The Role of of the Left Atrial Appendage

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Left Atrial Appendage
Atrial Fibrillation and Thrombus Formation

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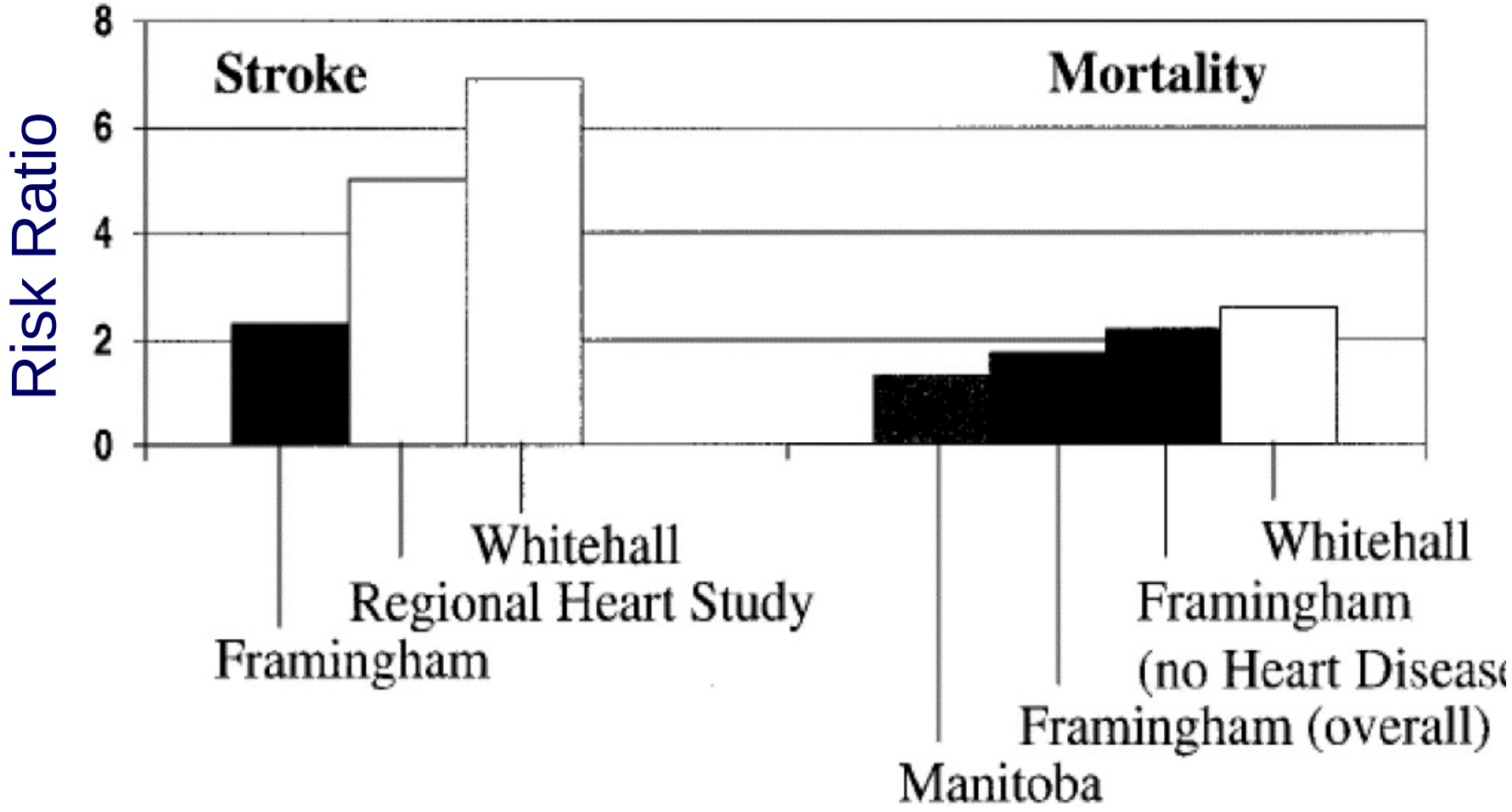
Stroke in AF patients ≈ Appendage-related stroke

