



LAA Occlusion for Stroke Prevention: What is the Ideal

David R. Holmes, Jr., M.D.
Mayo Clinic, Rochester

TCTAP 2017
Seoul, Korea
April 2017

Presenter Disclosure Information

David R. Holmes, Jr., M.D.

**“LAA Occlusion for Stroke Prevention:
What is the Ideal”**

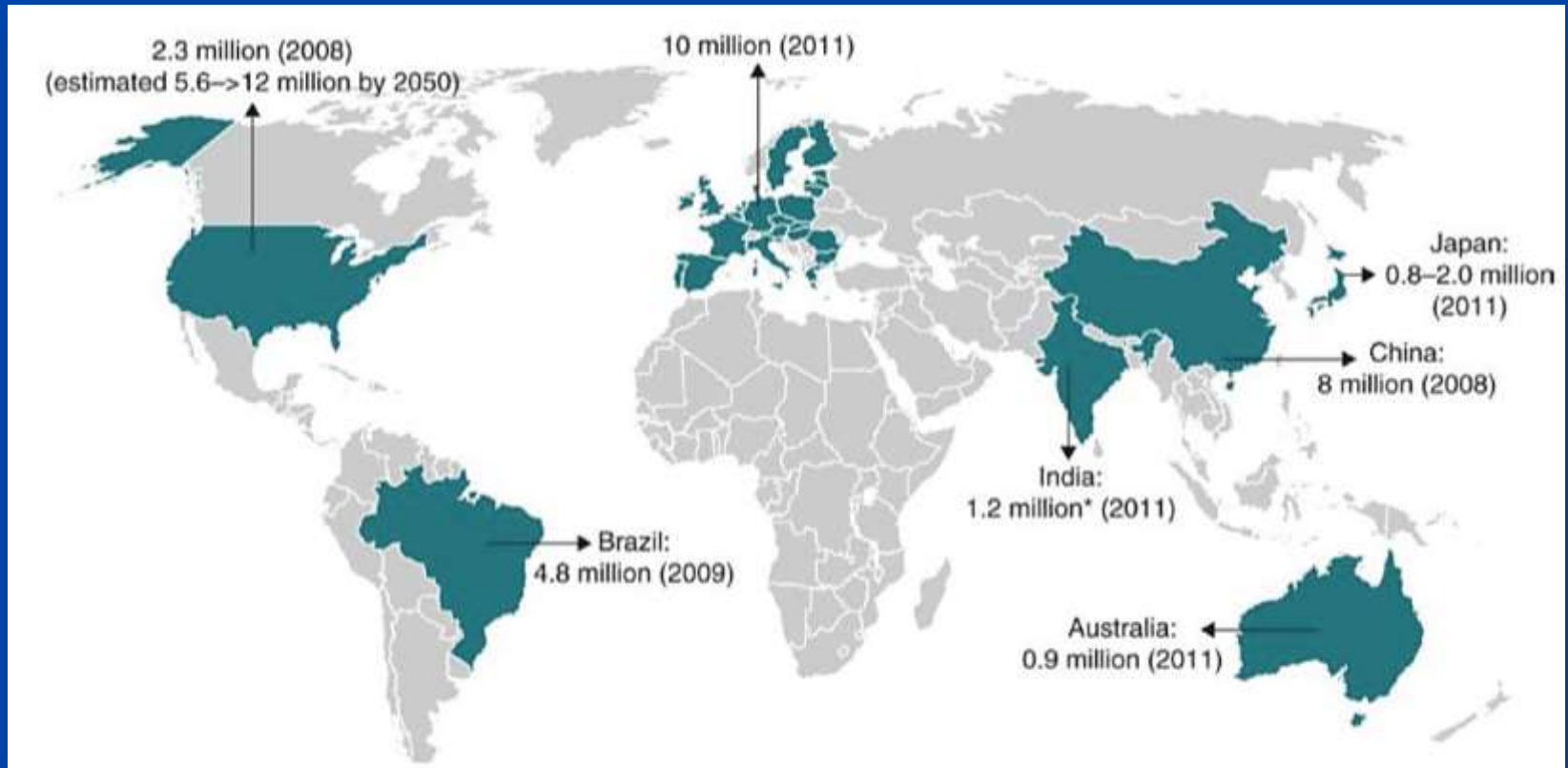
The following relationships exist related to this presentation:

Both Mayo Clinic and I have a financial interest in technology related to this research. That technology has been licensed to Boston Scientific.

LAA – What do we have?

- We have a huge and growing problem of patients with AF and increased risk of stroke and systemic thromboembolism
- We know the proximate pathophysiology
- Alternative medical treatments have significant limitations
- Alternative strategies to medical treatment also have significant limitations.

