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UTSW Cerebrovascular Diseases and Stroke Symposium 2025

The Heart-Brain Connection: Advances in Neurocardiology

Dharam J. Kumbhani, MD, SM, MRCP, FACC, FAHA, FSCAI

Jim and Norma Smith Distinguished Chair for Interventional Cardiology

Section Chief, Interventional Cardiology

Director, Cardiac Catheterization Laboratory, Clements University Hospital

Professor of Medicine

UT Southwestern Medical Center, Dallas, TX

December 13, 2025

Disclosures

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Honoraria, American College of Cardiology

Associate Editor, *Circulation*

Circulatory Devices Advisory Panel, US FDA


Giving a talk right after lunch

Outline

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- Epidemiology of cardioembolic strokes
- Left atrial appendage closure
- Patent foramen ovale closure

Highlight close collaboration between interventional cardiology and stroke neurology

Cardiac Sources of Stroke

	Higher-stroke risk	Lower-stroke risk
Rhythm	Atrial fibrillation/flutter Sick sinus syndrome	Paroxysmal supraventricular tachycardia
Valve	Rheumatic mitral stenosis Bioprosthetic valve, 1st 6 months Mechanical heart valve Endocarditis Papillary fibroelastoma	Bioprosthetic valve, >6 months Mitral annular calcification Lambl excrescence
Cardiac chamber	L-atrial myxoma L-atrial/ventricular thrombus L-ventricular assist device	L-atrial spontaneous echo contrast Wall motion abnormality, including apical AK Left ventricular hypertrophy Left ventricular non-compaction
Interatrial septum	Patent foramen ovale Atrial septal defect	Interatrial septal aneurysm

AF, Stroke, and LA Thrombus

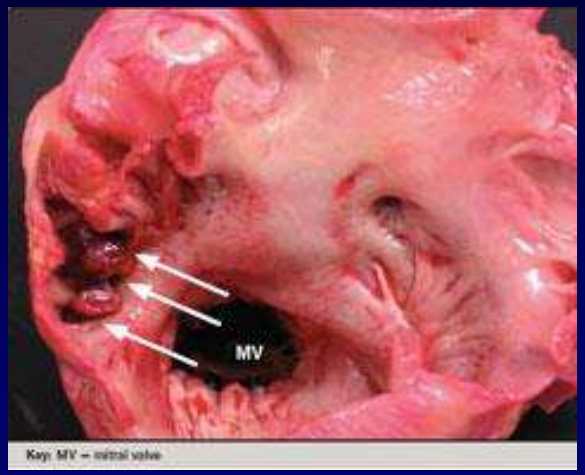
1) AF is the Most Common Arrhythmia
   - -2.66 million Americans in 2010, *over 12.1 million in 2030*
   - -AF present in 1% population under 60 and 8% over age 80
   - -estimated to costs $6.65 billion for care in 2005, $26 billion in 2019

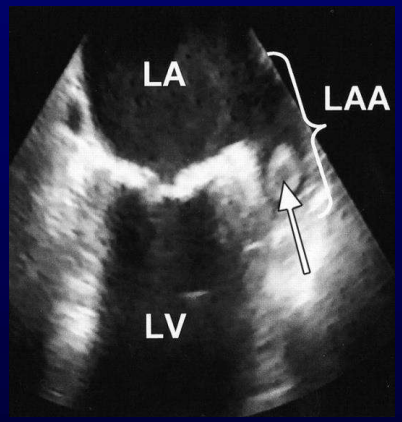
2) AF is responsible for 15-20% ischemic strokes
   - -130,000 to 160,000 per year in US
   - -120,000 are first or new strokes
   - -costs $53.9 billion in 2010, and the leading cause of disability

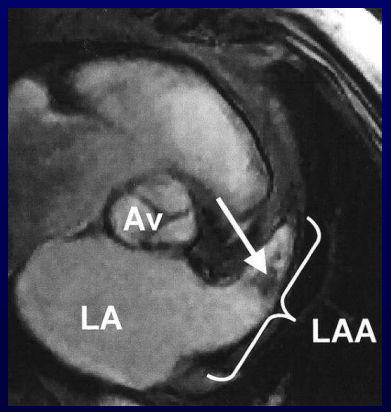
3) Left Atrial Thrombus
   - - occurs in ~15% with AF>48 hrs without anticoagulation
   - - when found, 90% are in left atrial appendage (LAA)

ACC/AHA/HRS 2011 AF Guidelines
Centers for Disease Control 2023
Manning, et al, JACC 1994

Left Atrial Thrombi can be quite large







Whitlock et al. Circ 2009;120:1927-32
Mohrs O K et al. AJR 2006;186:198-205
A-fib.com/bostona-fib symposium

NOACs better than VKA

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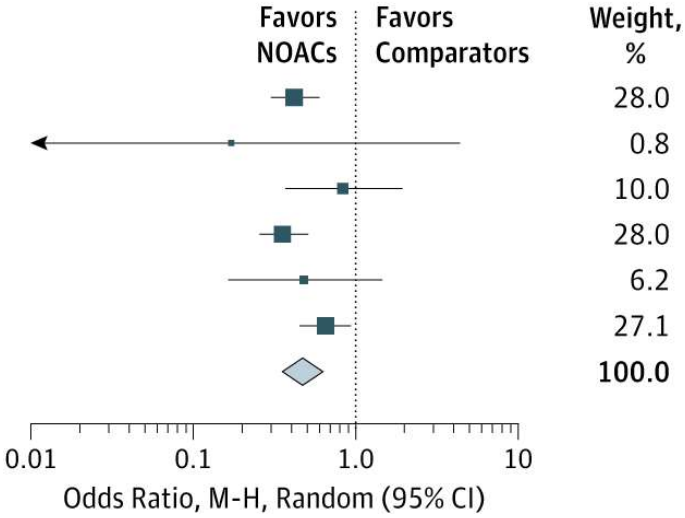
Risk of ICH

Source	NOACs, No. Events	NOACs, No. Total	Comparator, No. Events	Comparator, No. Total	Odds Ratio, M-H, Random (95% CI)
Granger et al,[5] 2011	52	9088	122	9052	0.42 (0.30-0.58)
Ogawa et al,[7] 2011	0	143	1	75	0.17 (0.01-4.30)
Connolly et al,[8] 2011	11	2808	13	2791	0.84 (0.38-1.88)
Connolly et al,[3] 2009	63	12091	87	6022	0.36 (0.26-0.49)
Hori et al,[6] 2012	5	639	10	639	0.50 (0.17-1.46)
Patel et al,[4] 2011	55	7061	84	7082	0.65 (0.46-0.92)
Total (95% CI)	**186**	**31830**	**317**	**25661**	**0.49 (0.36-0.65)**

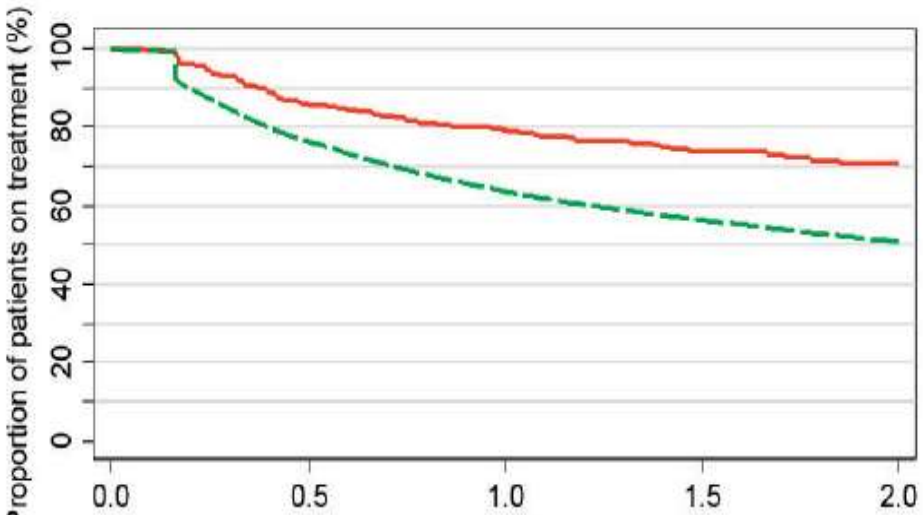
Heterogeneity: $\tau^2 = 0.05$; $\chi^2_5 = 9.13$ ($P = .10$); $I^2 = 45\%$
Test for overall effect: $Z = 4.87$, $P < .001$



Chatterjee S..Kumbhani DJ. JAMA Neurol. 2013

Despite NOAC adoption and ability to switch NOACs, adherence to anticoagulation remains a challenge

~30% of NOAC patients stop taking any drug at 2 years



NOAC	914	651	342	139	41
VKA	12307	8453	5762	3915	2506

Martinez C. Thromb Haemost. 2015

DOAC Trials – Adherence and Bleeding Issues

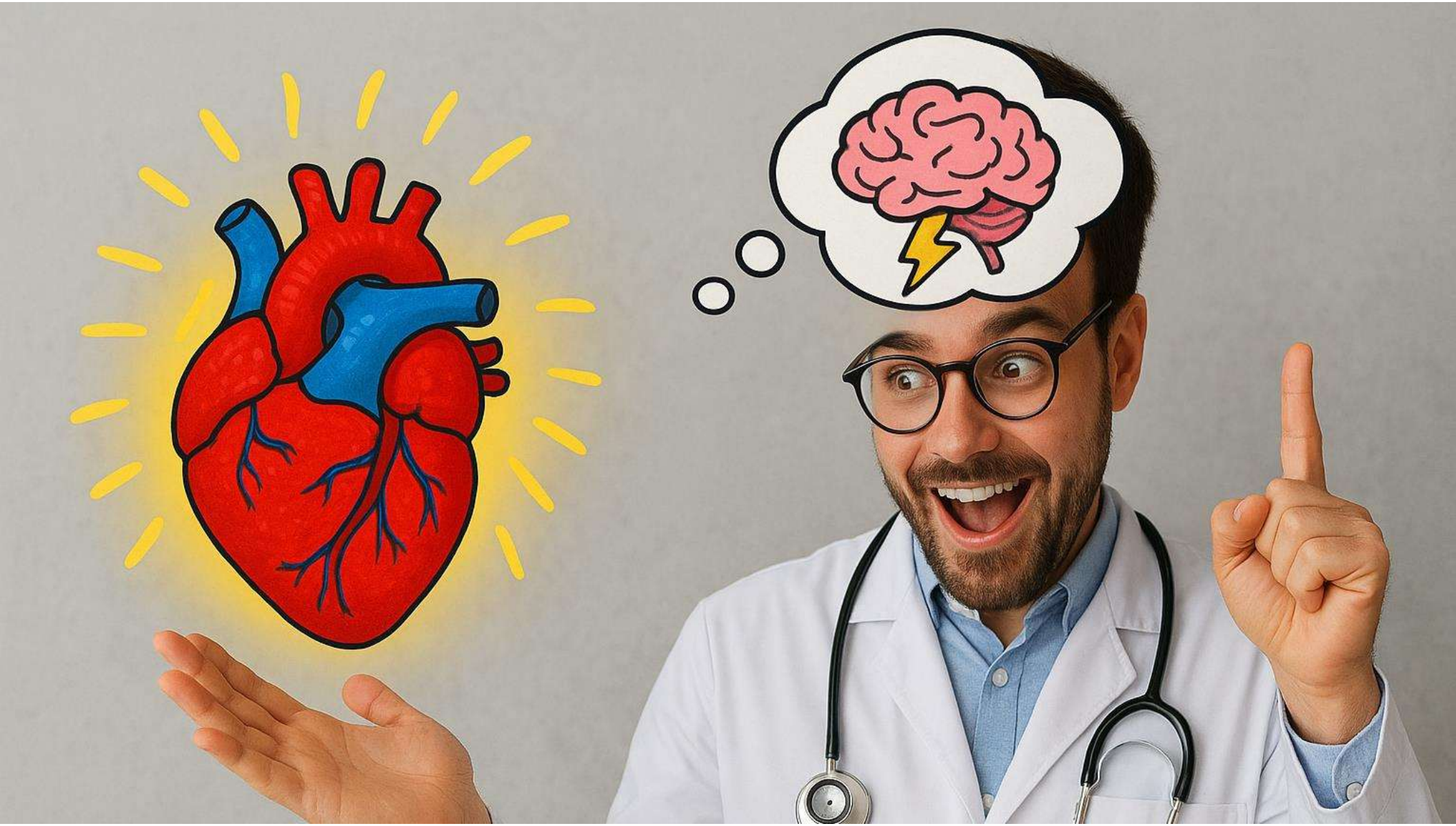
For those that remain adherent, bleeding risks persist

Treatment	Study Drug Discontinuation Rate	Major Bleeding (rate/year)
Rivaroxaban[1]	24%	3.6%
Apixaban[2]	25%	2.1%
Dabigatran[3] (150 mg)	21%	3.1%
Edoxaban[4] (60 mg / 30 mg)	34% / 33%	2.8% / 1.6%
Warfarin[1-4]	17 – 35%	3.1 – 3.4%

*Rivaroxaban: 1.9 years follow-up; Apixaban: 1.8 years follow-up; Dabigatran: 2 years follow-up; Edoxaban: 2.8 years follow-up

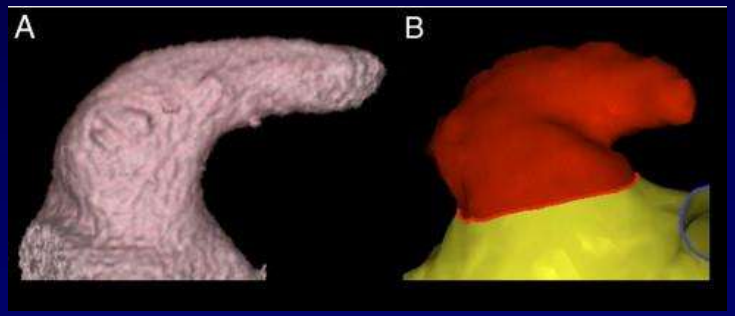
[1]Patel, M. NEJM 2011; 365(10):883-891. [2]Granger, C NEJM 2011; 365(11):981-992. [3]Connolly, S. NEJM 2009; 361(12): 1139-1151, [4]Giugliano, R. NEJM 2013; 369(22): 2093-2104.