1 Blackshear JL. Odell JA., *Annals of Thoracic Surgery.* 1996;61:755-759

Prognostic Implications

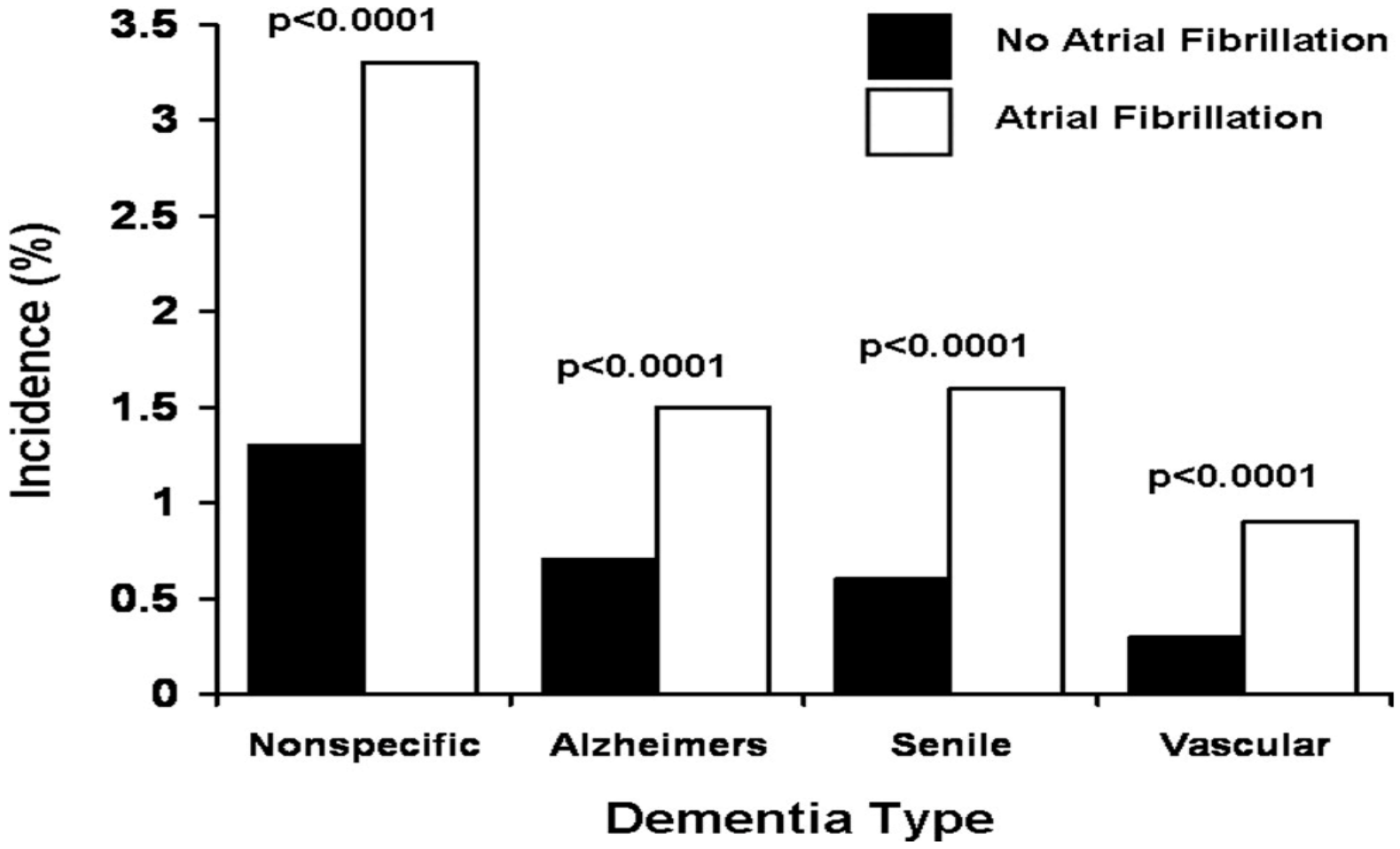
Stroke, Mortality



Hersi and Wyse *Curr Probl Cardiol.* 2005 Apr;30(4):175-233

Prognostic Implications

Dementia

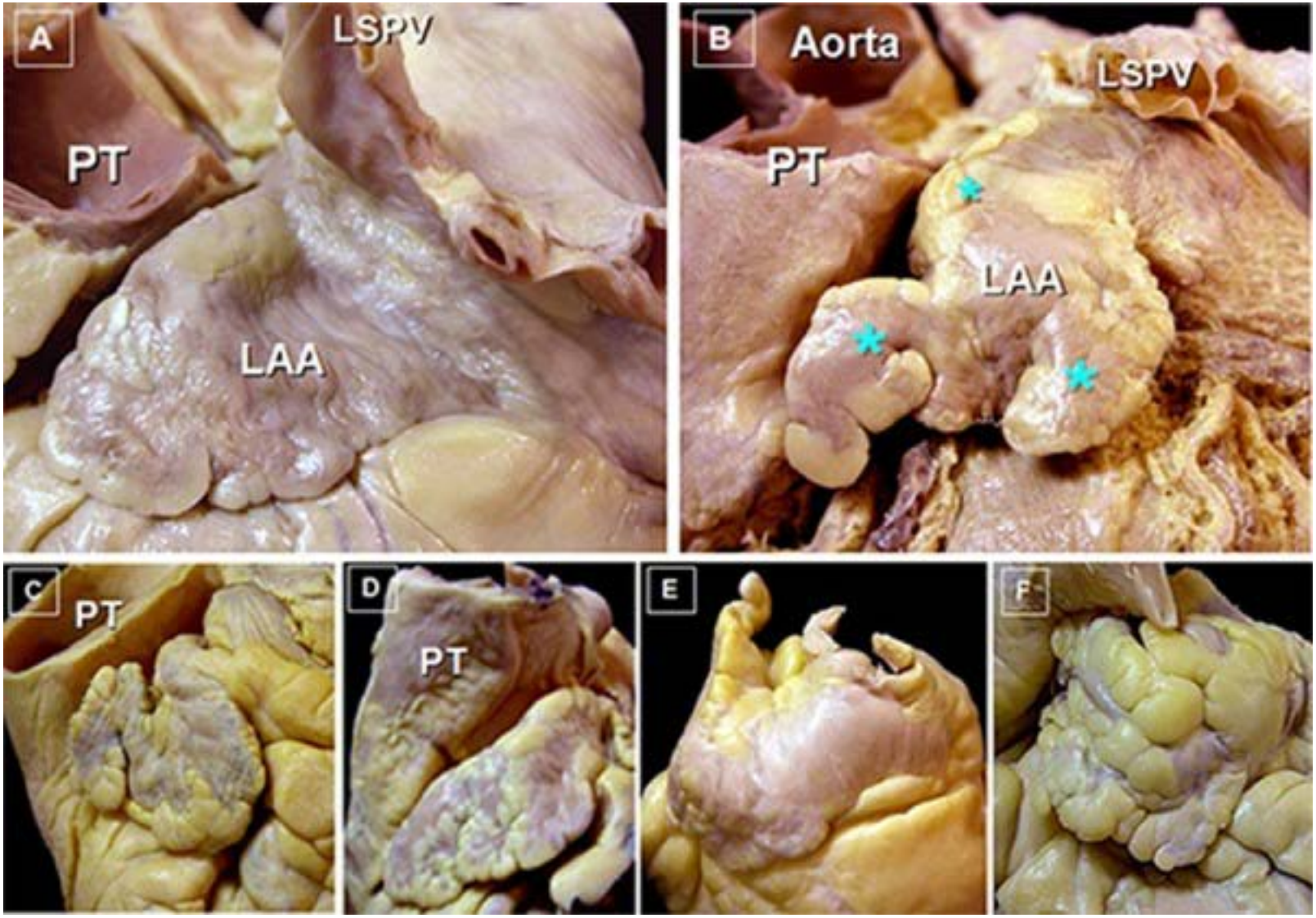


Bunch TJ et al *Heart Rhythm* 2010 Apr;7(4):433-7

