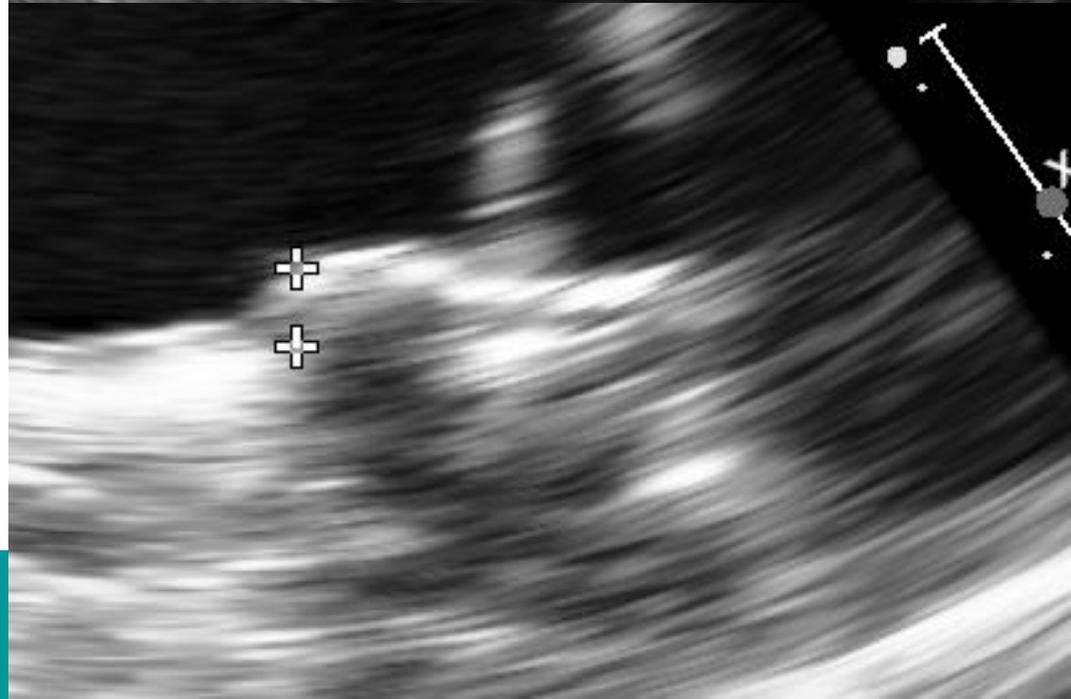
Watchman is deployed and Tug Test performed to assure stability



**First deployment
canted and less stable**



**Second deployment
more coaxial and stable**



The Watchman Device

PROTECT-AF: Overview

Randomized FDA-IDE Trial

Can the WATCHMAN device
replace Warfarin?

Efficacy Endpoint:

Stroke

CV death (& Unknown)