Worldwide Prevalence of Atrial Fibrillation



Anticoagulants – Tested in Trials With >60,000 Patients for Stroke Prevention

Bleeding rates

- Major 2-3 %
- Any 15-25%

Discontinuation rates

- 20-25% in major studies



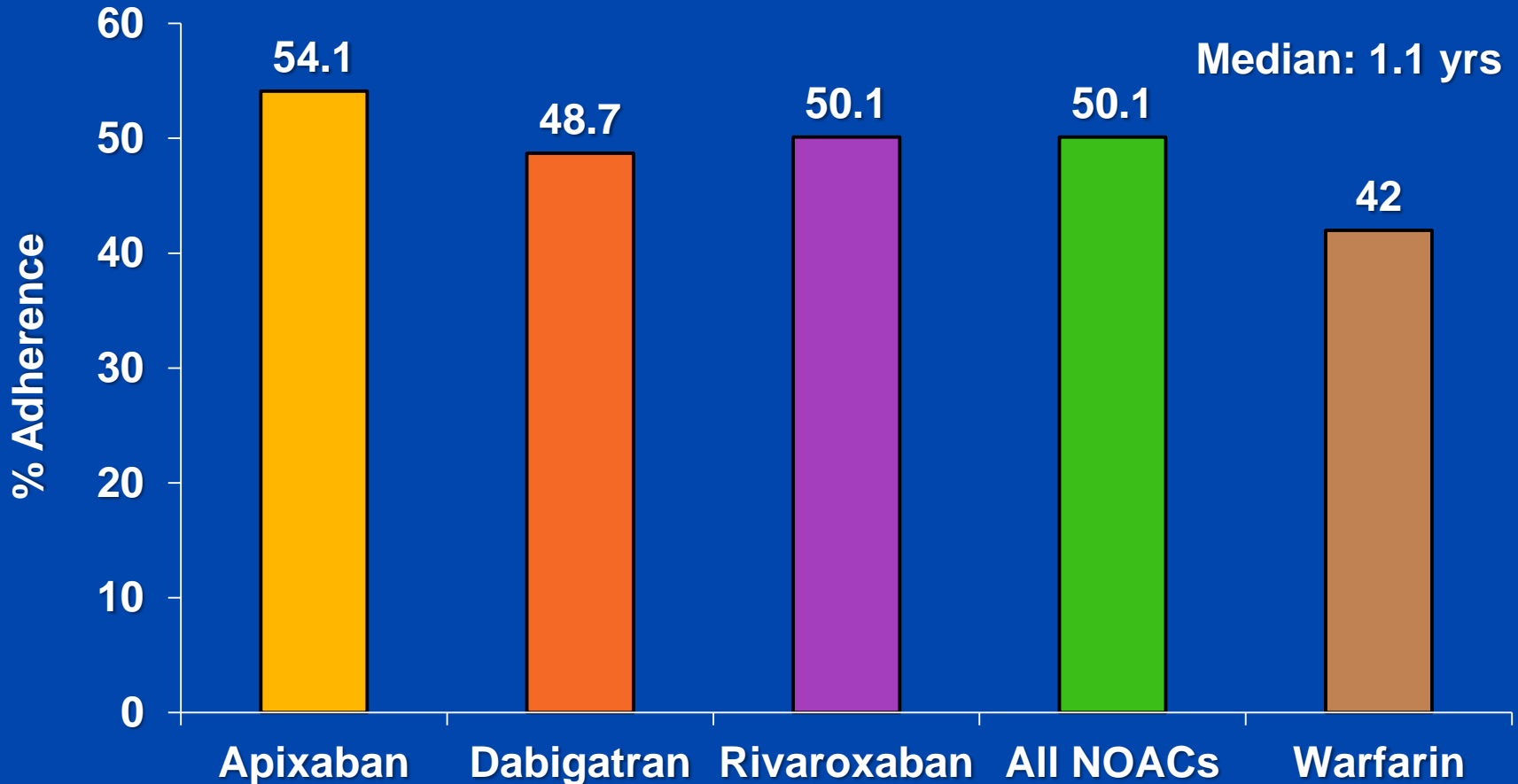
Concept: Avoid “systemic” complications by using “local” approach: & 100% adherence

Possibly control AF?

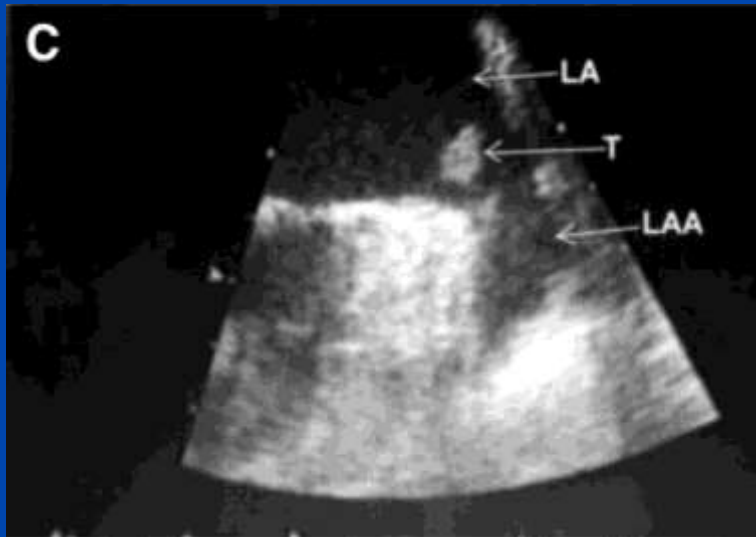
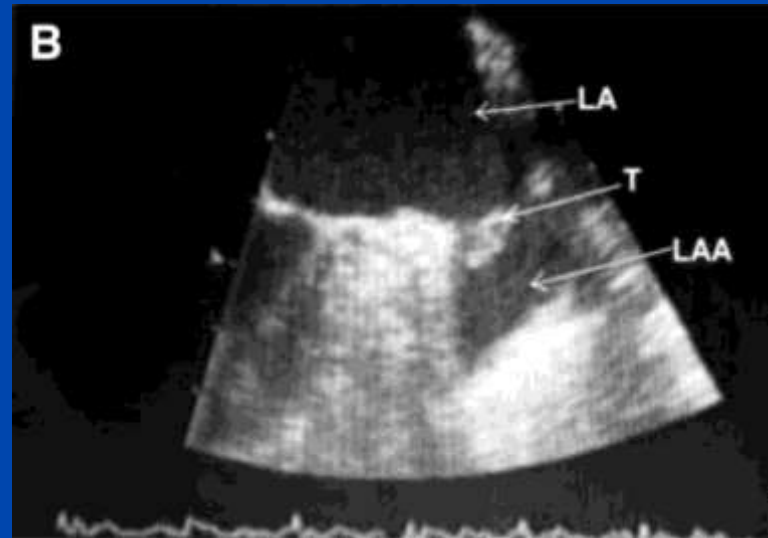
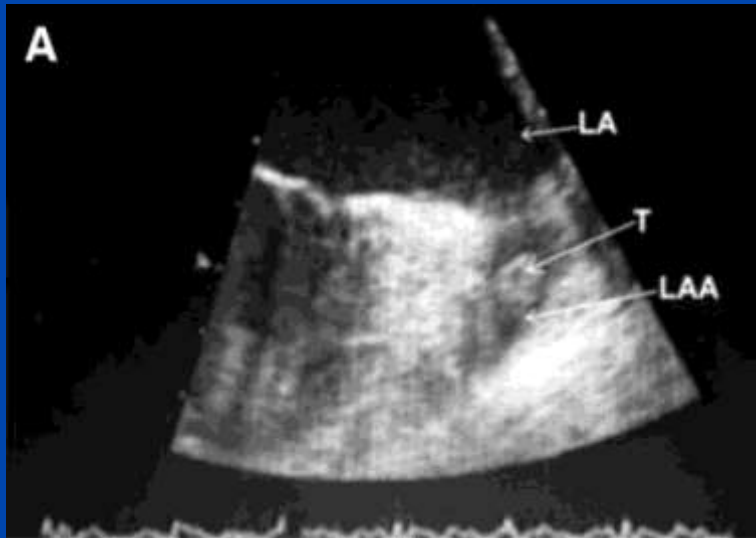
Adherence to OAC