Understanding LAA Anatomy

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

Cabrera et al *Heart.* 2014 Oct;100 (20):1636–50..



Understanding LAA Anatomy

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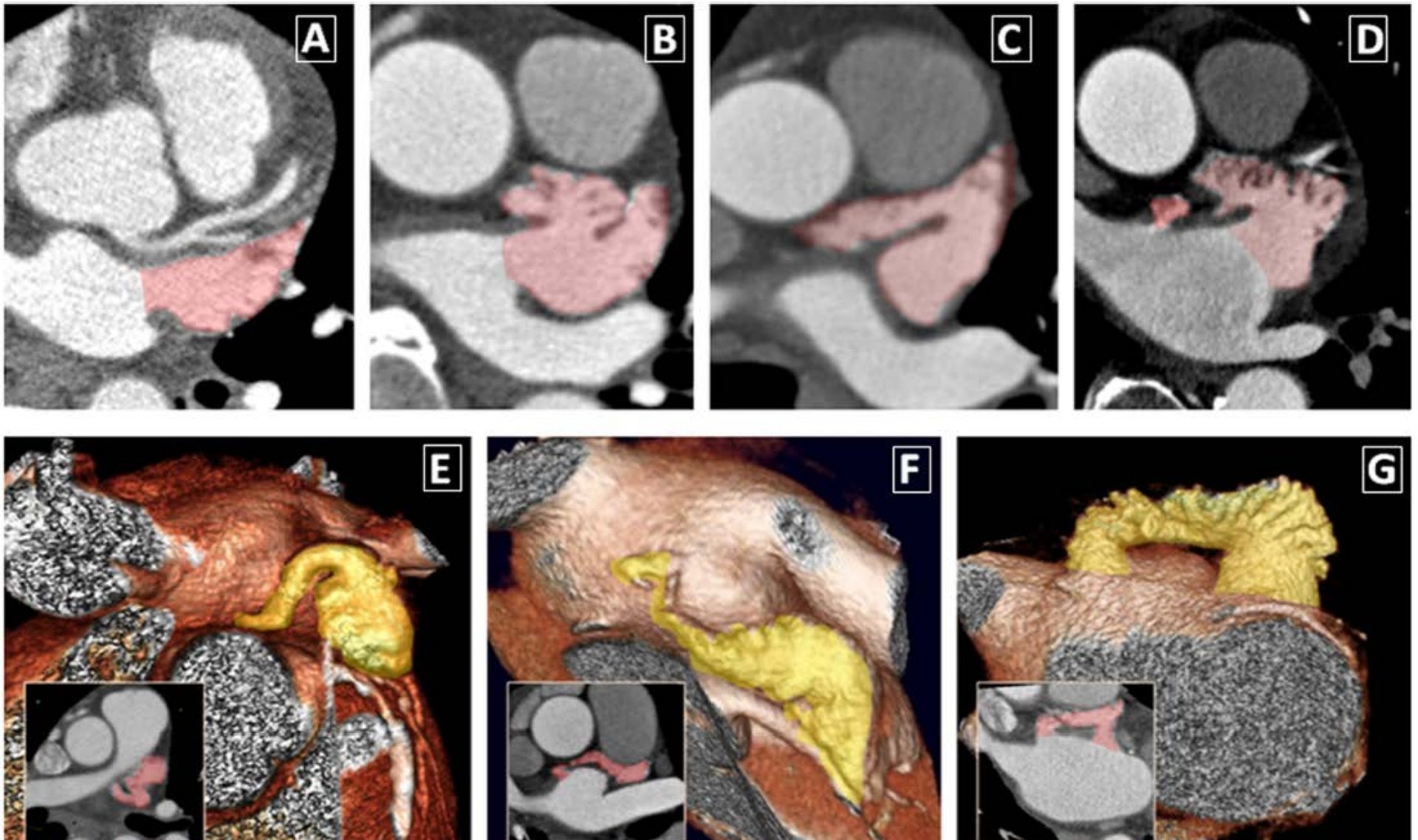
Cabrera et al *Heart.* 2014 Oct;100 (20):1636–50..