Left atrial appendage occlusion

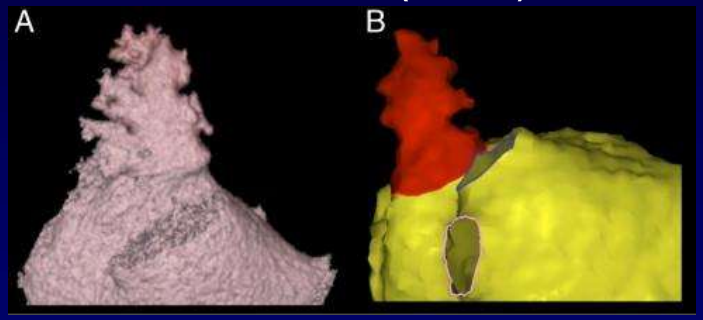


LAA Morphology

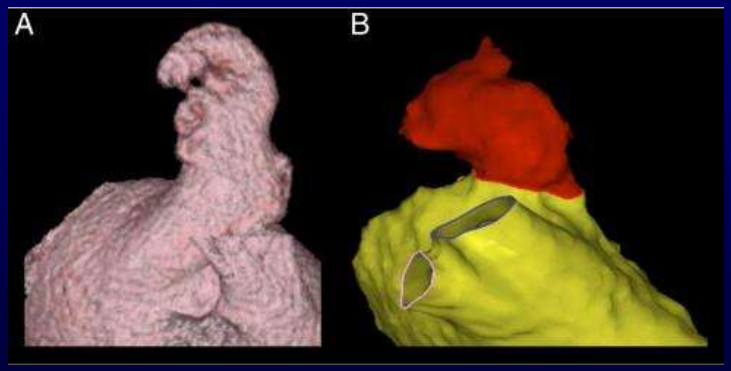
Chicken Wing (48%)



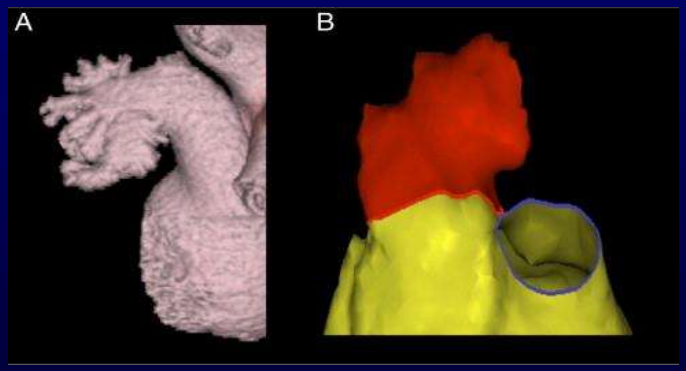
Cactus (30%)



Windsock (19%)

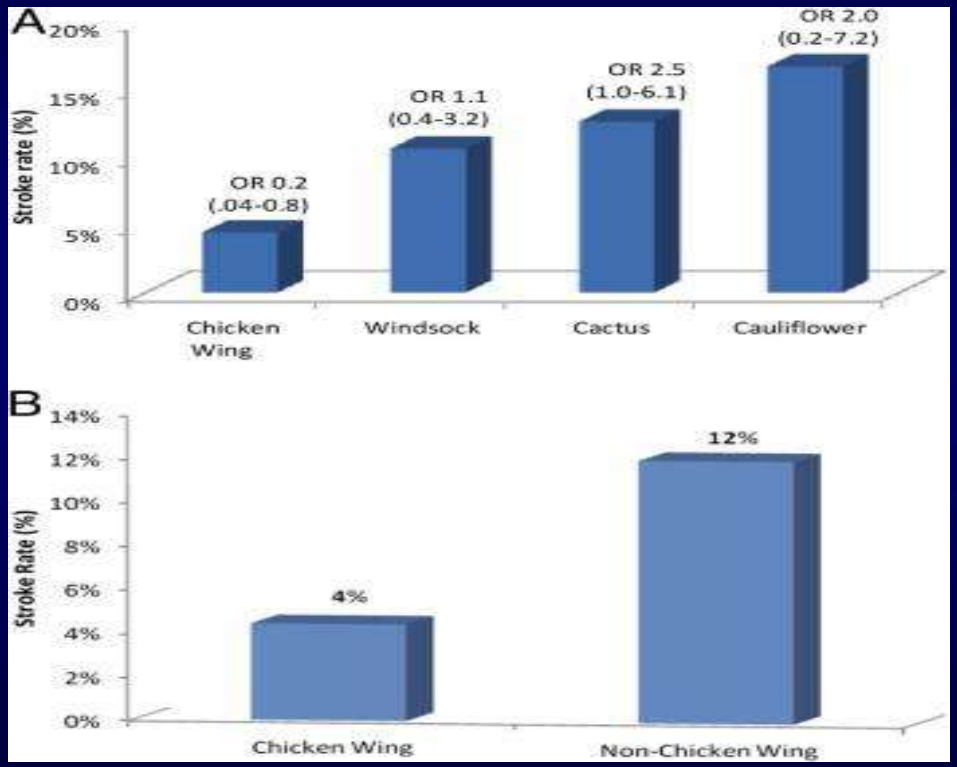


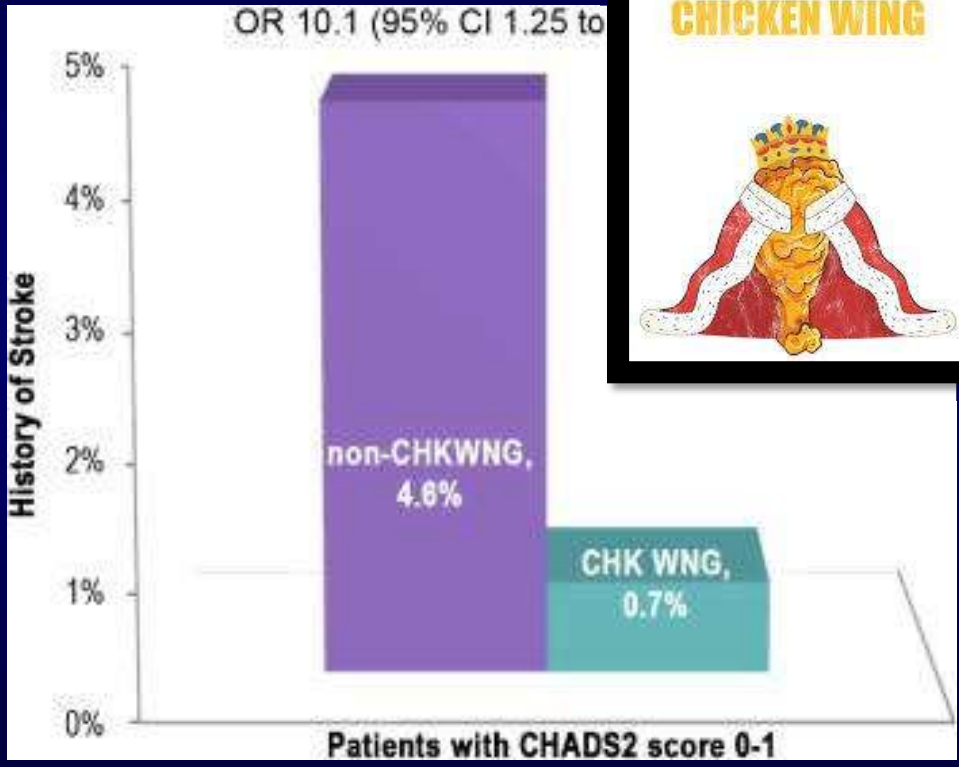
Cauliflower (3%)



Di Biase L. JACC 2012

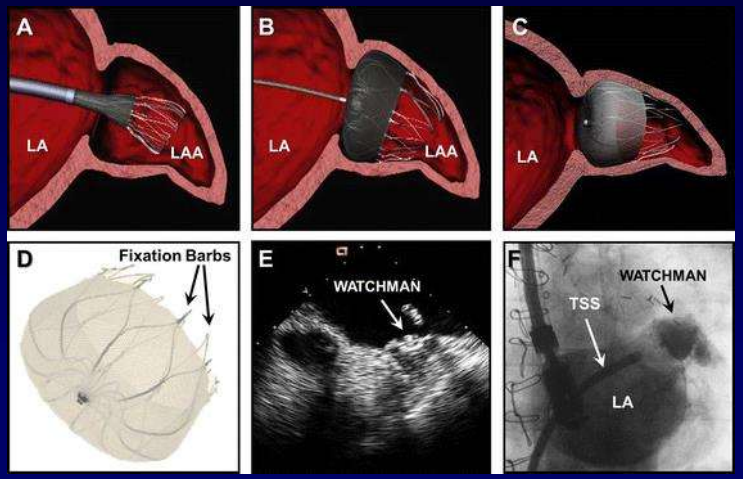
Prevalence of Prior Stroke/TIA According to LAA Morphologies