Proportion of Days Covered

CHA₂DS₂VASc score ≥ 4



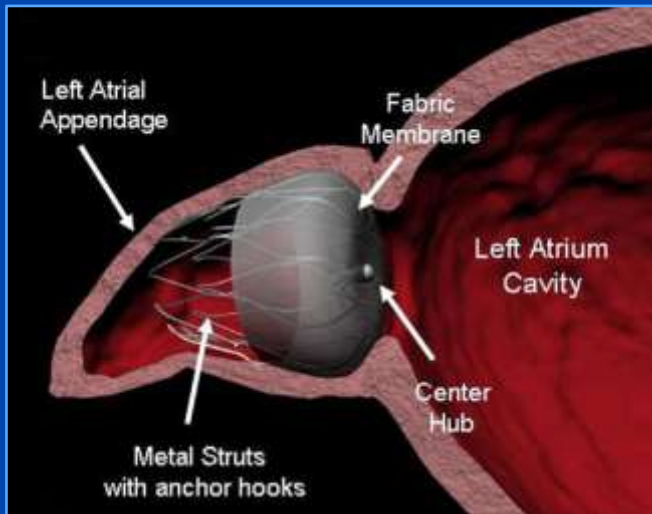
Disappearing LAA Thrombus Resulting in Stroke



Parekh A, Ezekowitz M et al: *Circ* 114:e513, 2006

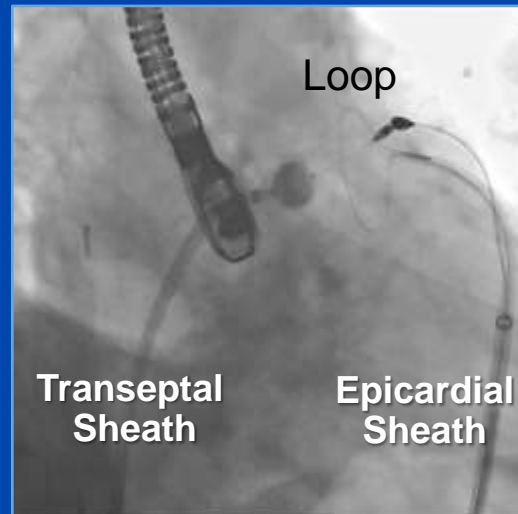
Types of Percutaneous Appendage Closure

Endocardial Plug



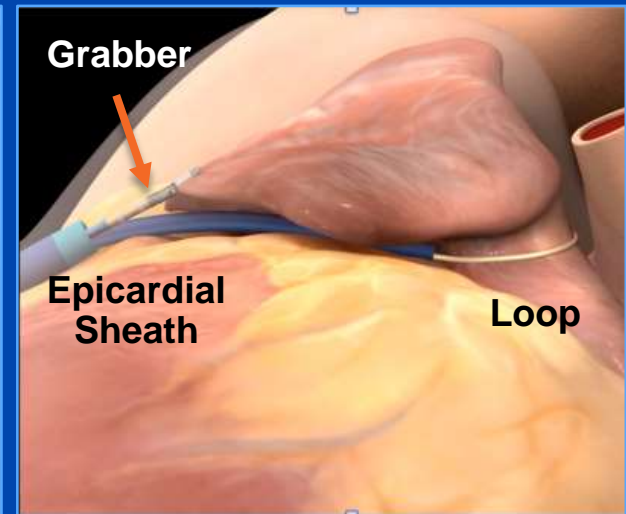
Watchman
WaveCrest
Amplatzer Cardiac Plug