Understanding LAA physiology

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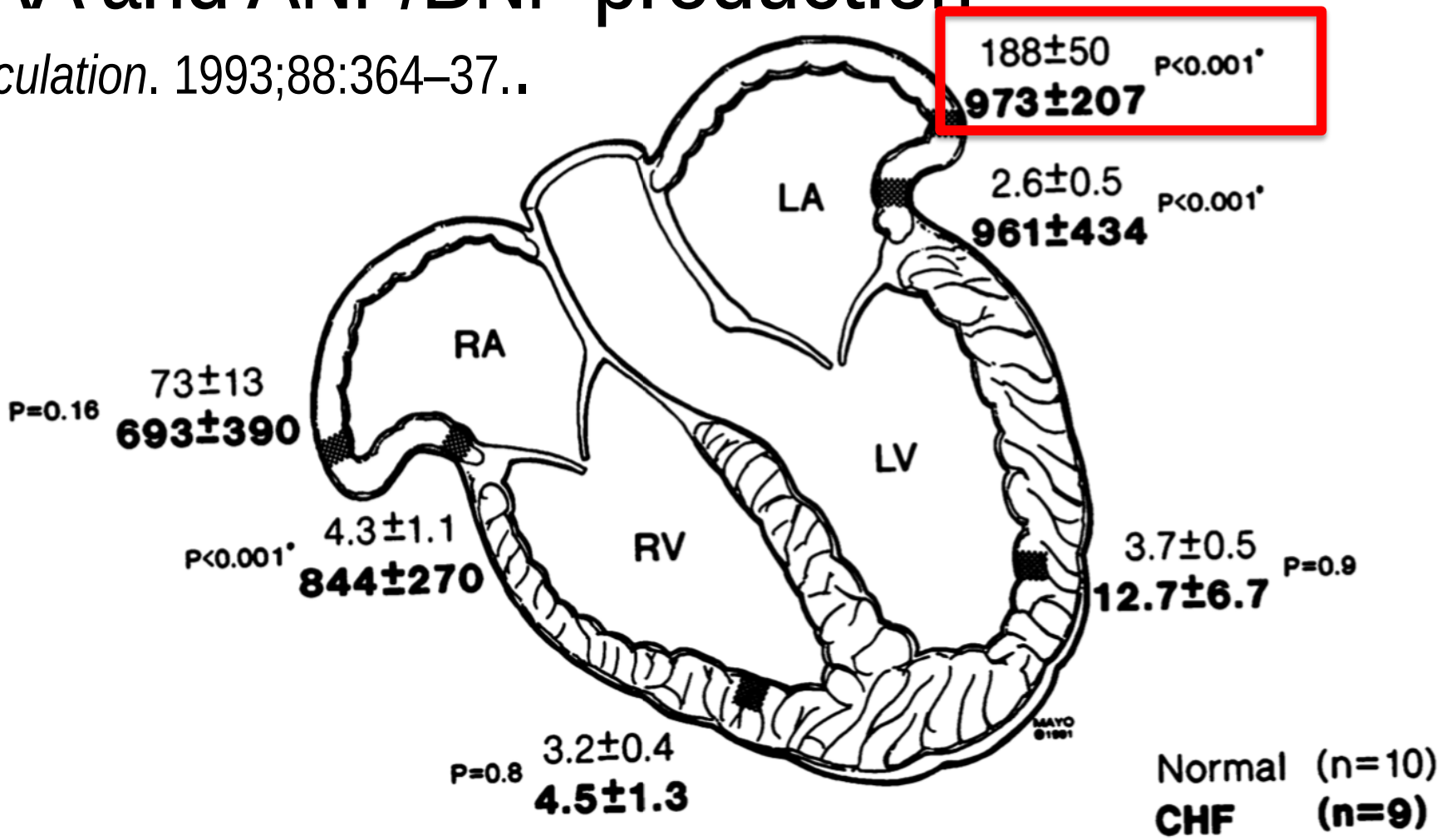
LAA and ANP/BNP production