Systemic embolism

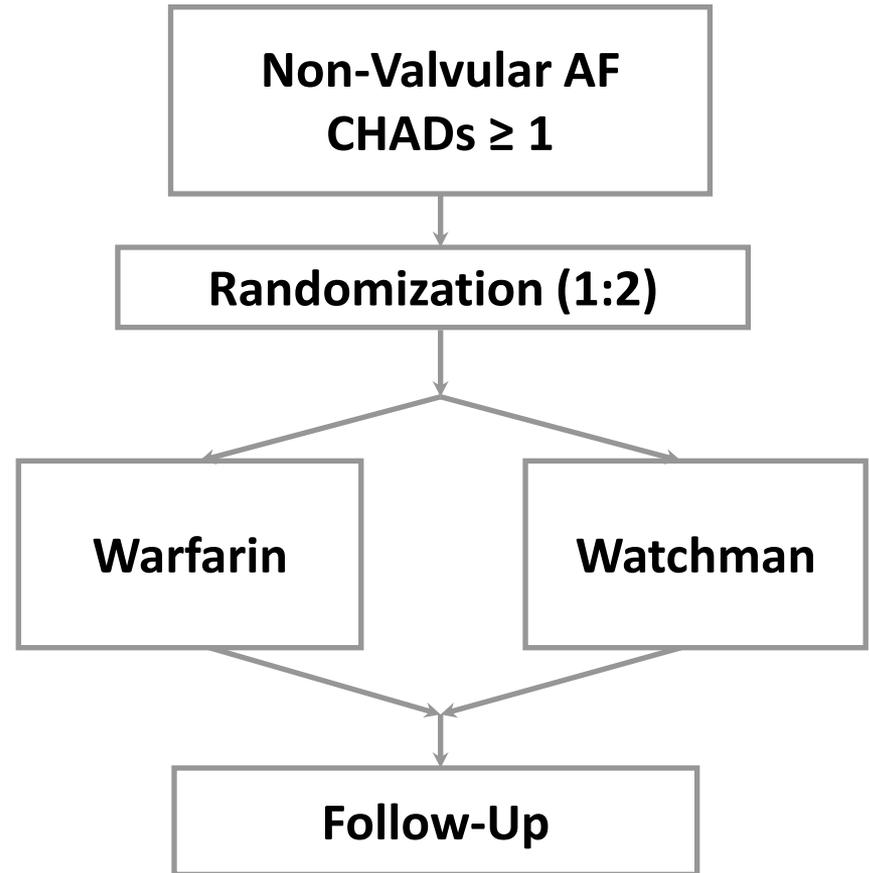
Safety Endpoint

Non-inferiority & Superiority

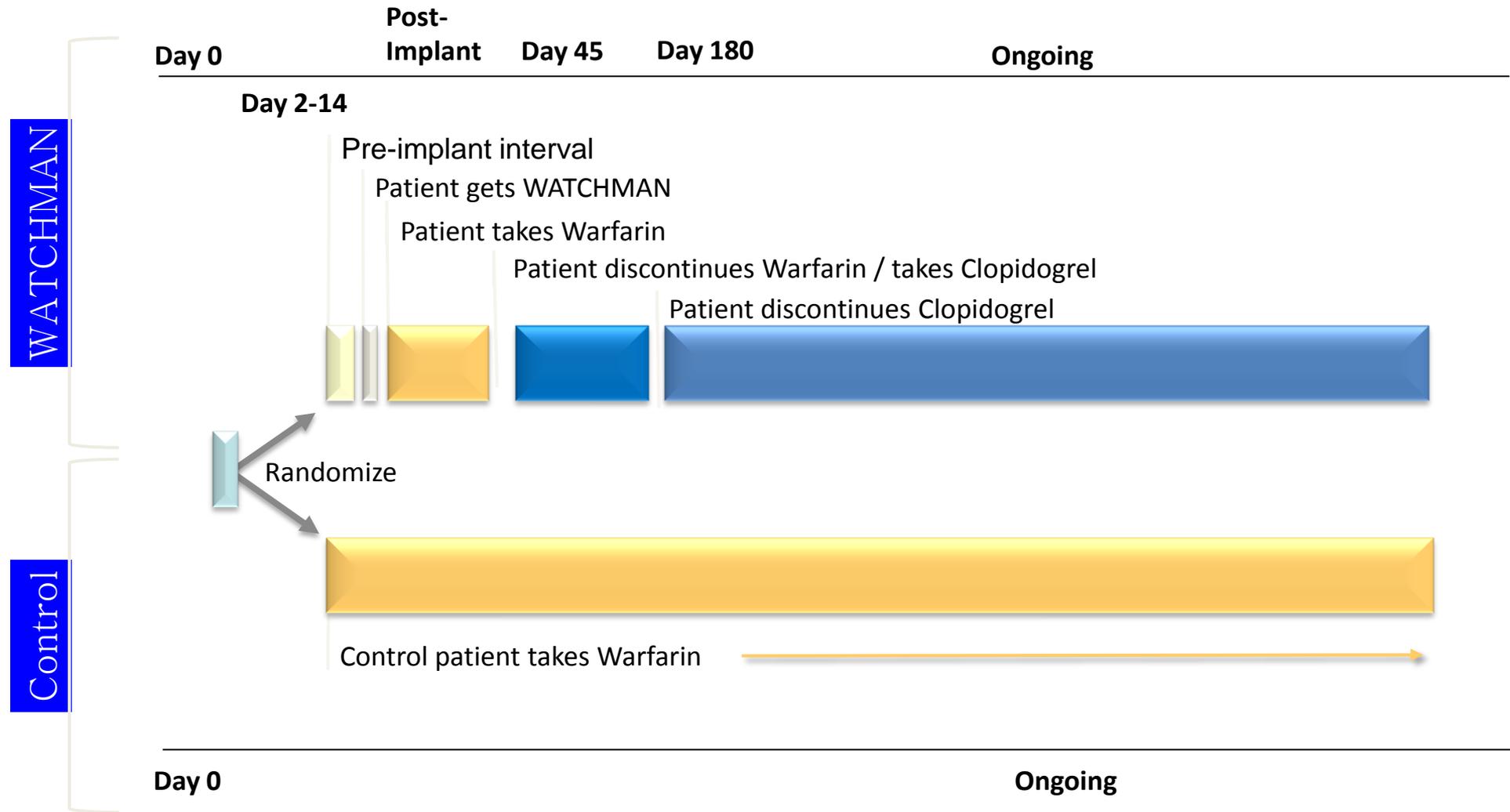
Bayesian Sequential Design

Analysis at 600 pt-yrs & every 150
pt-yrs thereafter → **1500 pt-yr**