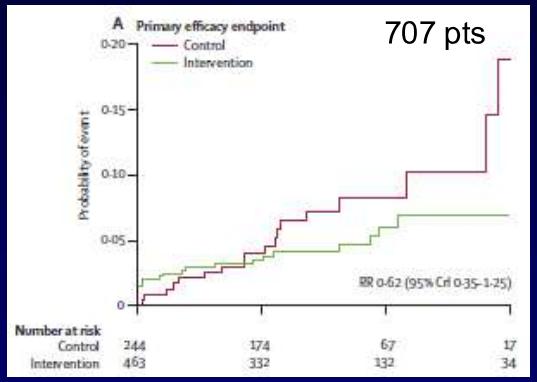


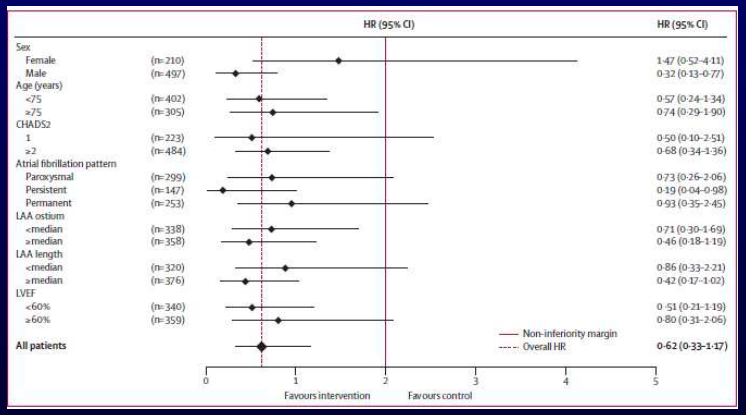


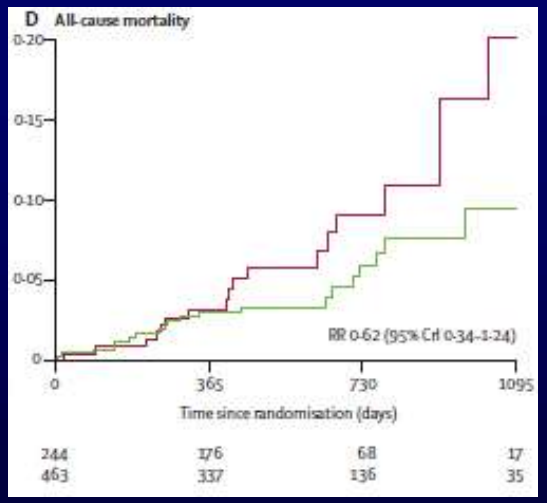
Di Biase L. JACC 2012

Watchman Device PROTECT-AF Trial



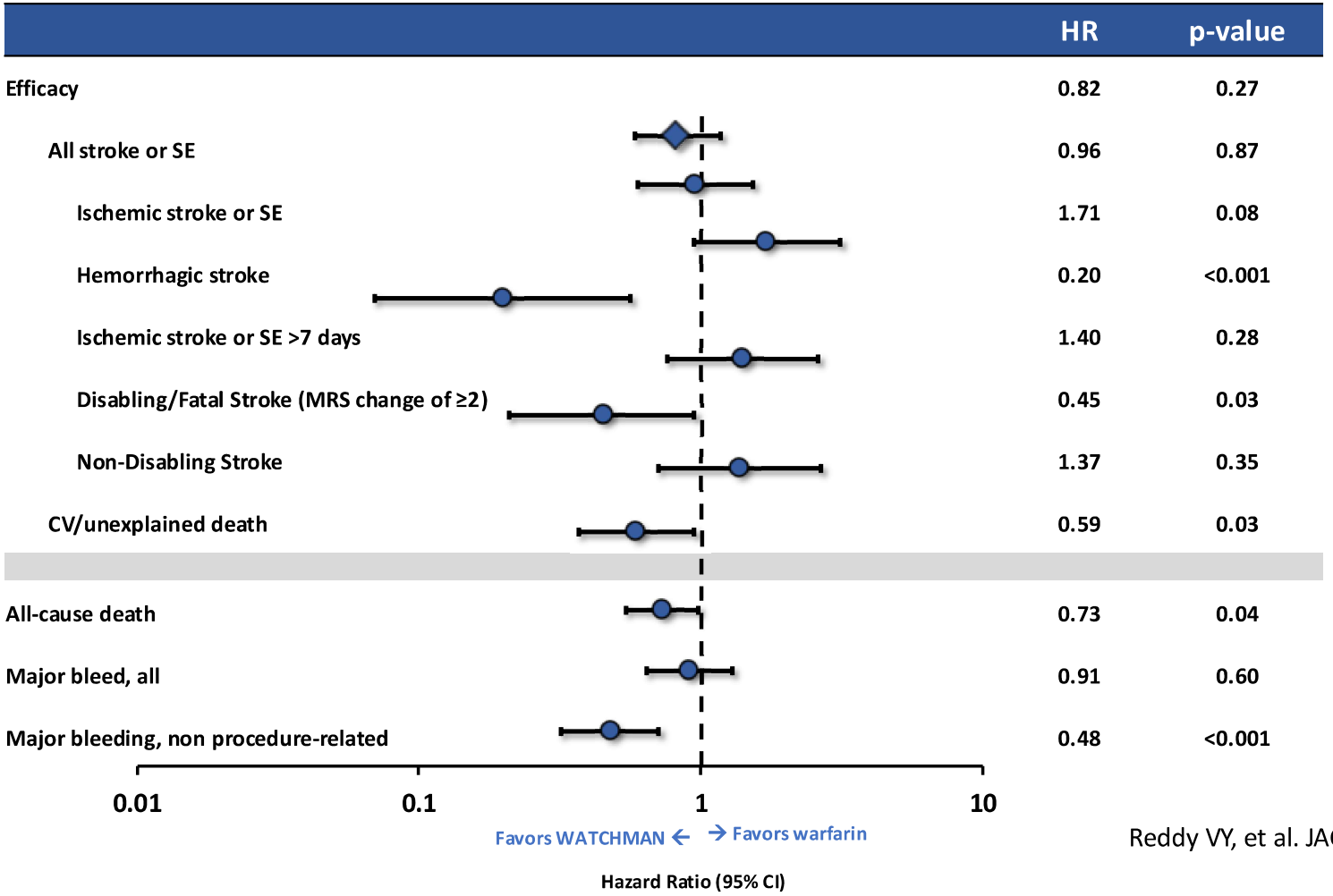






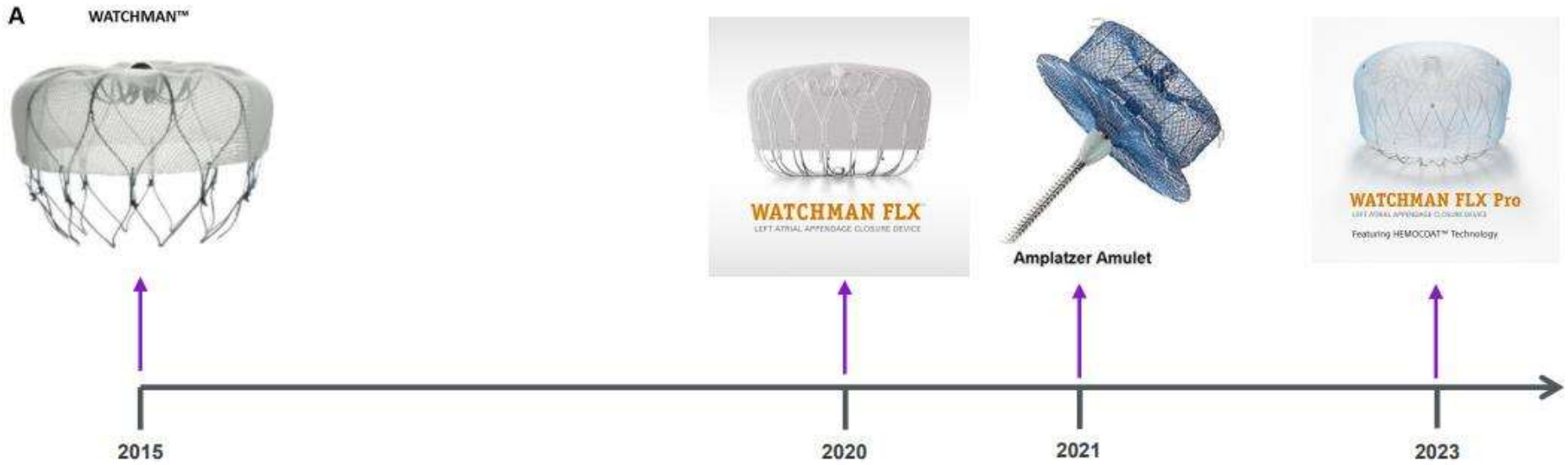
Holmes, Lancet 2009; 374: 534-42
Aryana, et al, Curr Treat CV Med, 2012

PROTECT AF & PREVAIL 5 Year Patient Level Meta-Analysis



Reddy VY, et al. JACC 2017; 70(24): 2964-2975.

Evolution of LAAO Devices



LAAO consideration

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CHA_2DS_2-VASc score

Age	**<65 0**	65-74 +1	≥75 +2
Sex	**Female +1**	Male 0	
CHF history	**No 0**	Yes +1	
Hypertension history	**No 0**	Yes +1	
Stroke/TIA/thromboembolism history	**No 0**	Yes +2	
Vascular disease history (prior MI, peripheral artery disease, or aortic plaque)	**No 0**	Yes +1	
Diabetes history	No 0	**Yes +1**	

HAS-BLED score

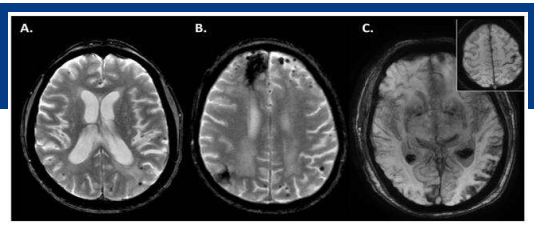
HAS-BLED Score for Major Bleeding Risk

Estimates risk of major bleeding for patients on anticoagulation to assess risk-benefit in atrial fibrillation care.

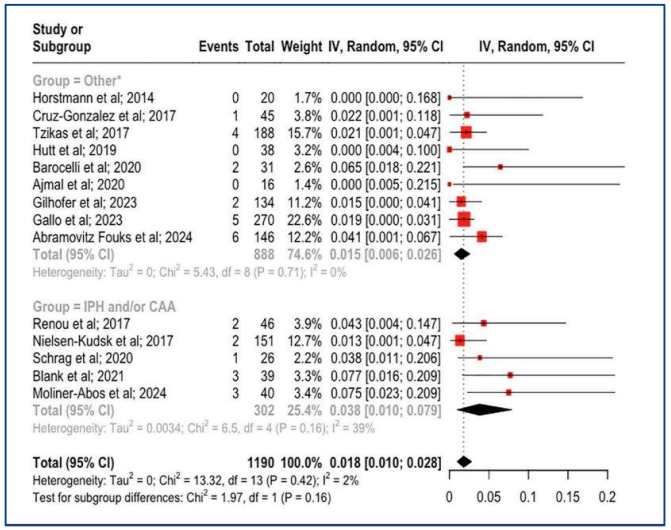
When to Use | Pearls/Pitfalls | Why Use

Hypertension Uncontrolled, >160 mmHg systolic	No 0	**Yes +1**
Renal disease Dialysis, transplant, Cr >2.26 mg/dL or >200 µmol/L	**No 0**	Yes +1
Liver disease Cirrhosis or bilirubin >2x normal with AST/ALT/AP >3x normal	**No 0**	Yes +1
Stroke history	No 0	**Yes +1**
Prior major bleeding or predisposition to bleeding	**No 0**	Yes +1
Labile INR Unstable/high INRs, time in therapeutic range <60%	**No 0**	Yes +1
Age >65	No 0	**Yes +1**
Medication usage predisposing to bleeding Aspirin, clopidogrel, NSAIDs	No 0	**Yes +1**
Alcohol use ≥8 drinks/week	**No 0**	Yes +1

LAAO in cerebral amyloid angiopathy

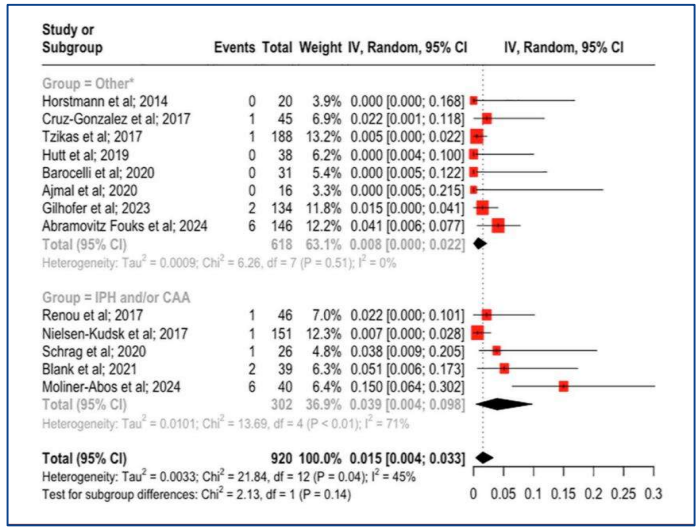


Ischemic stroke



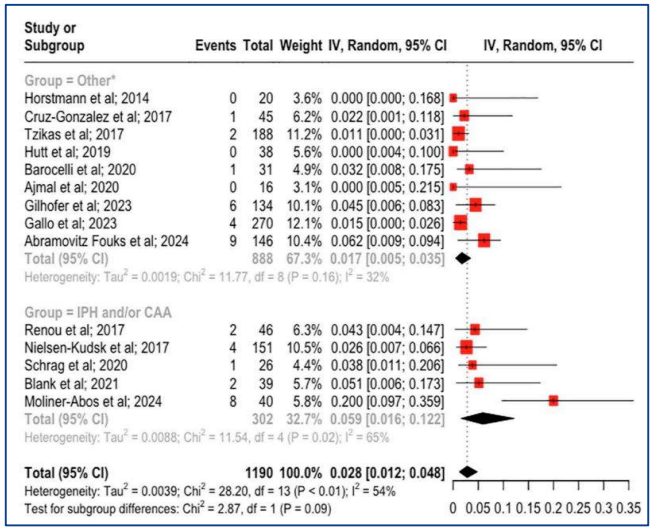
Mean: 17.1 months
Overall: 2%
IPH/CAA: 4%

Recurrent ICH



Mean: 18.6 months
Overall: 2%
IPH/CAA: 4%

Major hemorrhage



Mean: 18.6 months
Overall: 3%
IPH/CAA: 6%

Mavridis T. Int J Stroke 2025

Device related thrombosis (DRT)

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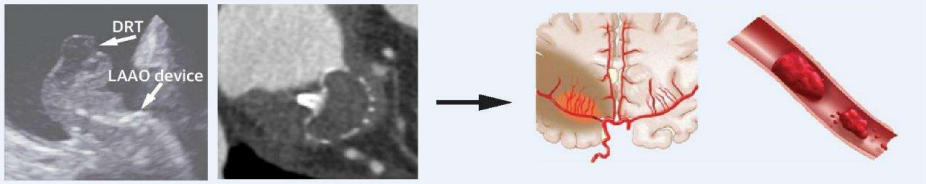
Device-Related Thrombus Following Left Atrial Appendage Occlusion

A Incidence and Clinical Impact

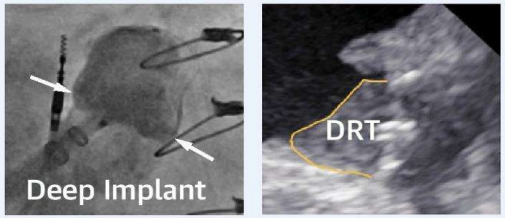


2%-4% within 1 year after LAAO

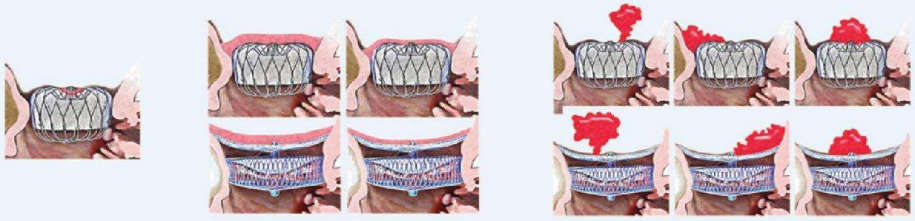
2- to 4-Fold ↑ Thromboembolism

B Independent Predictors of DRT

- Age
- Female
- Permanent AF
- LV Dysfunction
- CHA_2DS_2-VASc
- Coagulopathy
- Renal Disease