Hybrid Endo/Epi Loop



Lariat

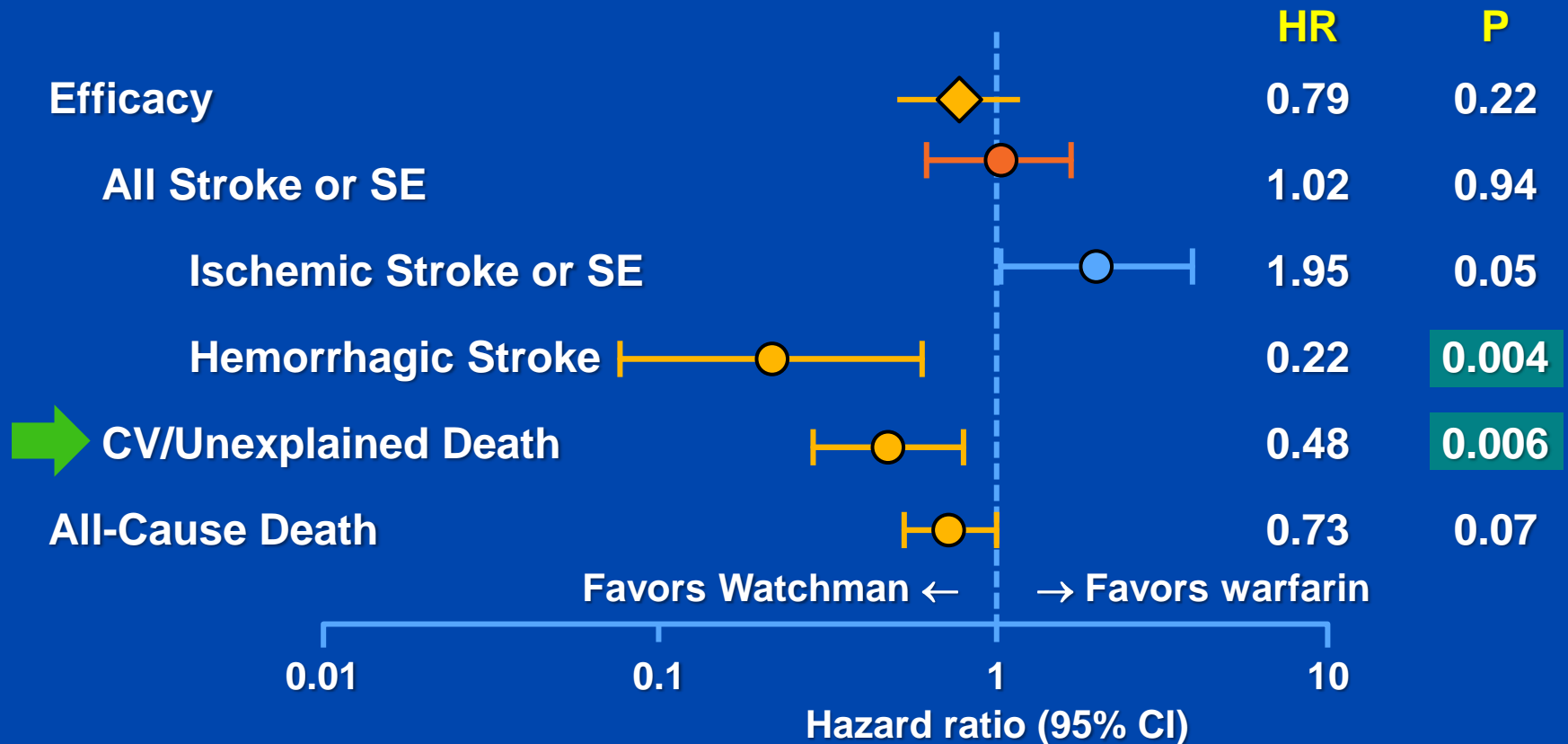
Epicardial Loop



Aegis/Mayo

Left Atrial Appendage Closure vs Warfarin in AF

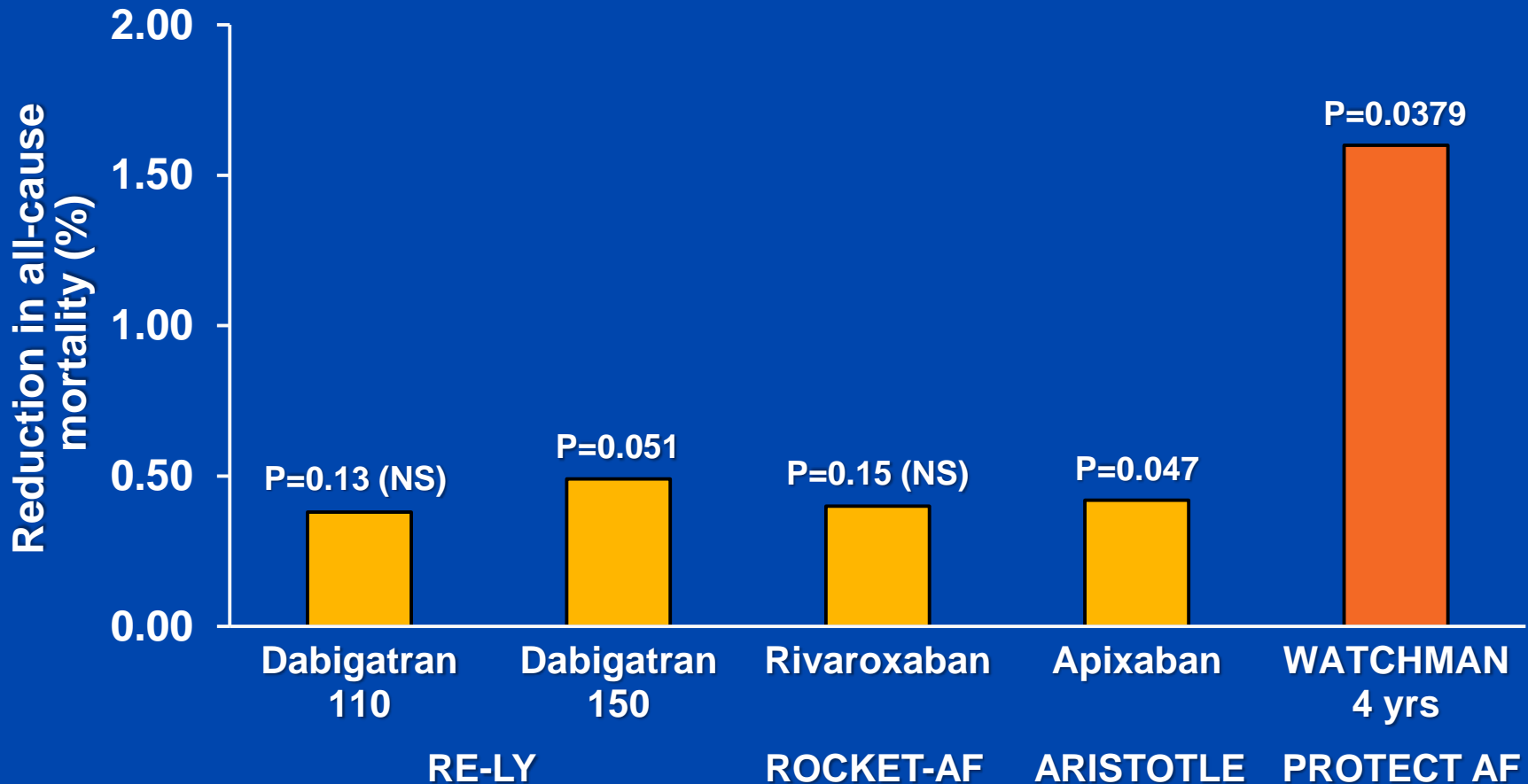
A Patient-Level Meta-Analysis



Combination of PROTECT AF and PREVAIL patients receiving the Watchman device, vs warfarin for overall stroke, ischemic stroke, and all-cause death.