Circulation. 1993;88:364–37..



Autonomic cardiac nerves

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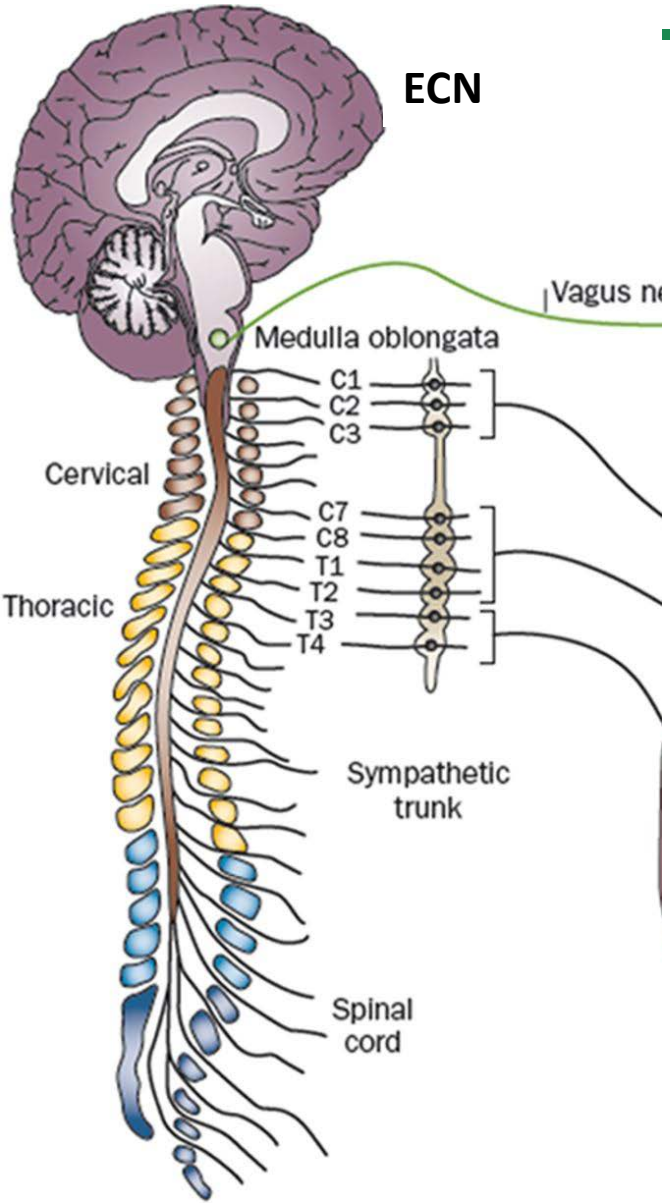
ECN