C Novel DRT Classification



No DRT | Low likelihood of DRT | High likelihood of DRT

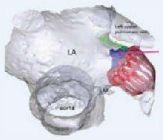
D Prevention and Treatment of DRT

Before LAAO

Surgical clipping for high-risk patients

After DRT

Long-term anticoagulation



Frequent surveillance

Alkhouli M. JACC Intv 2023

Peri-device leak (PDL)

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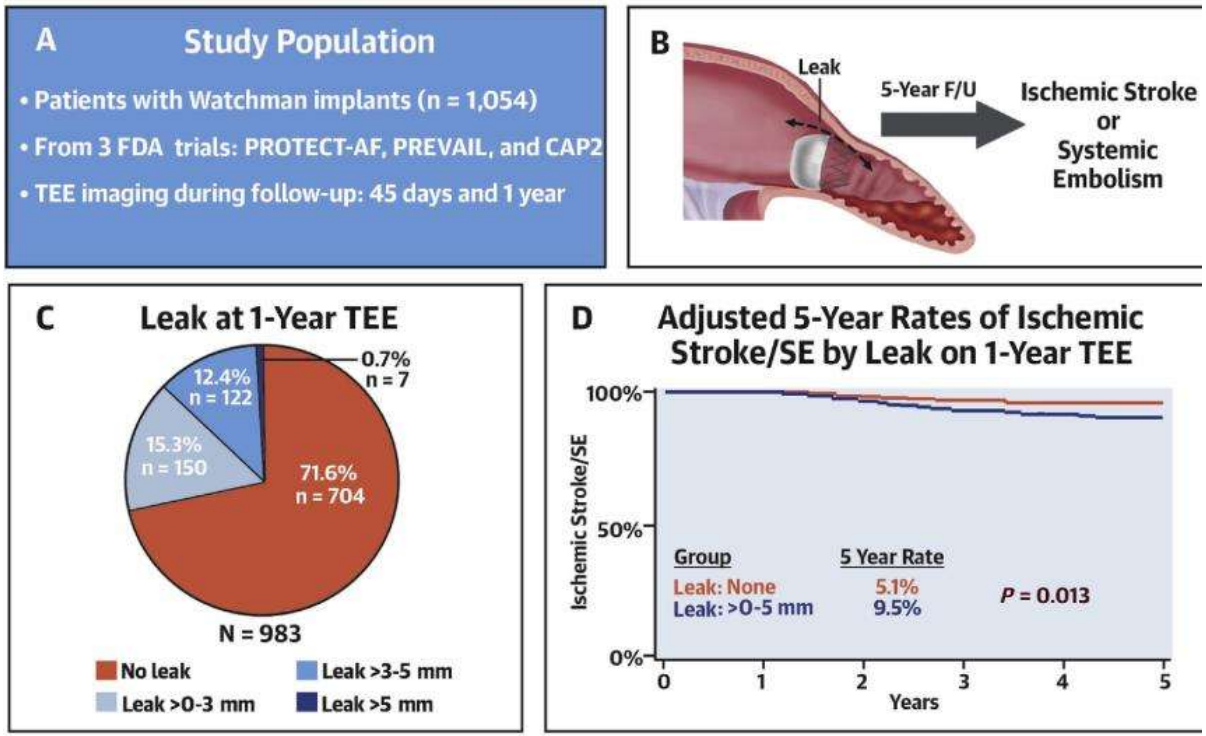
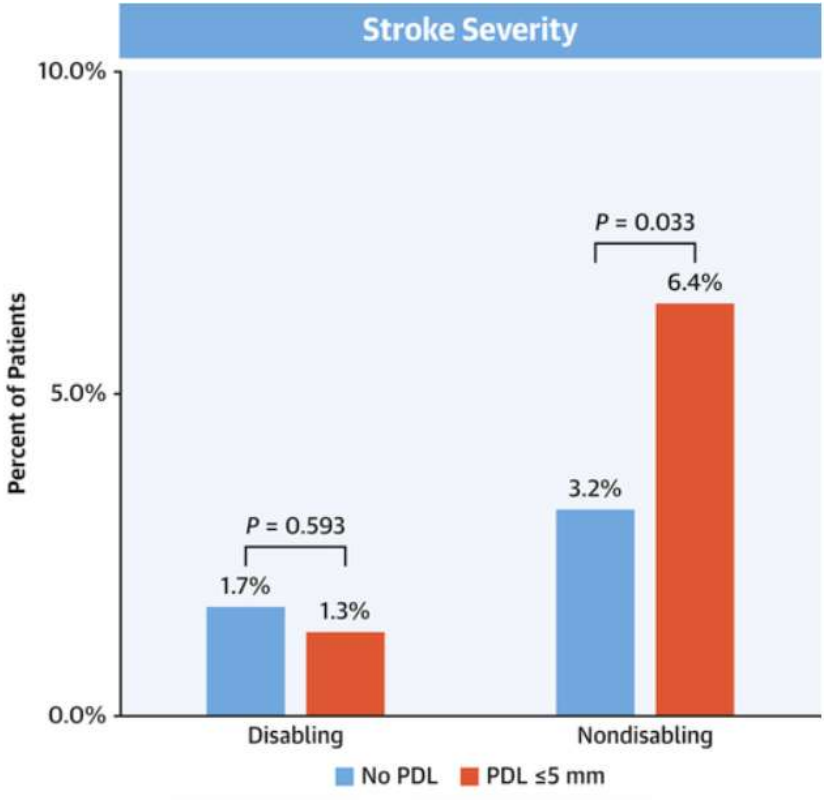
Increased risk with larger leaks:

Studies show a stronger association between larger peri-device leaks and higher stroke risk compared to small leaks.





Dukkipati SR. JACC 2022; 80 (5):469–483.

Antithrombotic regimen post LAAO

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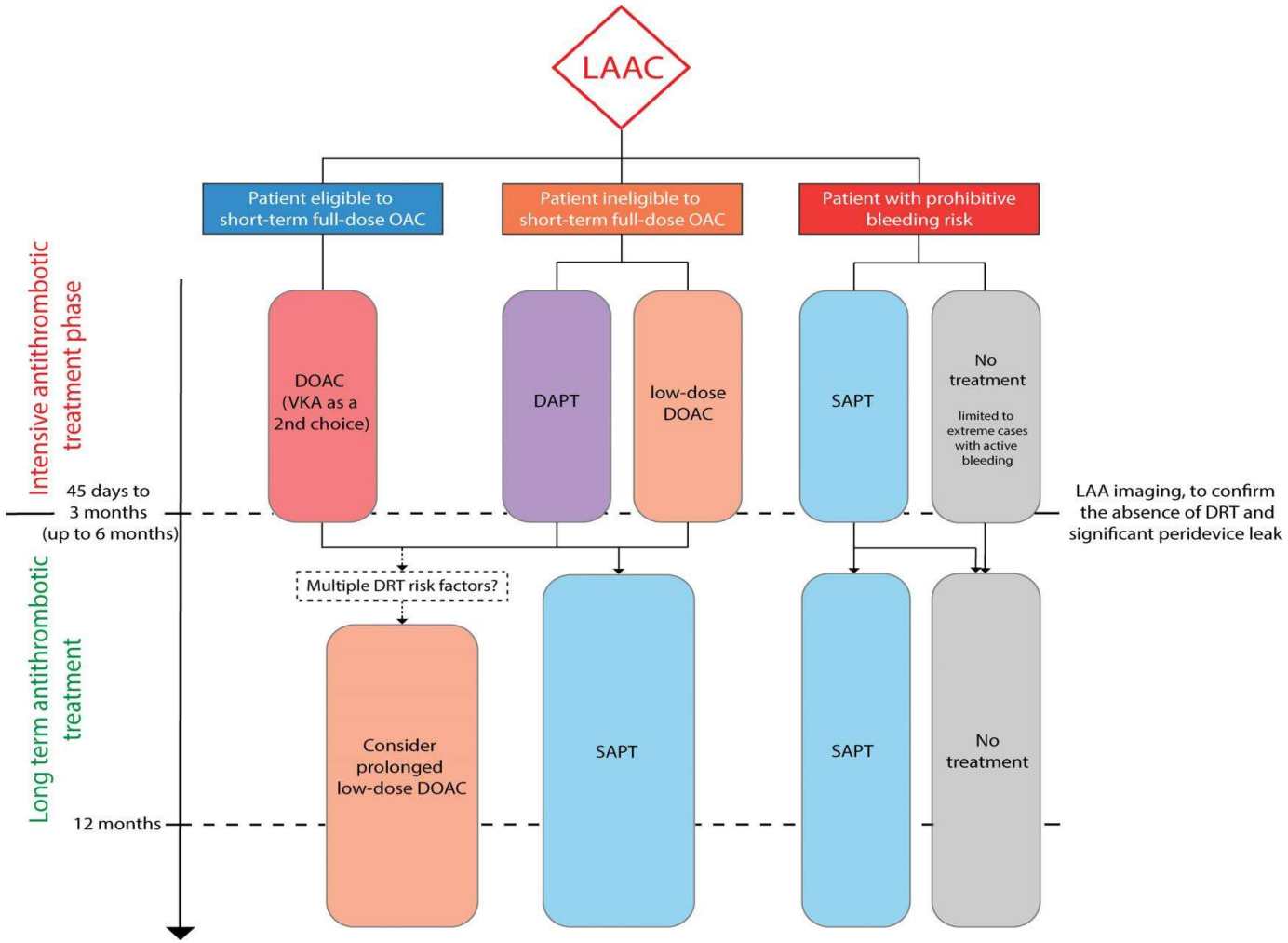

Mesnier J. Circ: CV Intv 2023

2023 ACC/AHA AF Guideline Recommendations for LAAO

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Recommendations for Percutaneous Approaches to Occlude the LAA Referenced studies that support the recommendations are summarized in the Online Data Supplement.		
COR	**LOE**	**Recommendations**
2a	**B-NR**	1. In patients with AF, a moderate to high risk of stroke (CHA_2DS_2-VASc score ≥2), and a contraindication (Table 14) to long-term oral anticoagulation due to a nonreversible cause, percutaneous LAAO (pLAAO) is reasonable.[1–4]
2b	**B-R**	2. In patients with AF and a moderate to high risk of stroke and a high risk of major bleeding on oral anticoagulation, pLAAO may be a reasonable alternative to oral anticoagulation based on patient preference, with careful consideration of procedural risk and with the understanding that the evidence for oral anticoagulation is more extensive.[1–3,5,6]
2b	**B-NR**	3. In patients with AF and conditions associated with high risk of recurrent ICH (eg, cerebral amyloid angiopathy) anticoagulation-sparing strategies (eg, LAAO) may be considered to reduce the risk of recurrent hemorrhage.[6,7]

Long-term OAC contraindicated

- Severe irreversible bleeding (GI, GU, pulm)
- Spontaneous intracranial/ intraspinal bleeding
- Bleeding from recurrent falls

Joglar J. Circ 2023

Patent Foramen Ovale

Epidemiology

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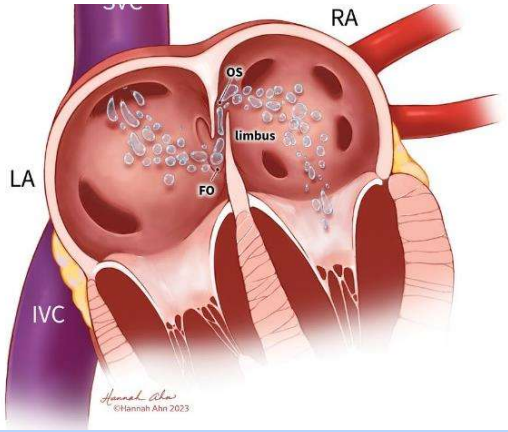
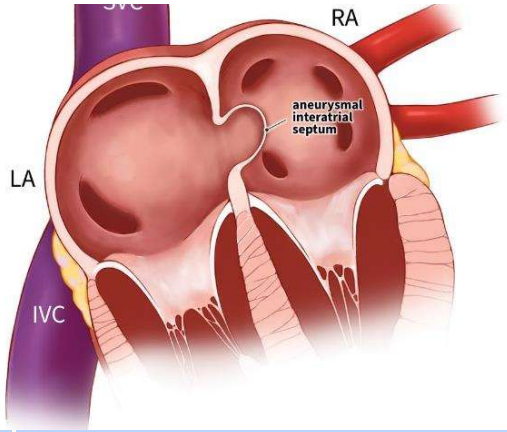
Prevalence ~25%