J Am Coll Cardiol; 65:2614, 2015

Mortality Reduction (vs warfarin)



Results from different clinical trials:

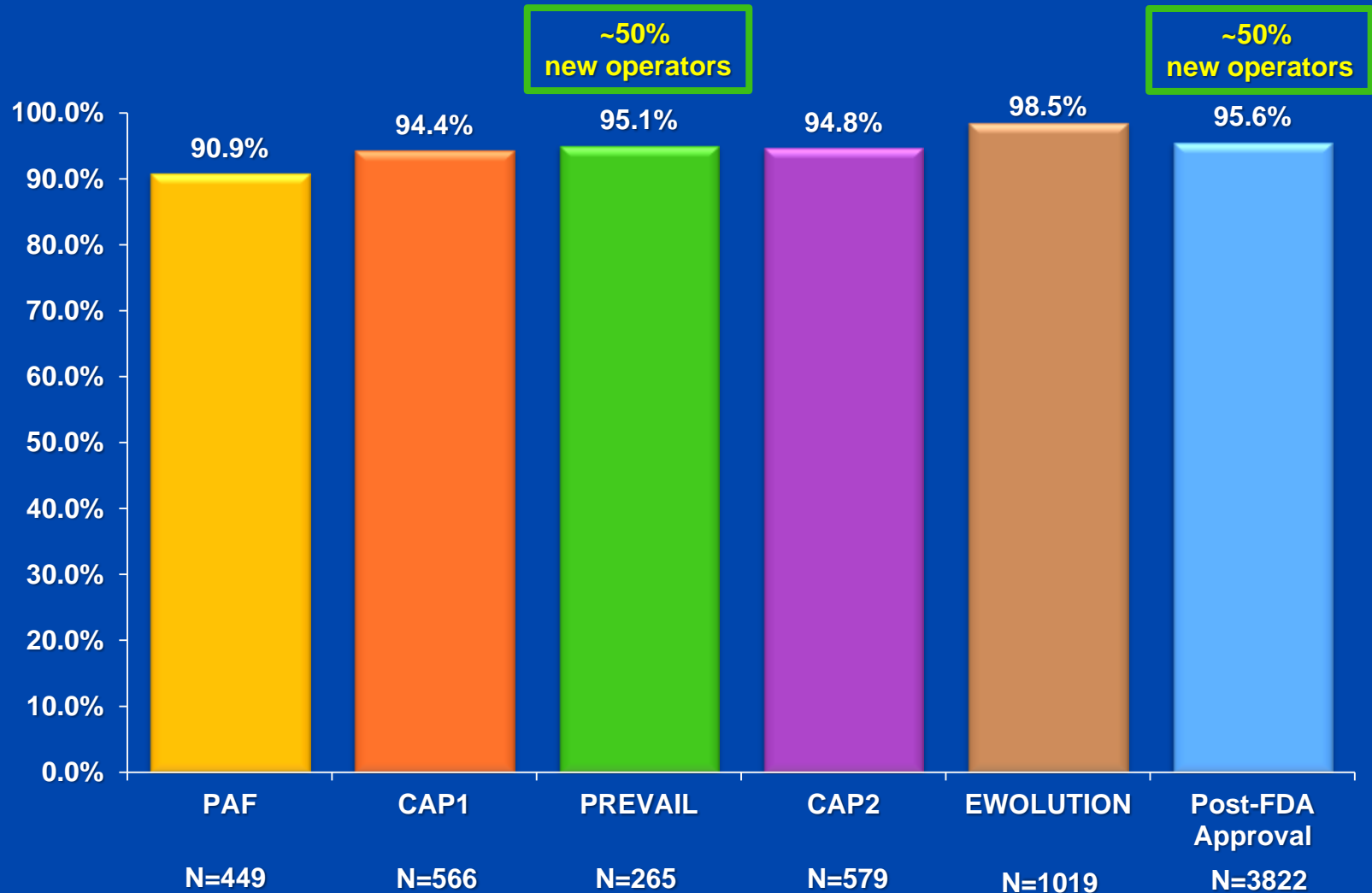
¹Connolly, S. NEJM 2009; 361:1139-1151 – 2 yrs f-up

²Patel, M. NEJM 2011; 365:883-891 – 1.9 yrs f-up, ITT

³Granger, C NEJM 2011; 365:981-992 – 1.8 yrs f-up

⁴Reddy, V. LBCT HRS 2013 – 4 yrs f-up

Procedural Success



Implant success defined as deployment and release of the device into the LAA; no leak \geq 5 mm