Follow-up till 5 years



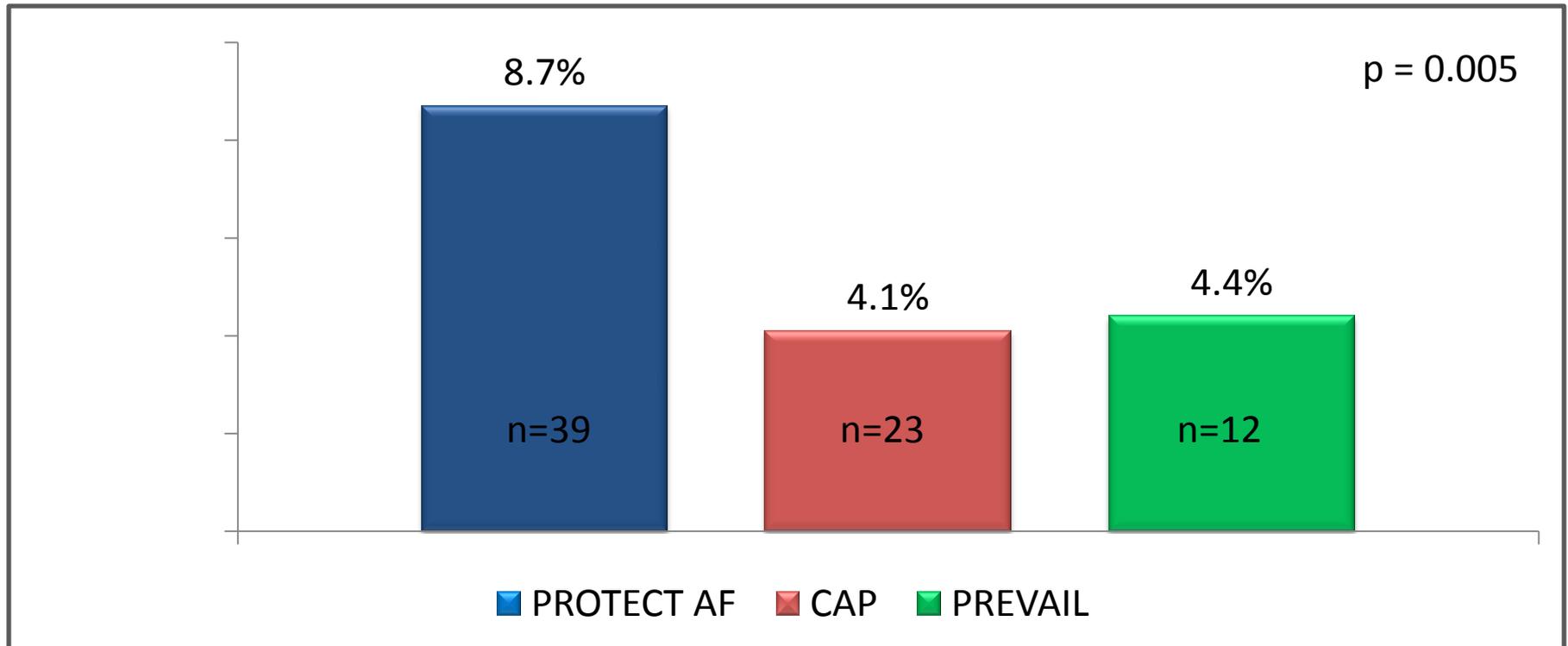
Patient Study Timeline



Vascular Complications

7 Day Serious Procedure/Device Related

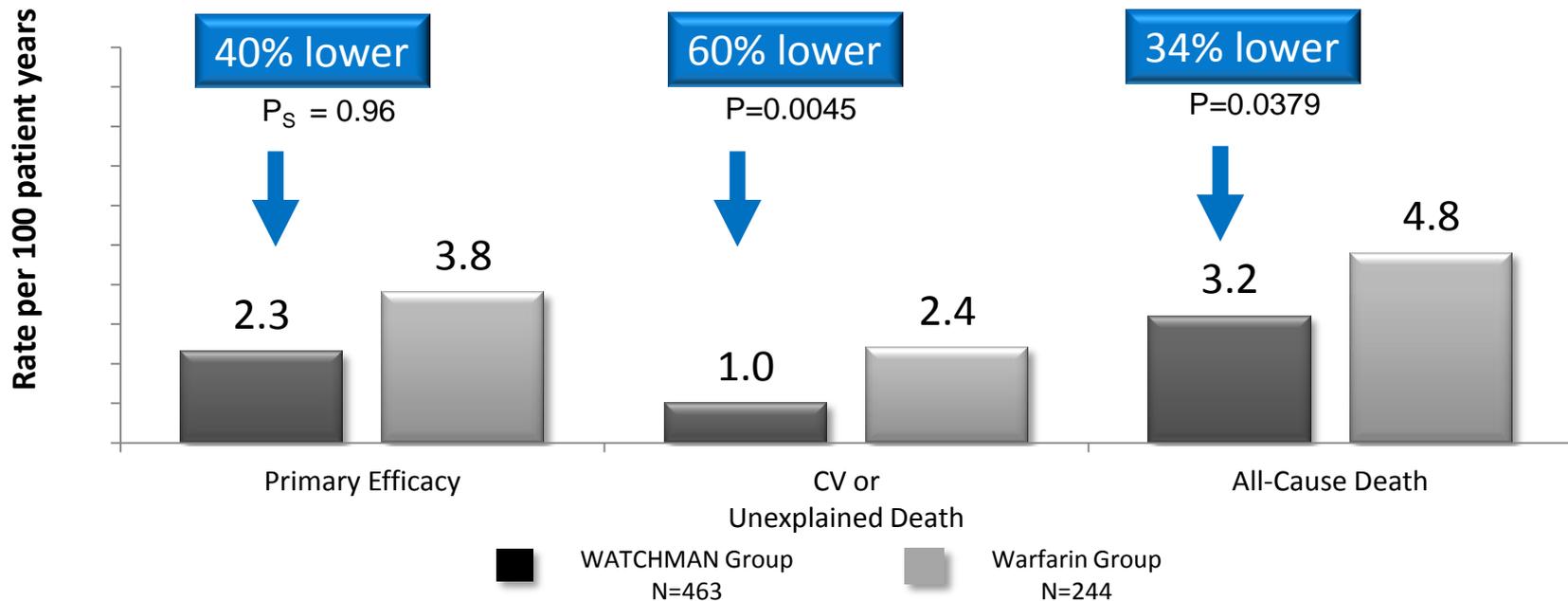
Composite of vascular complications includes cardiac perforation, pericardial effusion with tamponade, ischemic stroke, device embolization, and other vascular complications¹



No procedure-related deaths reported in any of the trials

PROTECT AF Long Term (4 Year Follow-up)