Evaluation

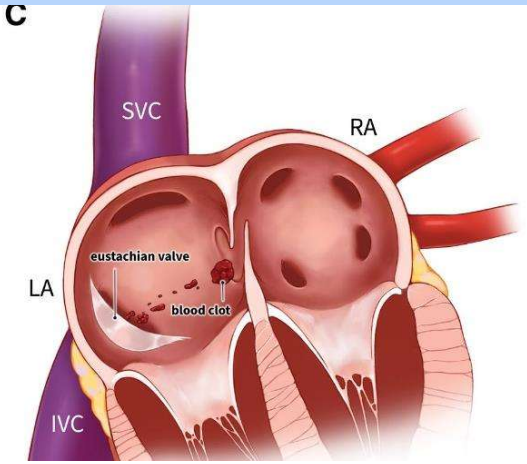
- TTE with bubble study -> initial test
- TEE -> test of choice
- ICE -> intra-procedure
- Transcranial Doppler -> more sensitive, less specific
- Right heart catheterization -> demonstration of wire crossing defect



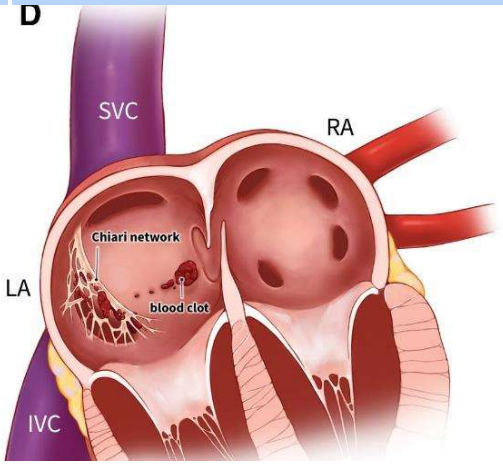
> 20 microbubbles in 3 beats



Atrial septal aneurysm



Prominent Eustachian valve



Chiari network

Sposato LA. Stroke 2024

Cryptogenic stroke

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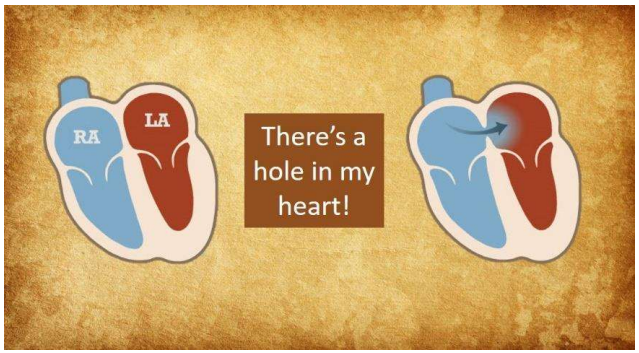
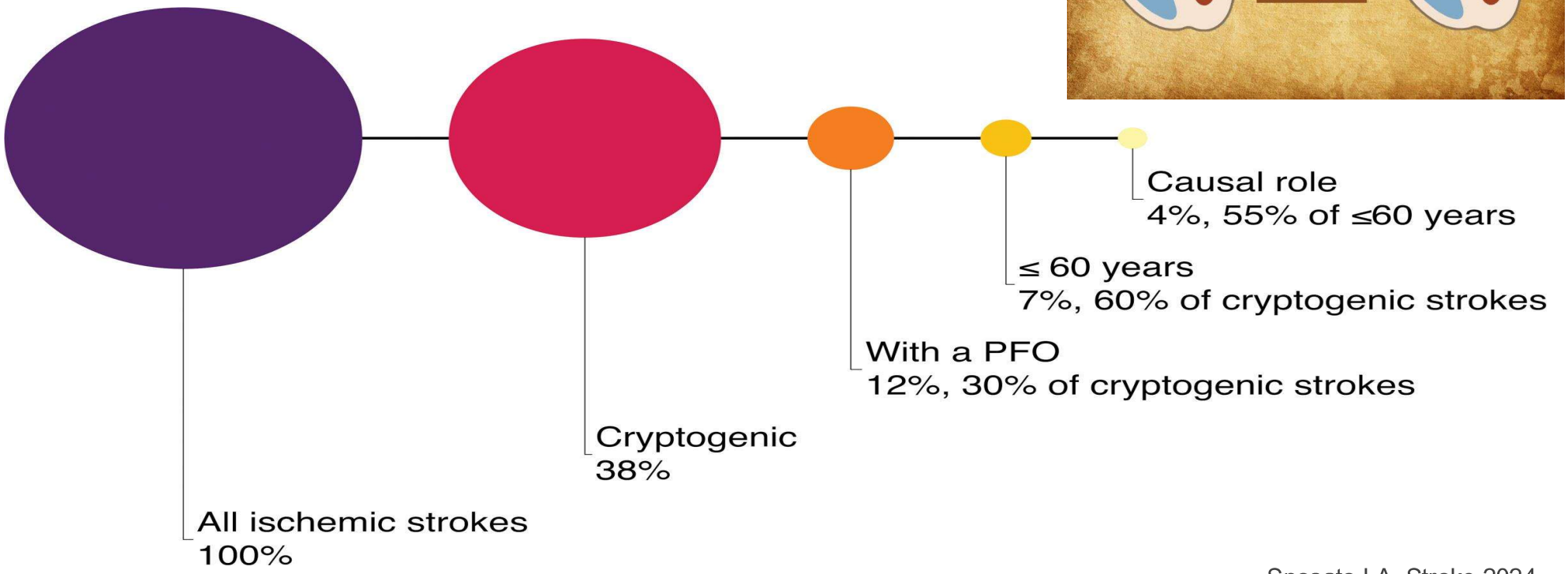
- Patients 18 to 60 years of age with non-lacunar stroke of undetermined cause
- PFO is not the cause, but mediator of stroke





Sposato LA. Stroke 2024

CLOSE trial

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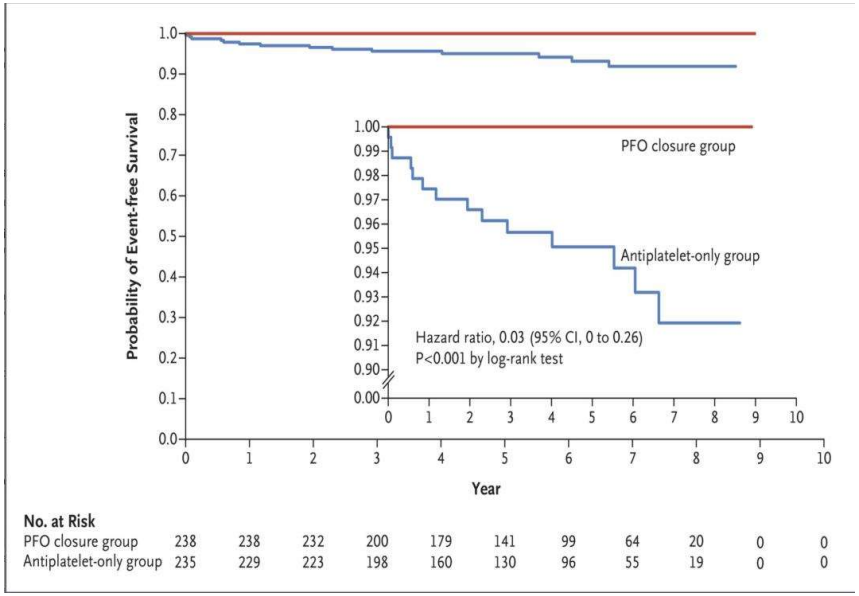
- Multicenter, randomized, open-label trial (n=663)
- Patients 16 to 60 years of age with recent stroke attributed to PFO, with an associated atrial septal aneurysm or large interatrial shunt
- Patients were assigned to transcatheter PFO closure plus long-term APT, APT alone, or OAC in a 1:1:1 ratio
- Primary outcome was the occurrence of stroke (Median: 5.3 years)



- AF: 4.6% vs. 0.9%, p=0.02
- 3 vs. 7 strokes for OAC vs. APT

Mas JL. NEJM 2013

Meta-analysis

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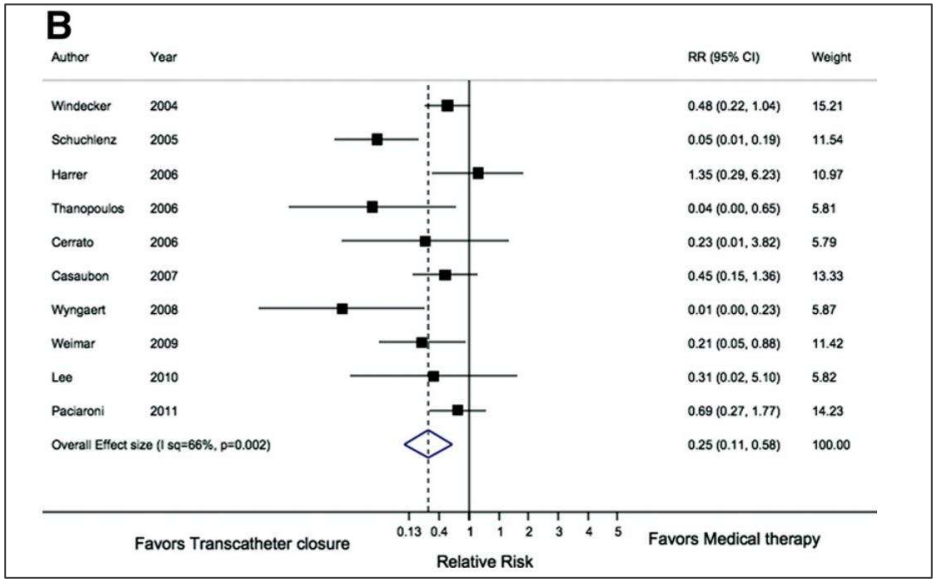