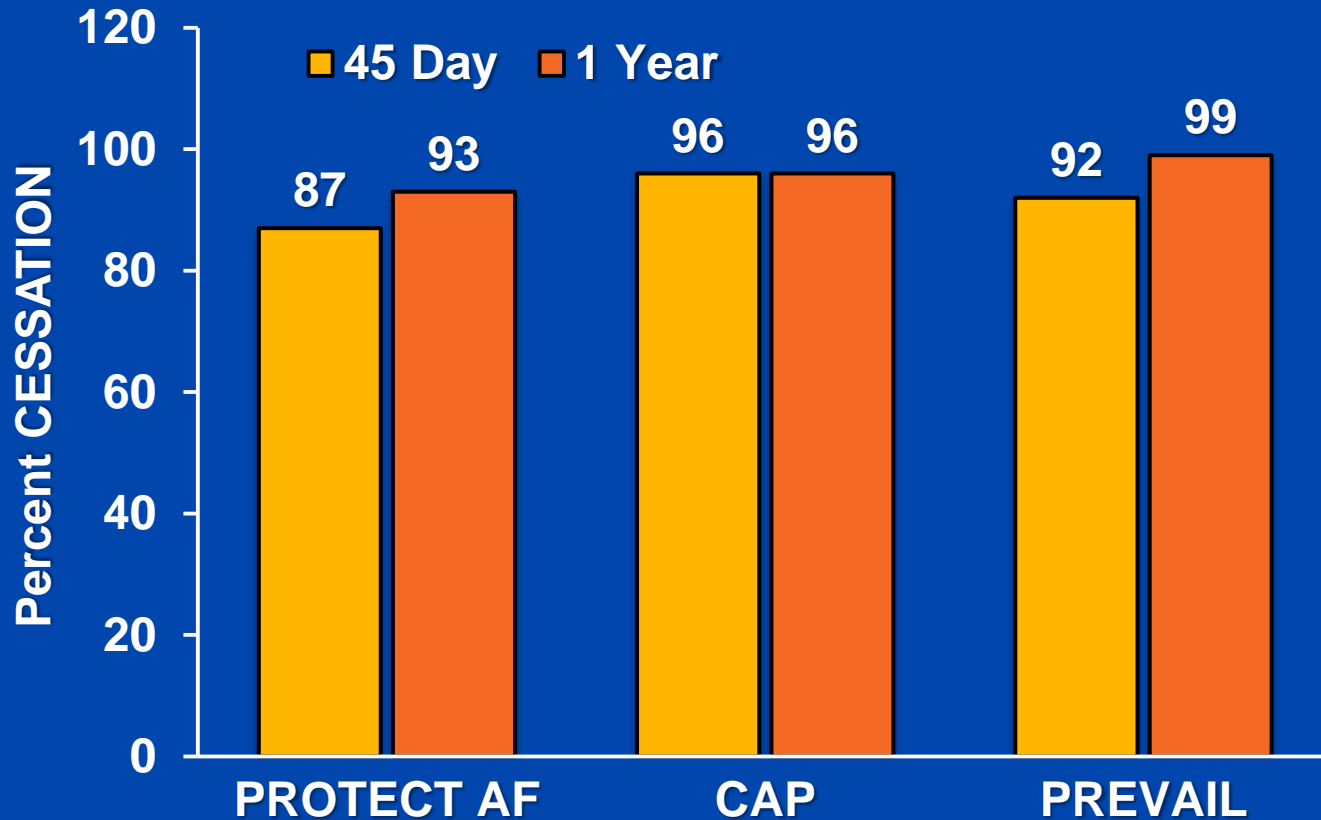
Comparison of Procedural Complications Across Watchman Studies

	PROTECT-AF	PREVAIL	CAP	CAP2	EWOLUTION	Post-FDA approval	Aggregate data
Pericardial tamponade	20 (4.3%)	5 (1.9%)	8 (1.4%)	11 (1.9%)	3 (0.29%)	39 (1.02%)	86 (1.28%)
Treated with pericardiocentesis	13 (2.8%)	4 (1.5%)	7 (1.2%)	NA	2 (0.20%)	24 (0.63%)	
Treated surgically	7 (1.5%)	1 (0.4%)	1 (0.2%)	NA	1 (0.10%)	12 (0.31%)	
Resulted in death	0	0	0	0	0	3 (0.78%)	
Pericardial effusion – no intervention	4 (0.9%)	0	5 (0.9%)	3 (0.5%)	4 (0.39%)	11 (0.29%)	27 (0.40%)
Procedure-related stroke	5 (1.15%)	1 (0.37%)	0	2 (0.35%)	1 (0.10%)	3 (0.078%)	12 (0.18%)
Device embolization	3 (0.6%)	2 (0.7%)	1 (0.2%)	0	2 (0.20%)	9 (0.24%)	17 (0.25%)
Removed percutaneously	1	0	0	0	1	3	
Removed surgically	2	2	1	0	1	6	
Death							
Procedure-related mortality	0	0	0	0	1 (0.1%)	3 (0.078%)	4 (0.06%)
Additional mortality within 7 days	0	0	0	1 (0.17%)	3 (0.29%)	1 (0.026%)	5 (0.07%)

¹WATCHMAN FDA Panel Sponsor Presentation. Oct 2014;