Events in PROTECT AF trial at 2,621 patient years

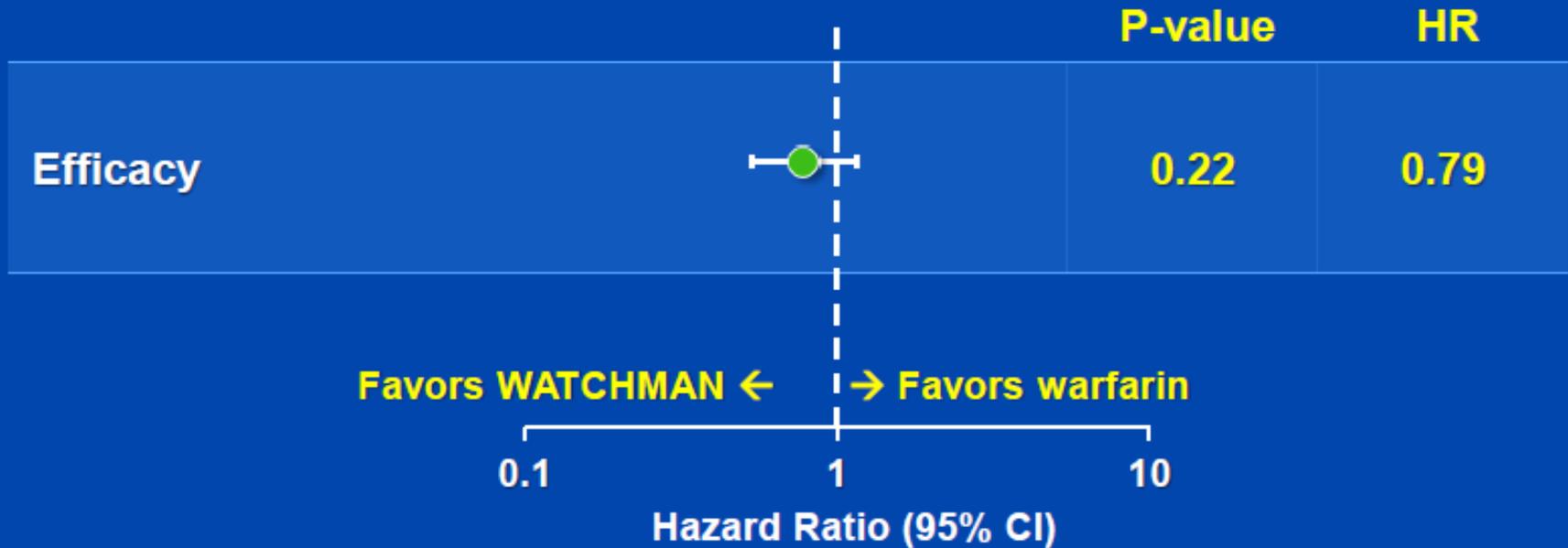


Ps = Posterior Probability for Superiority

All three endpoints met statistical superiority

Patient-Level Meta-Analysis

Efficacy



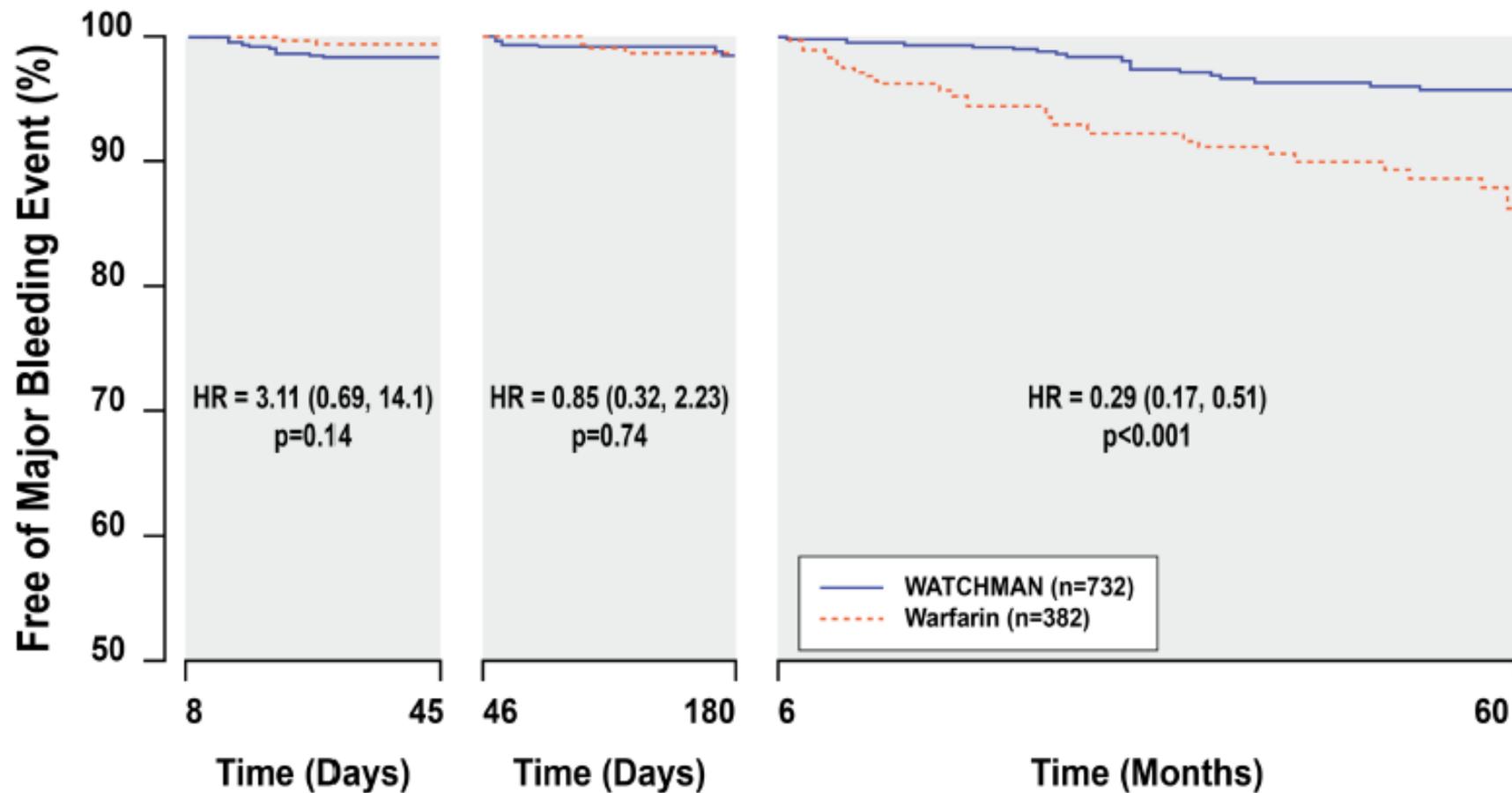
Protect AF and Prevail Pooled Analysis

Patient-Level Meta-Analysis

Stroke



Landmark Analysis: Bleeding Events after WATCHMAN LAAC vs Warfarin in the Pooled PROTECT-AF and PREVAIL Trials



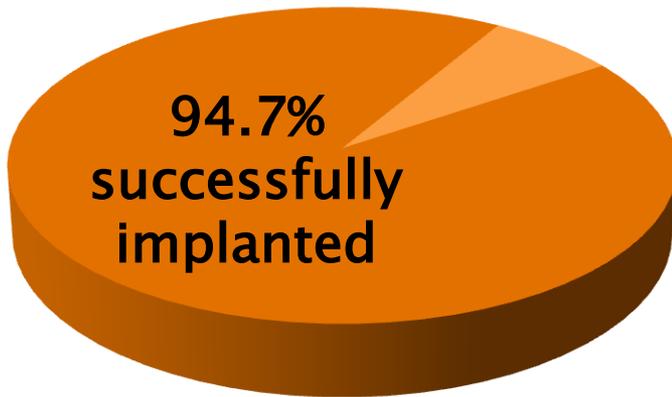
Significant differences in bleeding between treatment arms appear 6 months post-randomization

What About Absolute Oral AC Contraindicated Patients?