ICN

Vein of Marshall Anatomy and Histology

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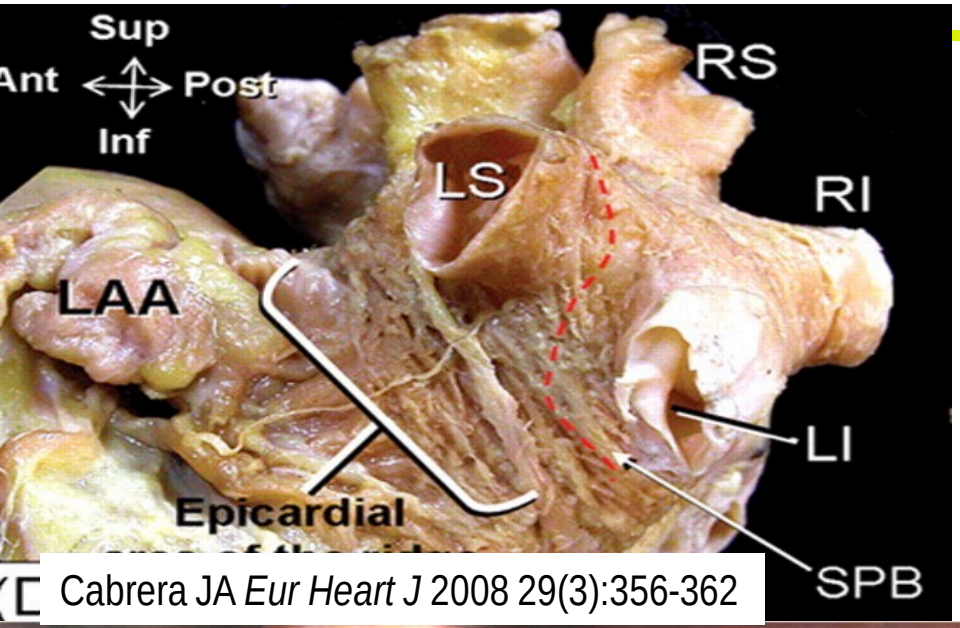
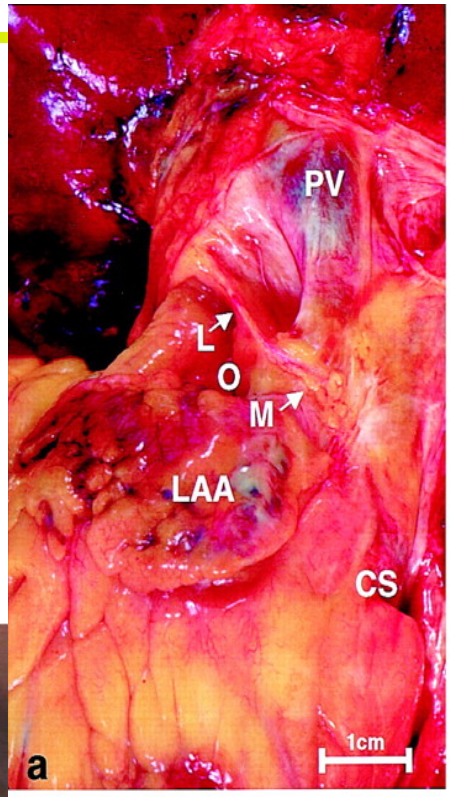
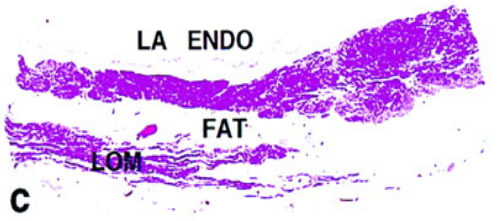
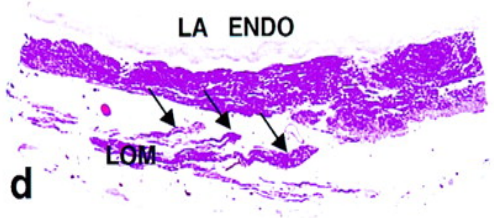
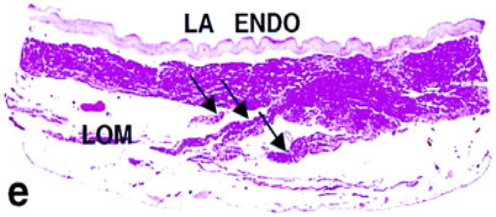


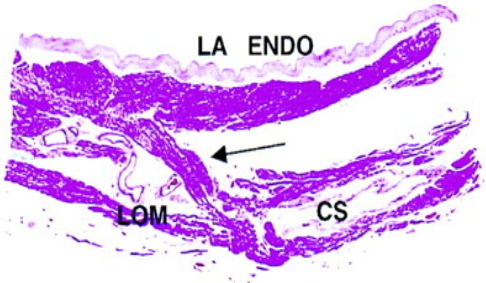
Cabrera JA *Eur Heart J* 2008 29(3):356-362