²Boersma et al: EHJ; published online Jan 2016 in press

Warfarin Cessation after WATCHMAN

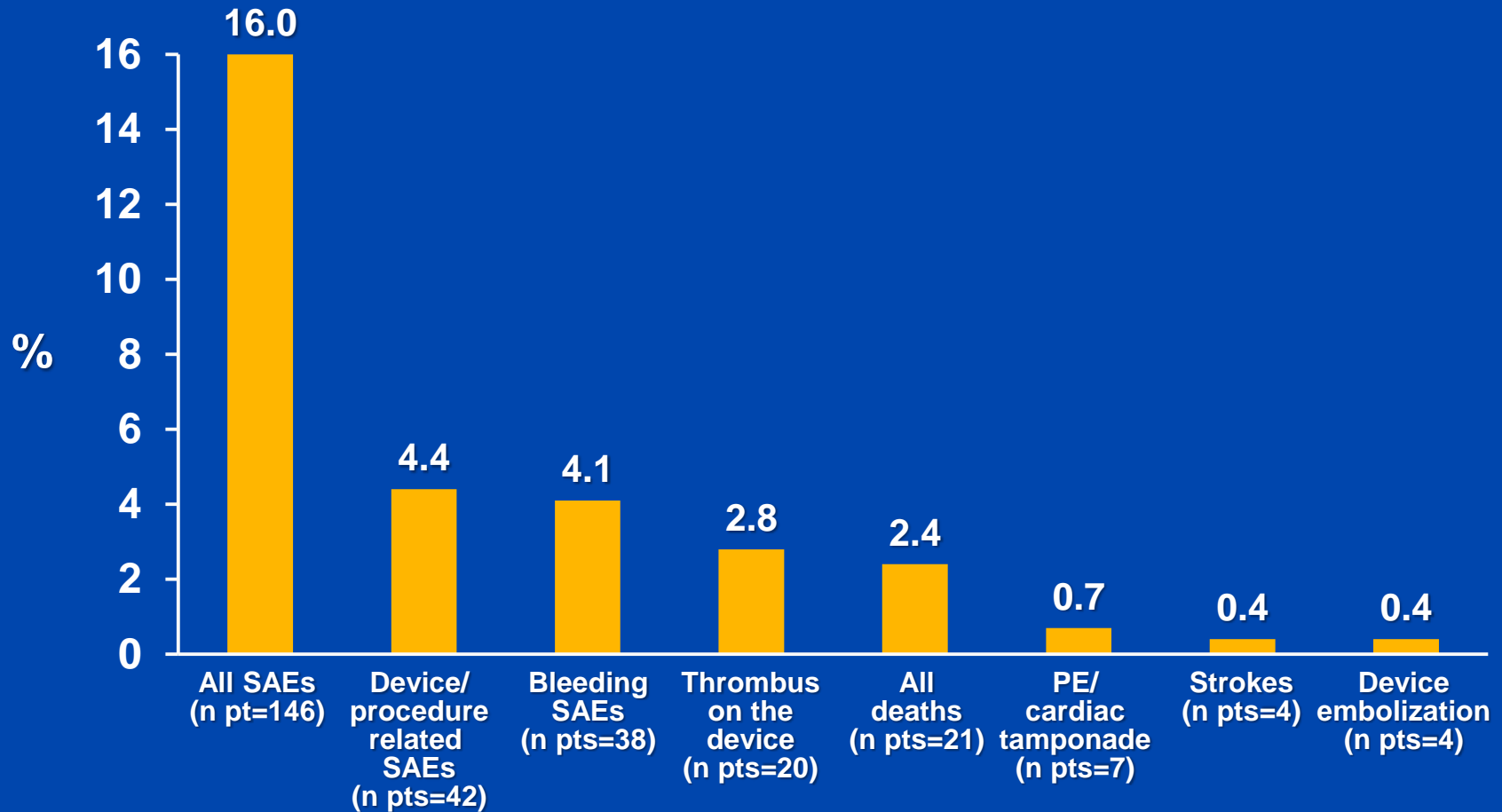




EWOLUTION

- **Multicenter registry of 1,021 patients treated with Watchman LAAC – 2013-2015**
 - **47 centers**
 - **13 countries**
- **Objective: obtain clinical data on**
 - **Procedural success and 30-day outcomes**
 - **Long-term outcomes**
 - **Bleeding**
 - **Stroke/TIA**

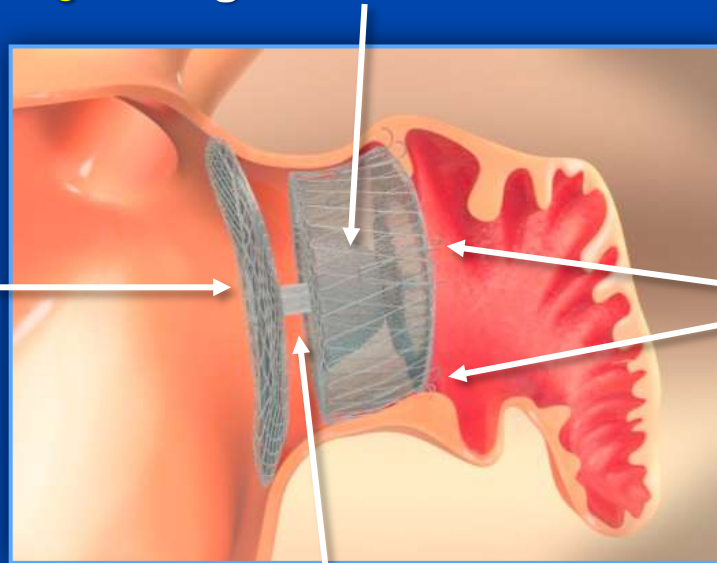
EWOLUTION: Safety Results @ 3 Months N=1025, AC contraindicated 72%



AMPLATZER™ Amulet™ Device

Lobe

- § Inside the LAA neck
- § Designed to conform to LAA anatomy



Disc

- Completely seal at the orifice

Stabilizing Wires

- § Engage with LAA wall
- § Help hold the device in place

Waist

- § Maintains tension between lobe and disc
- § Allows device to self-orient

Major Adverse Events

1,071 patients; major bleeding 73%

Device/Procedure Related MAE	No.	%
Death	3	0.3
Related to cardiac perforation	1	0.1
Related to myocardial infarction	1	0.1
Related to cardiorespiratory arrest	1	0.1
Stroke	3	0.3
Pericardial effusion	5	0.5
Resulted in pericardiocentesis	4	0.4
Resulted in surgical intervention	1	0.1
Embolization	1	0.1
Bleeding	10	0.9
Other	7	0.7
Total	29	2.7

Comparison to Other Studies

	ACP Registry¹	Watchman EVOLUTION²	Amulet (current study)
Implant success	97.3%	98.5%	98.8%
LAA closure rate (1-3 months) ≤5 mm	98.1%	99.3%	100.0%
Device or procedure- related complications	5.0%	2.7%	2.7%
Early mortality	0.8% (30-day)	0.7% (30-day)	0.3% (7-day)