ASAP Registry

150 AF patients contraindicated for LT warfarin therapy

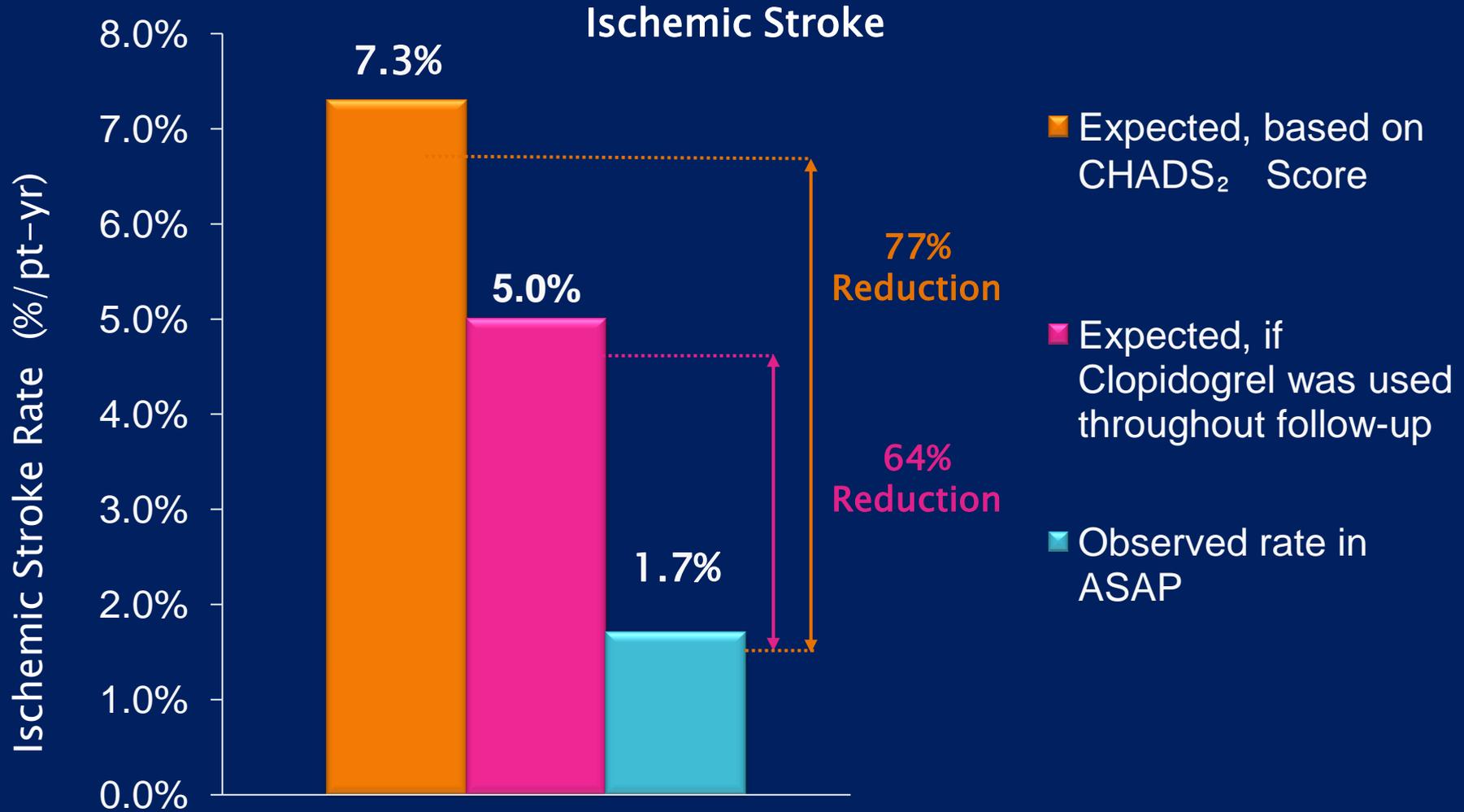
Rate of Success with
implantation in
warfarin
contraindicated
patients



- Patients had a history of hemorrhagic & bleeding tendencies or a hypersensitivity to warfarin
- 150 patients enrolled at 4 European centers
- Average CHADS₂ = 2.8
- Post procedure anti-platelet regimen
 - Clopidogrel through 6 months
 - Aspirin indefinitely
- Patients were followed for up to 1 year
 - Follow-up @ 3, 6, 12, 18 & 24 months
 - TEE at 3 and 12 months