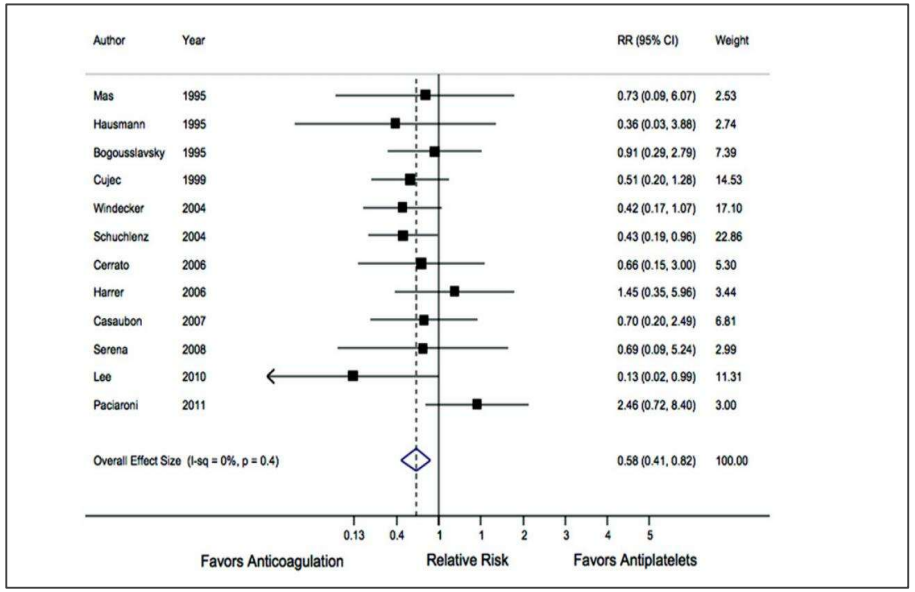

PFO closure better than medical therapy

OAC better than antiplatelets

Agarwal S..Kumbhani DJ..Kapadia S. JACC Intv 2012

PFO Closure Devices

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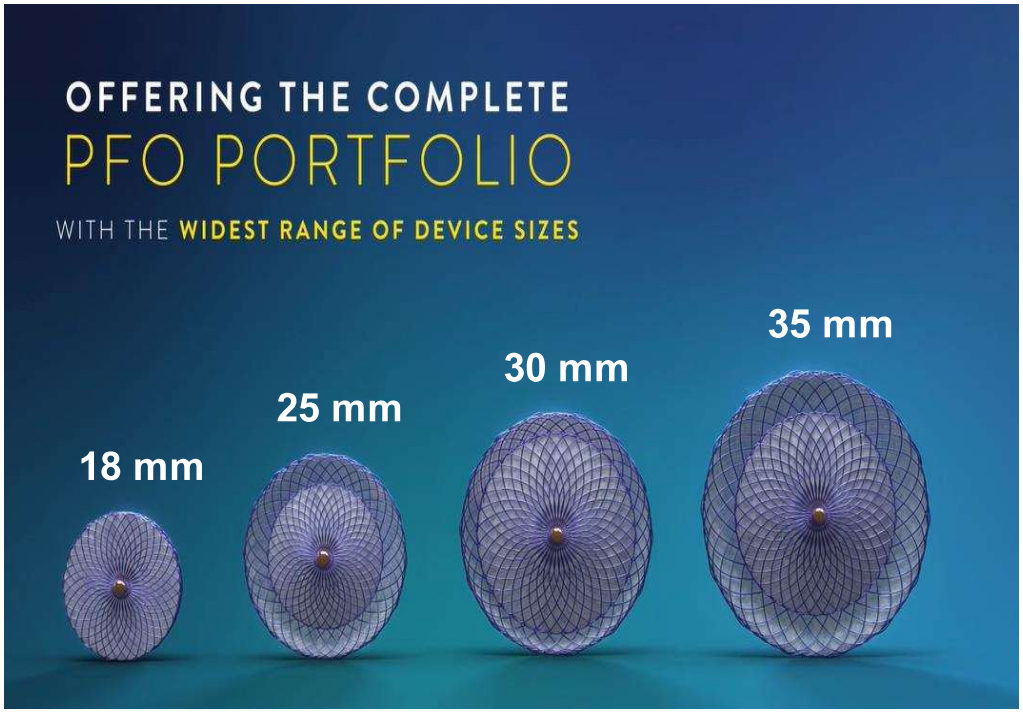
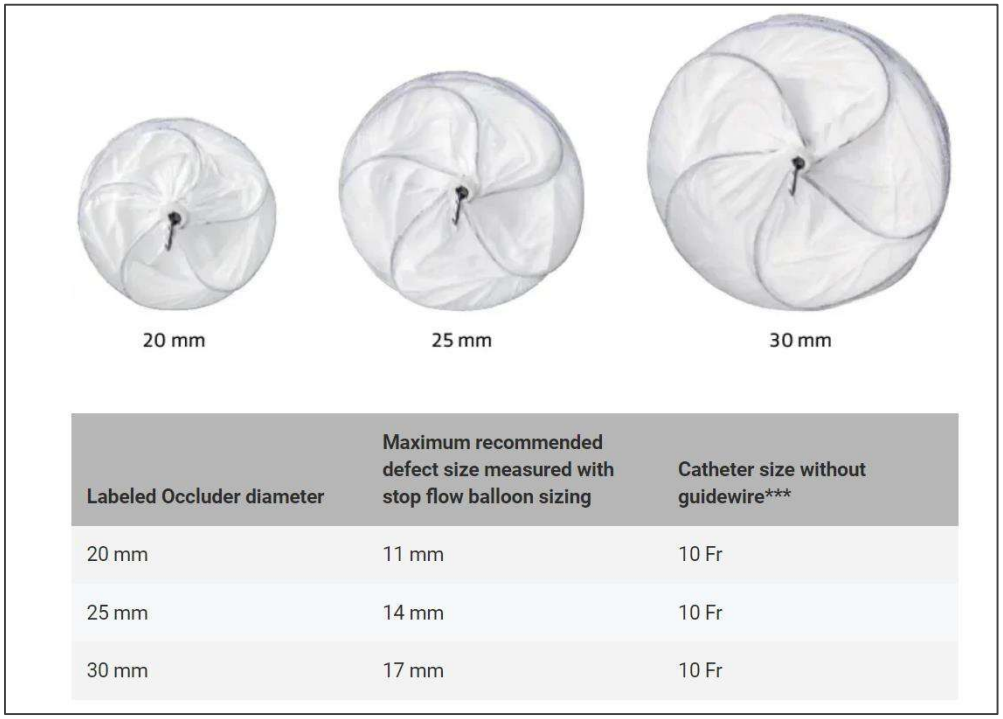


Amplatzer Talisman PFO device



Labeled Occluder diameter	Maximum recommended defect size measured with stop flow balloon sizing	Catheter size without guidewire***
20 mm	11 mm	10 Fr
25 mm	14 mm	10 Fr
30 mm	17 mm	10 Fr

Gore Cardioform device

RESPECT trial (Amplatzer PFO device)

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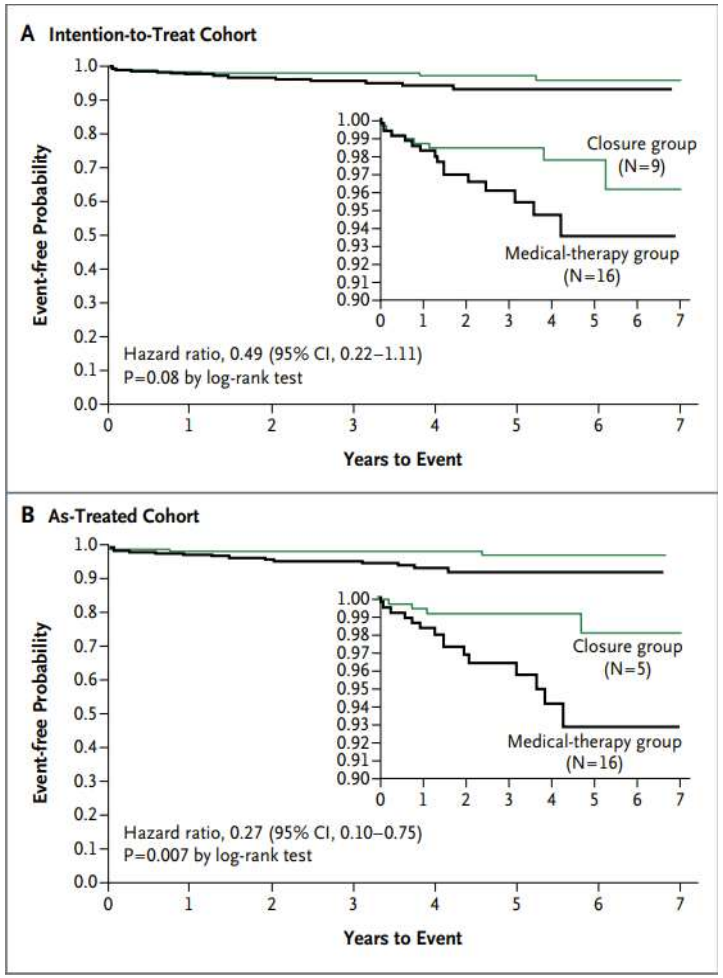

- DAPT for 1 month, ASA 81 mg
- Minimal or no shunt: 94%
- Atrial fibrillation: 0.4%
- Device-related thrombus: 0

Long-term f/u: Median 5.9 years

End Point	PFO Closure Group (N=499)		Medical-Therapy Group (N=481)		Hazard Ratio (95% CI)	P Value
	Patients with Event	Event Rate per 100 Patient-Yr	Patients with Event	Event Rate per 100 Patient-Yr		
	no. (%)		*no. (%)*			
Recurrent ischemic stroke	18 (3.6)	0.58	28 (5.8)	1.07	0.55 (0.31–0.999)	0.046

Carroll J, et al. NEJM 2013
Saver JL. NEJM 2017

Anatomic considerations

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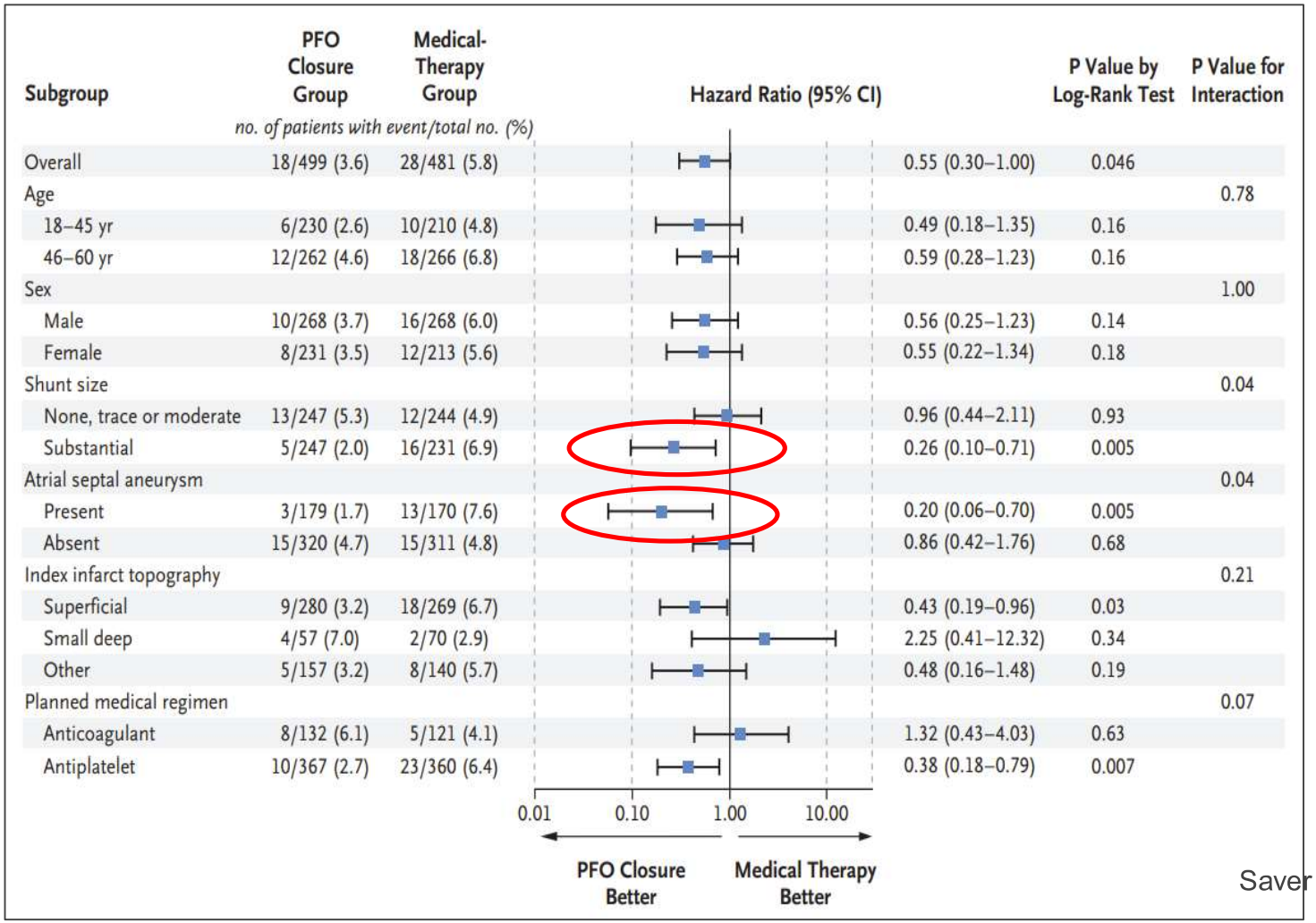

Subgroup	PFO Closure Group	Medical-Therapy Group	Hazard Ratio (95% CI)	P Value by Log-Rank Test	P Value for Interaction
	no. of patients with event/total no. (%)				
Overall	18/499 (3.6)	28/481 (5.8)	0.55 (0.30–1.00)	0.046	
Age					0.78
18–45 yr	6/230 (2.6)	10/210 (4.8)	0.49 (0.18–1.35)	0.16	
46–60 yr	12/262 (4.6)	18/266 (6.8)	0.59 (0.28–1.23)	0.16	
Sex					1.00
Male	10/268 (3.7)	16/268 (6.0)	0.56 (0.25–1.23)	0.14	
Female	8/231 (3.5)	12/213 (5.6)	0.55 (0.22–1.34)	0.18	
Shunt size					0.04
None, trace or moderate	13/247 (5.3)	12/244 (4.9)	0.96 (0.44–2.11)	0.93	
Substantial	5/247 (2.0)	16/231 (6.9)	0.26 (0.10–0.71)	0.005	
Atrial septal aneurysm					0.04
Present	3/179 (1.7)	13/170 (7.6)	0.20 (0.06–0.70)	0.005	
Absent	15/320 (4.7)	15/311 (4.8)	0.86 (0.42–1.76)	0.68	
Index infarct topography					0.21
Superficial	9/280 (3.2)	18/269 (6.7)	0.43 (0.19–0.96)	0.03	
Small deep	4/57 (7.0)	2/70 (2.9)	2.25 (0.41–12.32)	0.34	
Other	5/157 (3.2)	8/140 (5.7)	0.48 (0.16–1.48)	0.19	
Planned medical regimen					0.07
Anticoagulant	8/132 (6.1)	5/121 (4.1)	1.32 (0.43–4.03)	0.63	
Antiplatelet	10/367 (2.7)	23/360 (6.4)	0.38 (0.18–0.79)	0.007	

Saver JL, et al. NEJM 2017

REDUCE trial (Cardioform device)