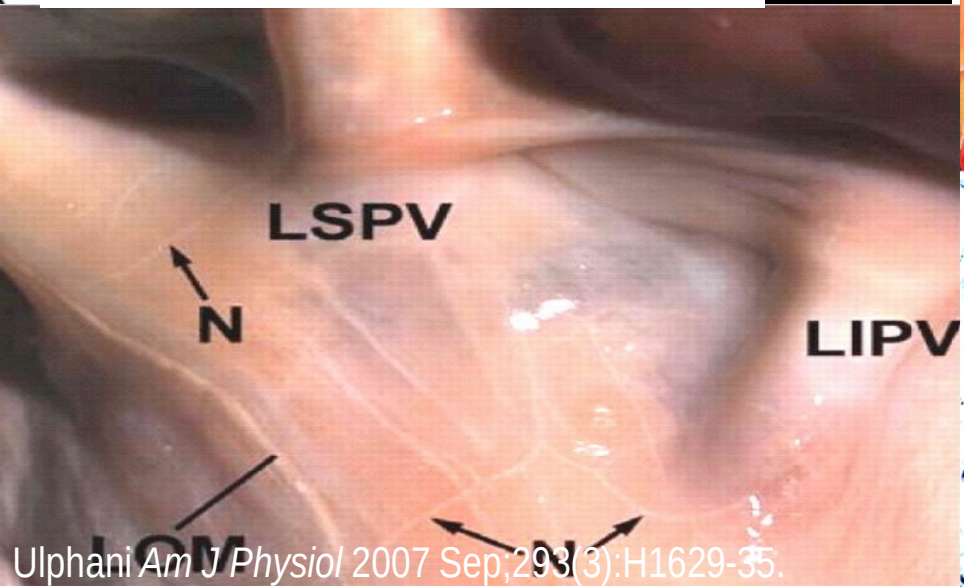




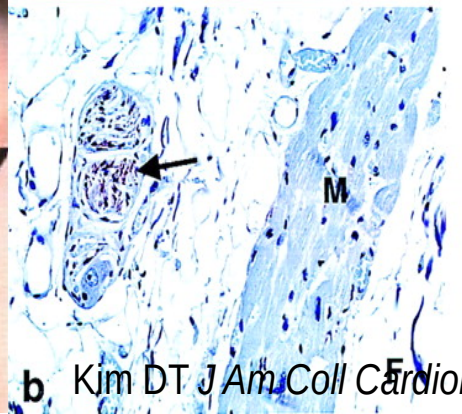








Ulphani *Am J Physiol* 2007 Sep;293(3):H1629-35.



Kim DT *J Am Coll Cardiol*, 2000; 36:1324-7

Left Atrial Cardiac Innervation

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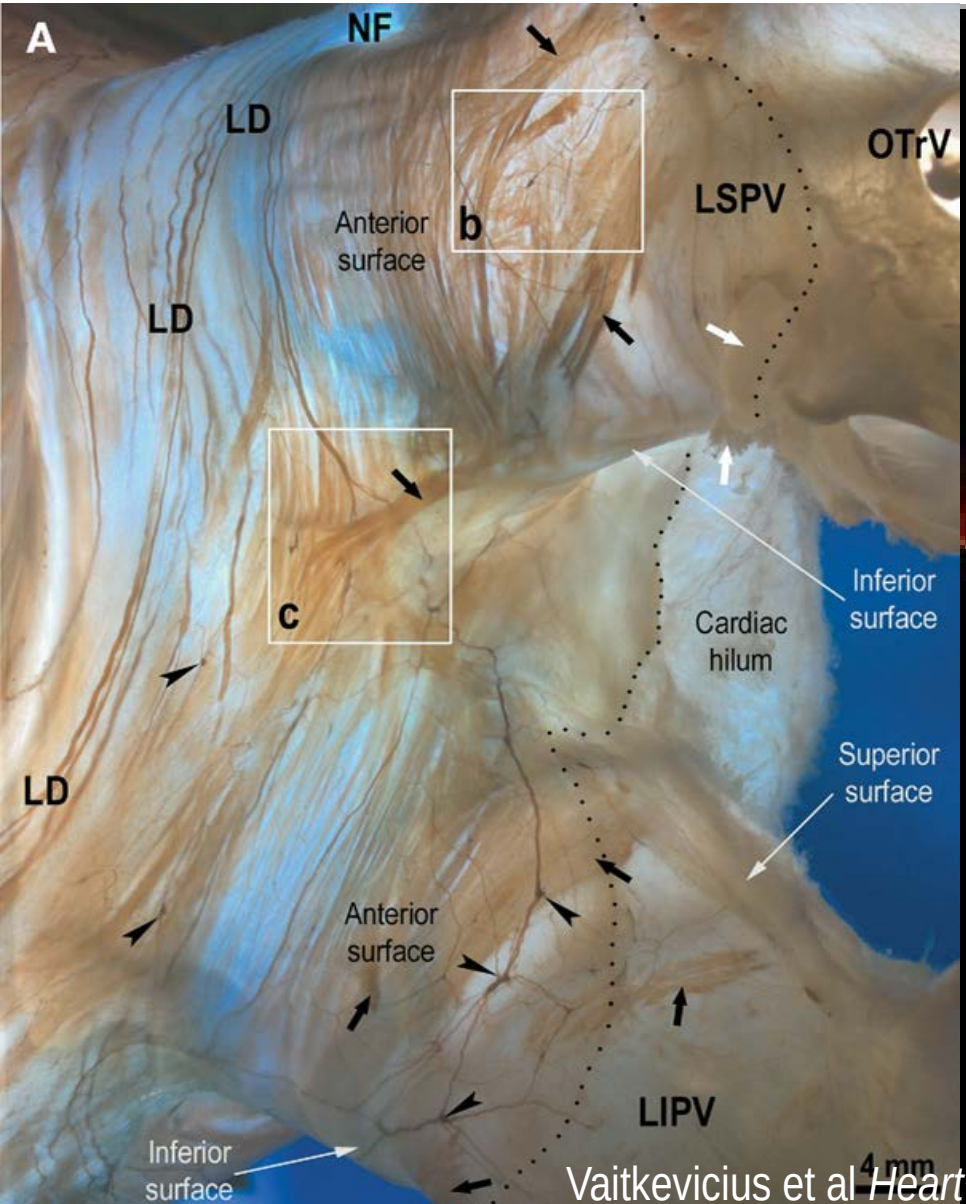