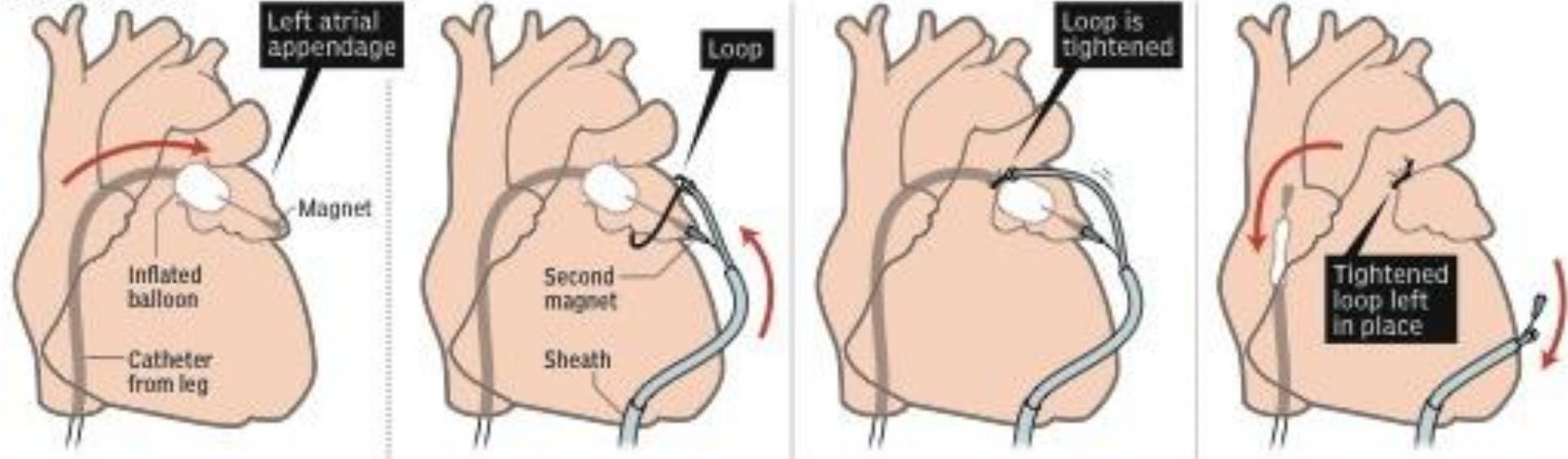
ASAP Registry

Efficacy outcome versus expected



Percutaneous Suture LAA Ligation Sentreheart Lariat

HOW IT WORKS



One



Carolinan HealthCare System

US Transcatheter LAA Ligation Consortium

Objective	<ul style="list-style-type: none"> • Peri-Procedural Safety (24h) • Efficacy (Closure) at 90days
# Patients	154
Age	72+ /-9.4
Sex	M: 96 (62%)
CHADS ₂	Mean 3
CHA ₂ DS ₂ -VASc	Mean 4.1

Major Bleeding	14 (9%)
Pericardial Effusion	16 (10%)
Tamponade	7 (4.5%)
Emergency Surgery	3 (2%)
Death	1
Strokes	0
Procedural Failure	22 (14%)
Stump thrombus at f/u (63)	3 (5%)
Stroke at median 112d f/u	2 (1%)

Anatomical Contraindications To Lariat

Additional exclusion criteria based on LAA anatomy included:

- LAA width > 40mm,
- Significantly posteriorly rotated heart.
- Prior cardiac surgery or pericarditis

My Take On Lariat

- **Benefits**

- Available for no AC patients
- Cool procedure

- **Risks**

- Procedural risk higher than Watchman
- Safety profile for Watchman is narrow thus probably Risks>Benefits
- No RCT data
- Potential for stump and thrombus

Conclusions

- Oral Anticoagulation is under utilized for stroke prevention in AF
- NOACs are a major advance over warfarin for stroke prevention in AF
 - No monitoring
 - Equal or superior stroke protection
 - 50% reduction in IC bleeding
 - Expensive
 - Can not be used in severe renal failure

Conclusions

- LAA Closure with Watchman is an effective alternative to warfarin for stroke prevention in AF
- Superiority over warfarin for mortality, bleeding, IC hemorrhage
- Equivalent to warfarin for all strokes with higher risk of embolic stroke balanced by lower risk of hemorrhagic stroke
- May be particularly well suited to patients with relative or absolute contraindications to oral AC
- Untested vs. NOACs

One



Carolinan HealthCare System