¹ Tzikas et al: EuroIntervention 10, 2015

³ Boersma et al: Eur Heart J 37(31):2465, 2016

Residual Issues

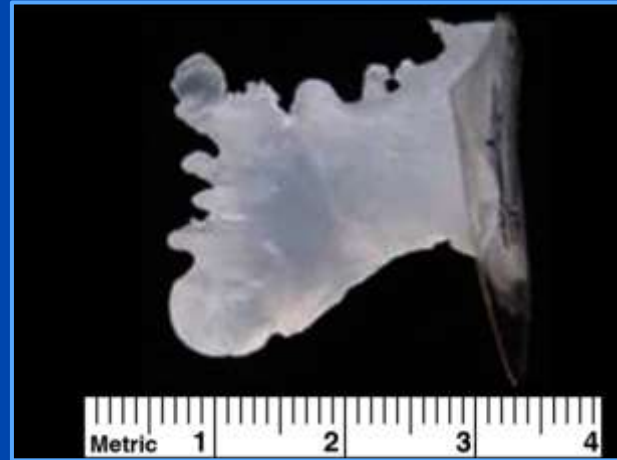
- **Variable anticoagulation strategies**
- **Residual leak**
- **Device thrombus**

Endocasts Obtained From 2 Explanted Hearts Showing the Different LAA Intraluminal Morphologies

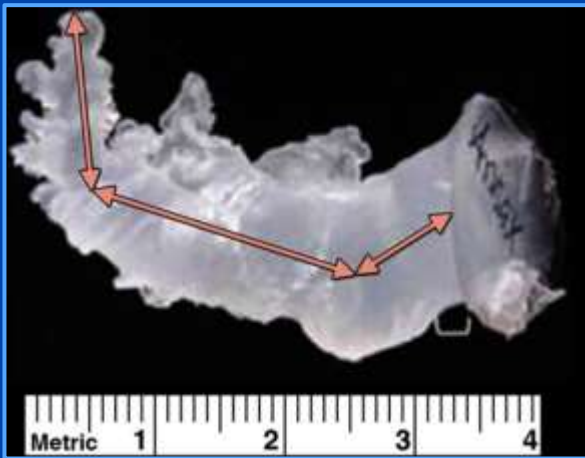
Chicken wing



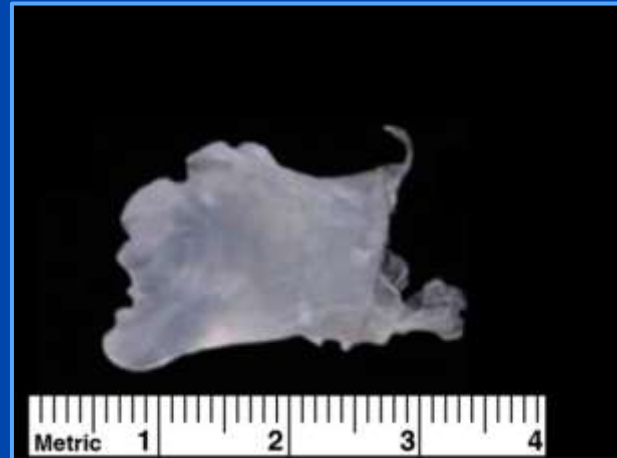
Cauliflower



Windsock



Cactus



Beigel et al: J Am Coll Cardiol Img 7:1251, 2014

Conclusions

- **LAA occlusion devices have very high technical implant success rates**
- **Implantation is associated with low rates of peri-procedural and early adverse events**
- **LAAO is associated with marked decrease in hemorrhage stroke, cardiac/noncardiac mortality & decreased hemorrhage**
- **Post procedure anticoagulation strategies vary but result in excellent outcome**
- **Additional long-term data is being collected to confirm these findings**

LAA – What is Ideal?

The wish list

- A predictable, safe and effective device for reducing ischemic and hemorrhagic strokes
- Is minimally invasive and can be used in hybrid procedures
- Does not require adjunctive AC/APT therapy
- Can be delivered by IC, EP and CV surgery
- Can be used to treat a variety of LAA sizes and shapes
- Is stable, heals fully and completely without residual leaks

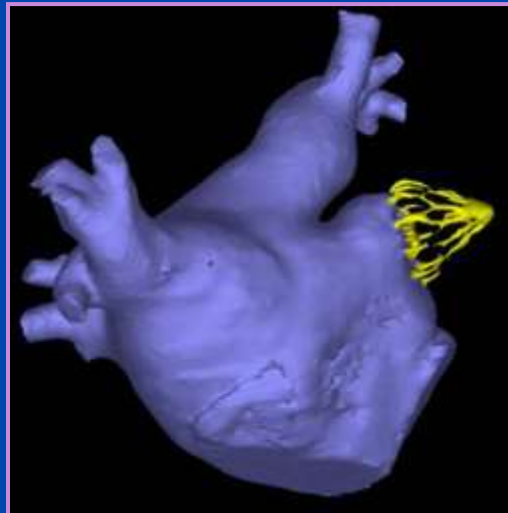
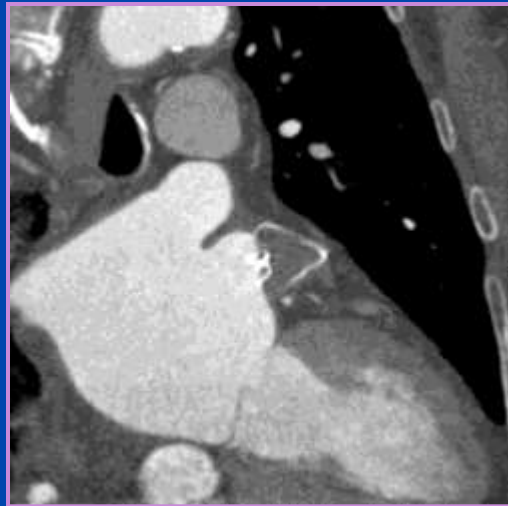


PATIENCE

Is A Virtue

Stroke and Atrial Fibrillation

Alternative to Warfarin or NOACS



- Patients who could be treated with warfarin/NOACS
- Patients who choose not to be treated with warfarin/NOACS
- Contraindications to warfarin/NOACS
- In concert with ablation