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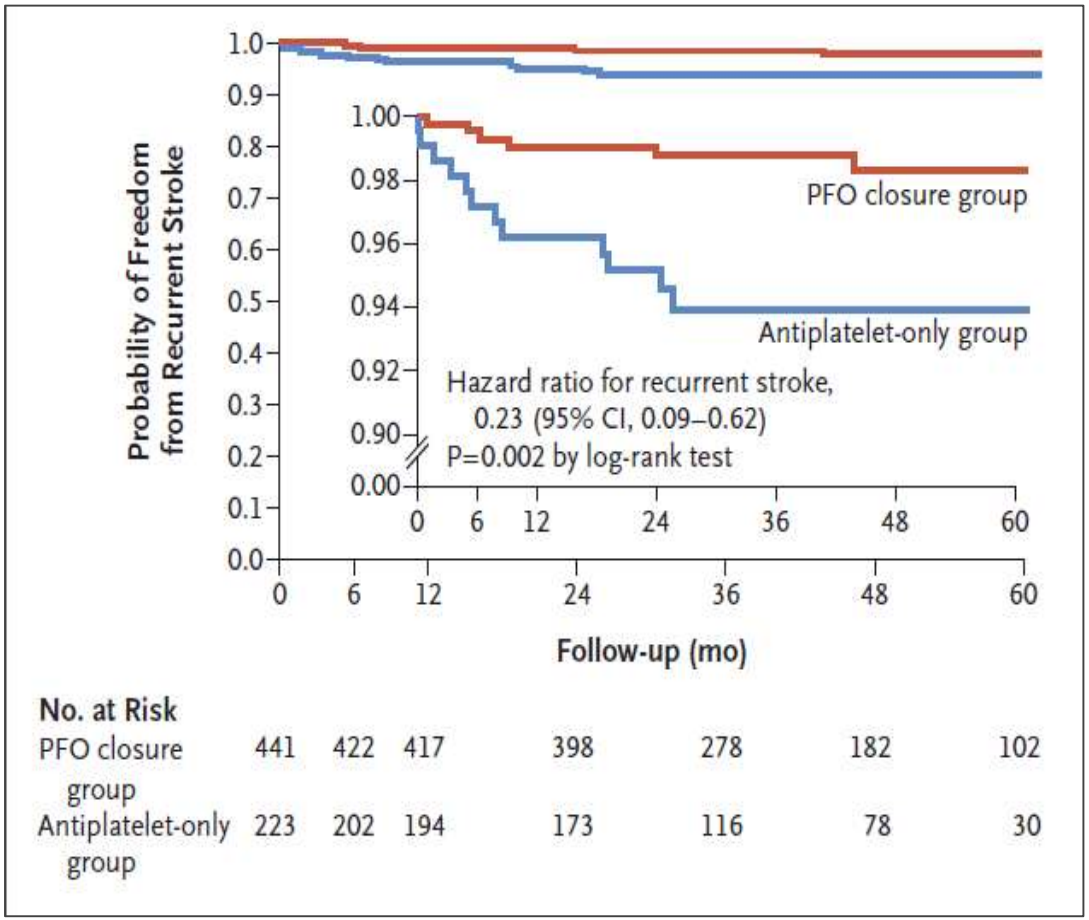

- Minimal or no shunt: 95%
- Atrial fibrillation: 0.5%
- Device-related thrombus: 0.5%

Long-term f/u: Median 5.0 years

1.4% vs. 5.4%, HR 0.31, 95% CI 0.13-0.76

Sondergaard L, et al. NEJM 2017
Kasner S. NEJM 2021

Risk stratification: RoPE score

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Risk of Paradoxical Embolism (RoPE) Score

☆

Identifies stroke-related PFO in patients with cryptogenic stroke.

INSTRUCTIONS

Use in patients with cryptogenic stroke found to have PFO and no other compelling cause for stroke.

History of hypertension	**No +1**	Yes 0
History of diabetes	**No +1**	Yes 0
History of stroke or TIA	**No +1**	Yes 0
Smoker	**No +1**	Yes 0
Cortical infarct on imaging	No 0	**Yes +1**
Age	45	years

8 points

84% chance that stroke is due to PFO.

6% risk of 2 year recurrence of stroke/TIA.

Copy Results | Next Steps »

Risk stratification: PASCAL classification

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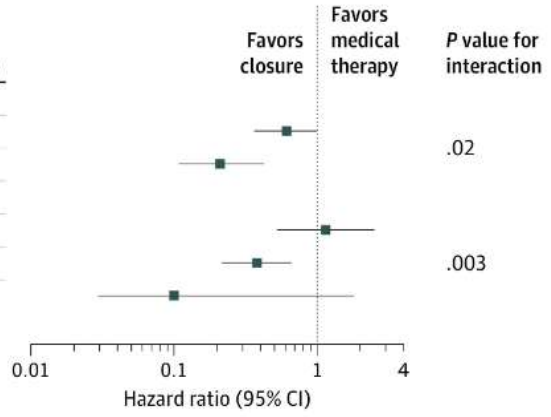
PFO-Associated Stroke Causal Likelihood (PASCAL)

High-risk = large shunt, aneurysmal septum

		RoPE	
		<7	≥7
High-risk PFO	Present	Possible	Probable
	Absent	Unlikely	Possible

A Hazard ratios of the primary outcome of recurrent ischemic stroke

	Device, overall events/No. of patients	Medical therapy, overall events/ No. of patients	Hazard ratio (95% CI)
RoPE categories			
<7	29/700	41/704	0.61 (0.37 to 1.00)
≥7	11/1189	41/1147	0.21 (0.11 to 0.42)
PASCAL categories			
Unlikely	17/293	11/254	1.14 (0.53 to 2.46)
Possible	19/897	46/914	0.38 (0.22 to 0.65)
Probable	3/700	25/683	0.10 (0.03 to 0.35)



Kent DM, et al. JAMA 2021

Bottom line: PFO closure

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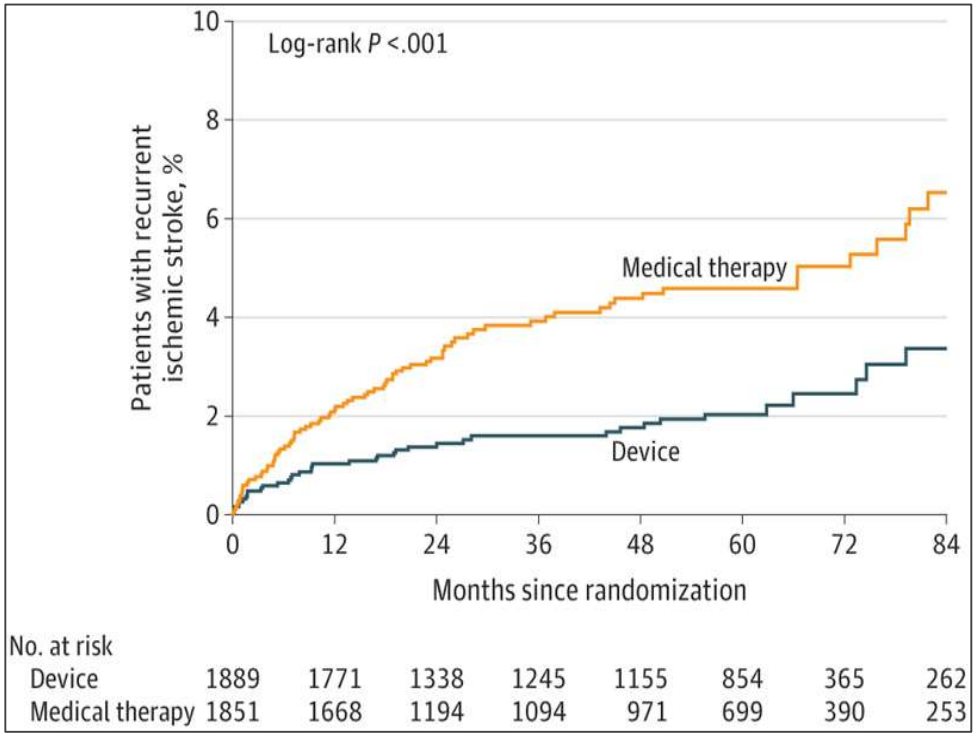

Recurrent ischemic stroke
0.47% vs. 1.09%/year
HR 0.41 (0.28-0.60), p<0.001

Median time to recurrent stroke: 13.7 months

Safety endpoints	Device	No device	Relative risk (95% CI)
Atrial fibrillation (all)	5.0%	1.1%	4.54 (2.78-7.39) p<0.001
Atrial fibrillation beyond 45 days	2.4%	0.8%	2.60 (1.44 – 4.70), p=0.001
Major bleeding	1.4%	1.7%	p=0.45
VTE event	1.4%	0.5%	2.59 (1.26 – 5.36), p=0.007

DAPT (ASA 81, clopidogrel 75) for at least 1 month, can be 3-6 months, then lifelong ASA 81

Kent DM, et al. JAMA 2021
Kavinsky CJ. JSCAI 2022

Bottom line: PFO closure

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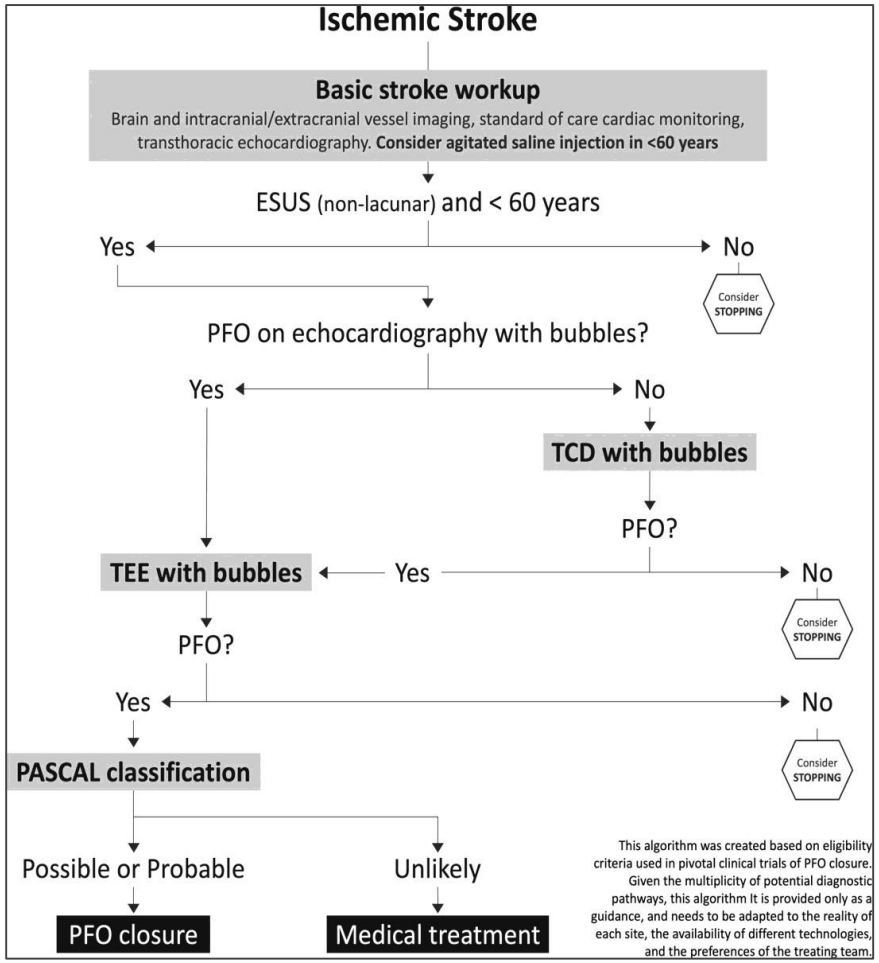
Statement 2a

In patients younger than 60 years with a PFO and an embolic-appearing infarct and no other mechanism of stroke identified, clinicians may recommend closure following a discussion of potential benefits (reduction of stroke recurrence) and risks (procedural complication and atrial fibrillation) (level C).

Neurocardiology team

- FDA statement endorses joint evaluation by neurology and cardiology



Sposato LA. Stroke 2024
Messe S. Neurology 2020

Conclusions

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- Cardioembolic strokes are common.
- Special considerations, patients benefit from close collaboration between neurology and cardiology.
- Left atrial appendage occlusion can be considered in patients with AF and high bleeding risk.
- PFO closure can be considered in young patients with cryptogenic stroke and PFO.

Acknowledgement

UT Southwestern Medical Center

Dr. Richard Wu

Dr. Anthony Bavry

Conclusions

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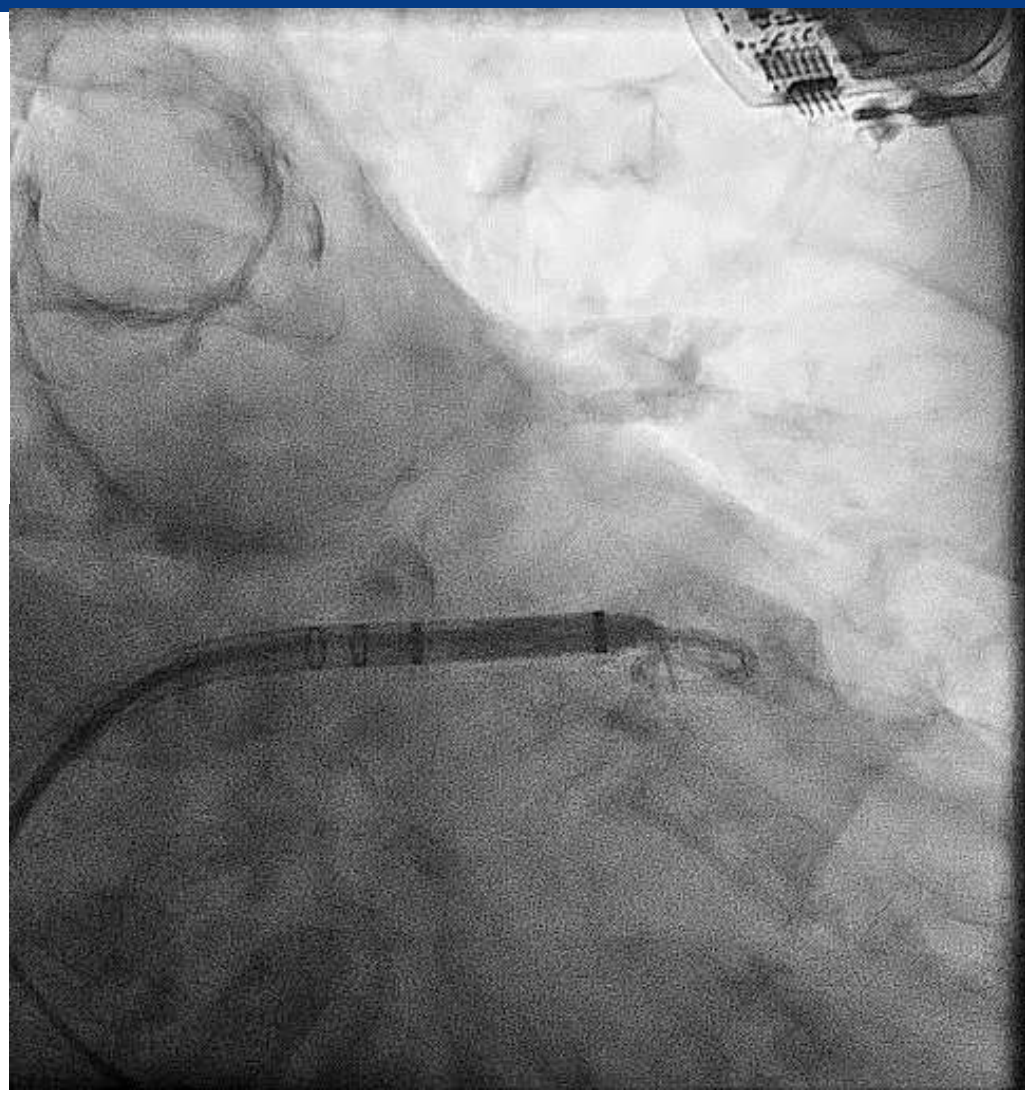
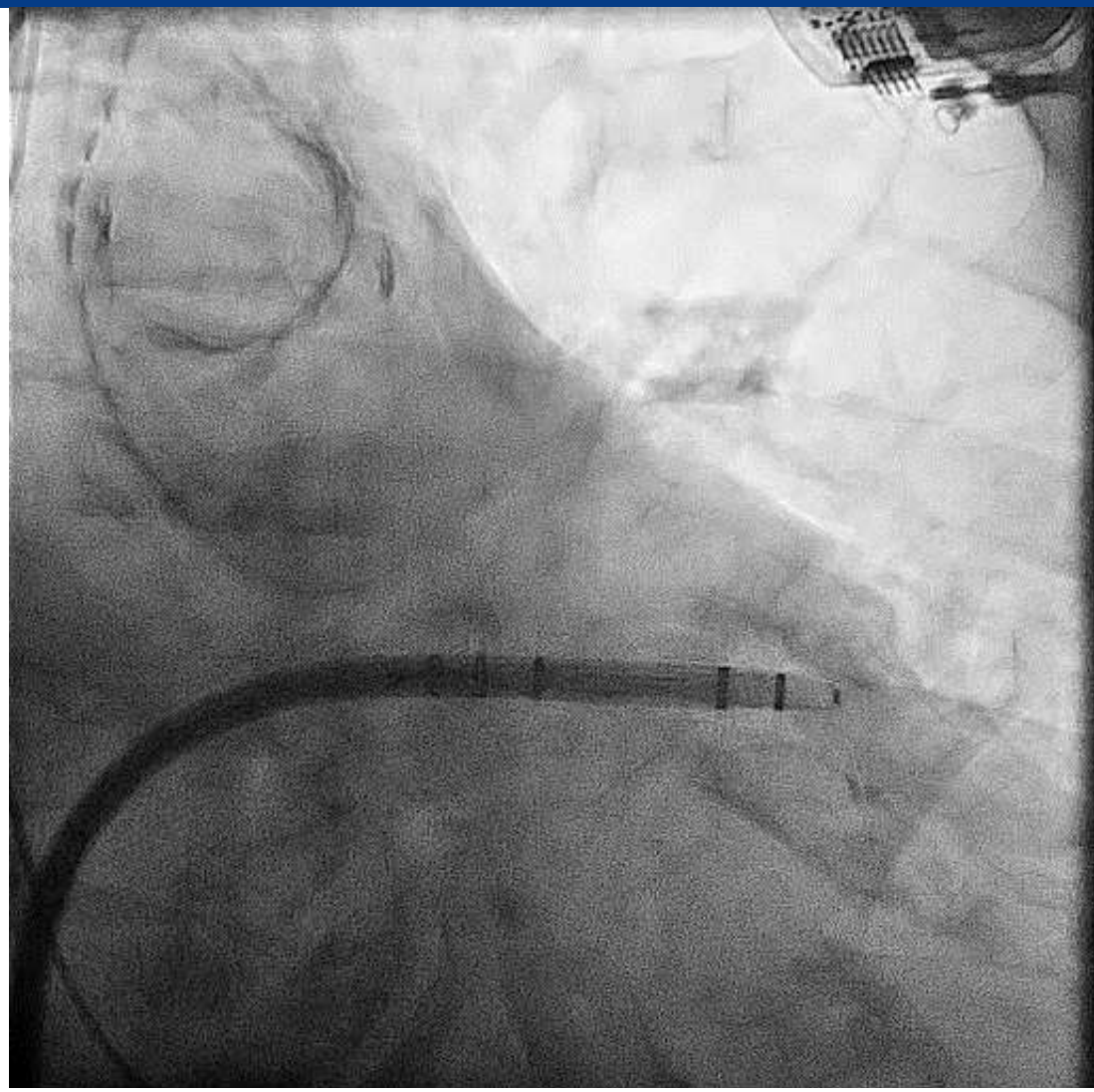
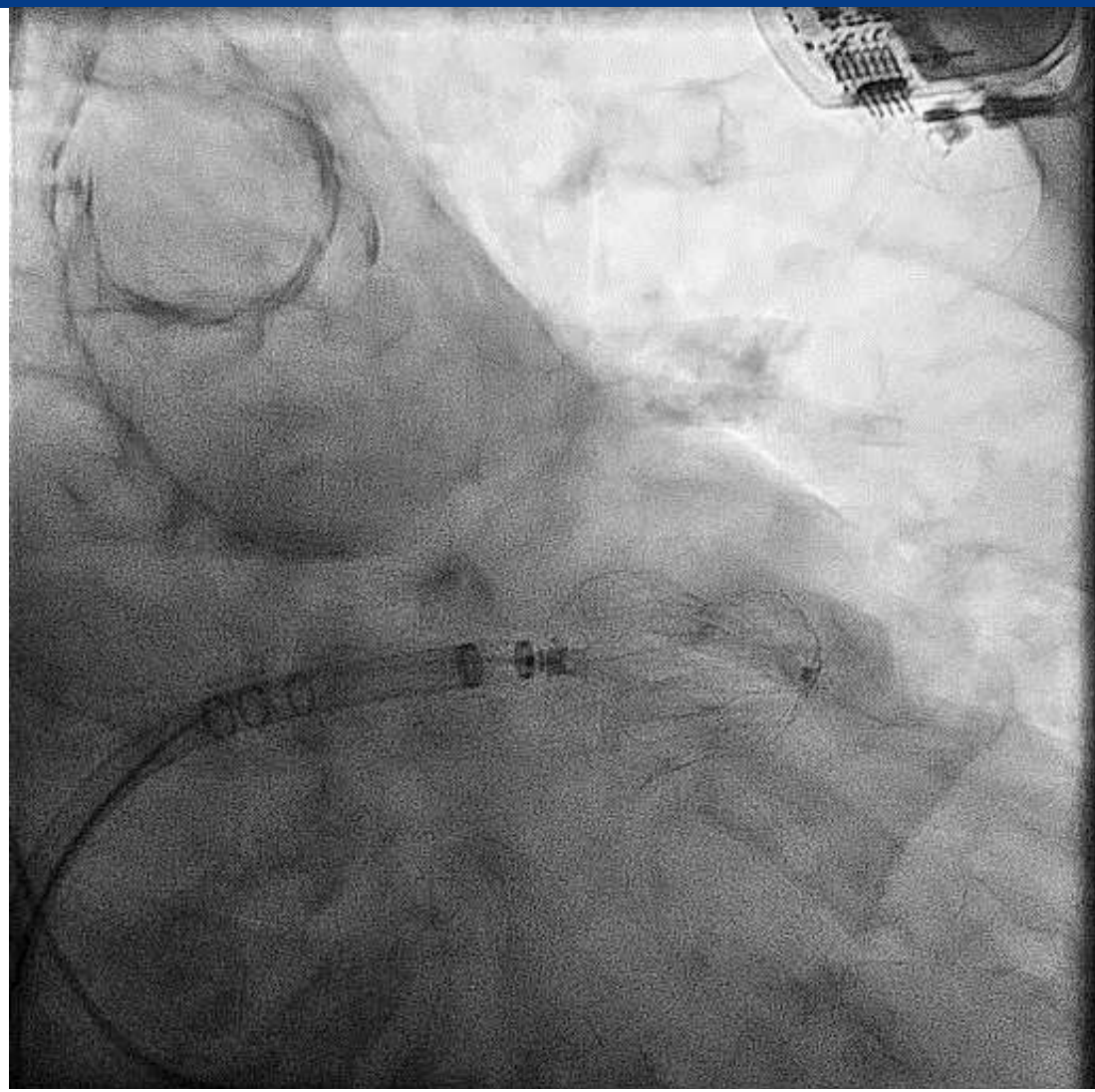
GA + TEE
UFH -> ACT ~300
16 Fr sheath R-CVF
Trans-septal puncture
Watchman access sheath over pigtail
Angio



1) Form FLX-ball
2) Deploy entire device

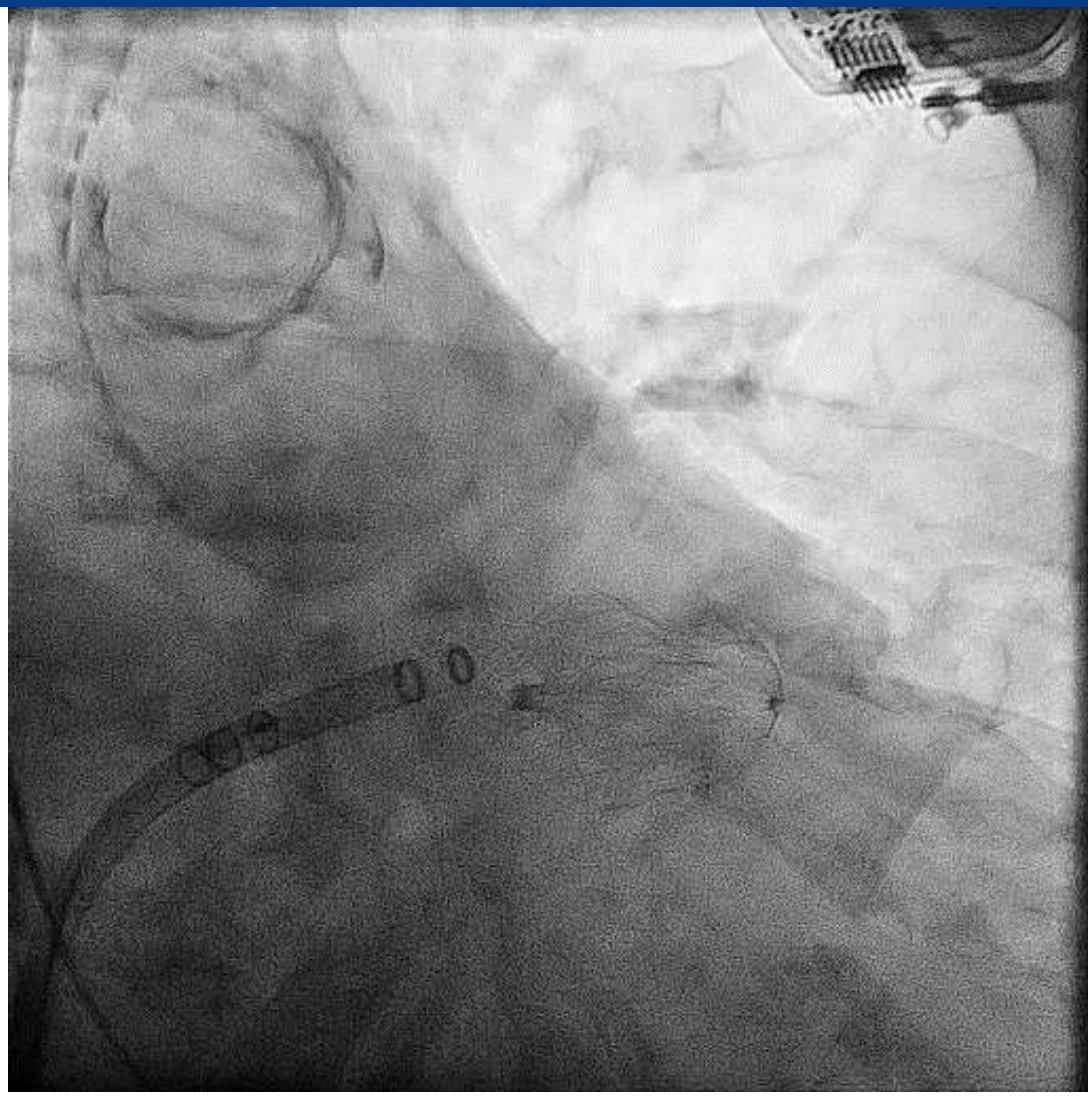


Angio



PASS criteria for release:

1) Position
2) Anchor
3) Size
4) Seal



6-week TEE