Vaitkevicius et al *Heart Rhythm*. 2009 Feb;6(2):221-8

Role of LAA in atrial fibrillation

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- Source of thromboembolic events
- Source of atrial fibrillation triggers/substrate
  - Autonomic innervation
  - Reentrant circuits
  - AF Triggers
- Source of atrial natriuretic peptide
  - Potential role in fluid retention post-ligation or post-ablation

Goal #1: Stroke Prevention
Not all patients have equal risk

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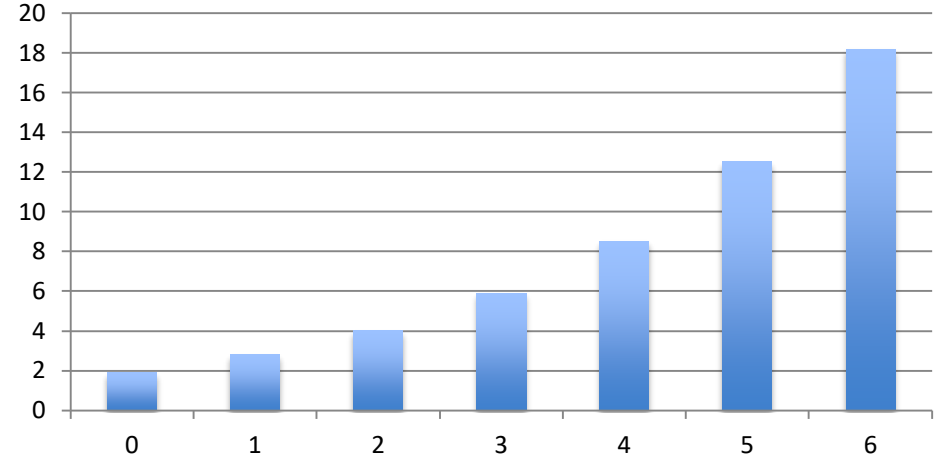
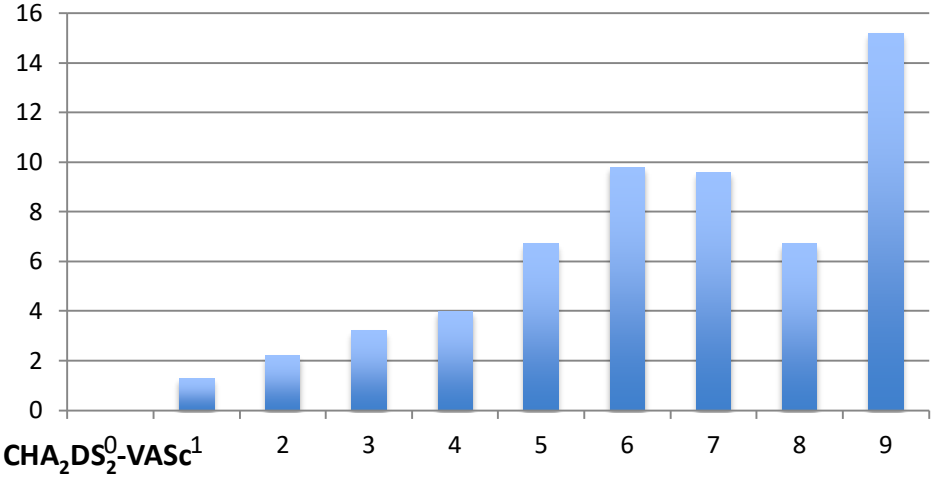
- $CHADS_2$-CHA_2DS_2-VASc Scores

Adjusted Stroke Rate (% per y)



$CHADS_2$	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum score	6

Adjusted Stroke Rate (% per y)



CHA_2DS_2-VASc	
Congestive HF	1
Hypertension	1
Age ≥75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum score	9

J Am Coll Cardiol. 2014;64(21):2246-2280. doi:10.1016/j.jacc.2014.03.021

Validation of CHADS-VASc

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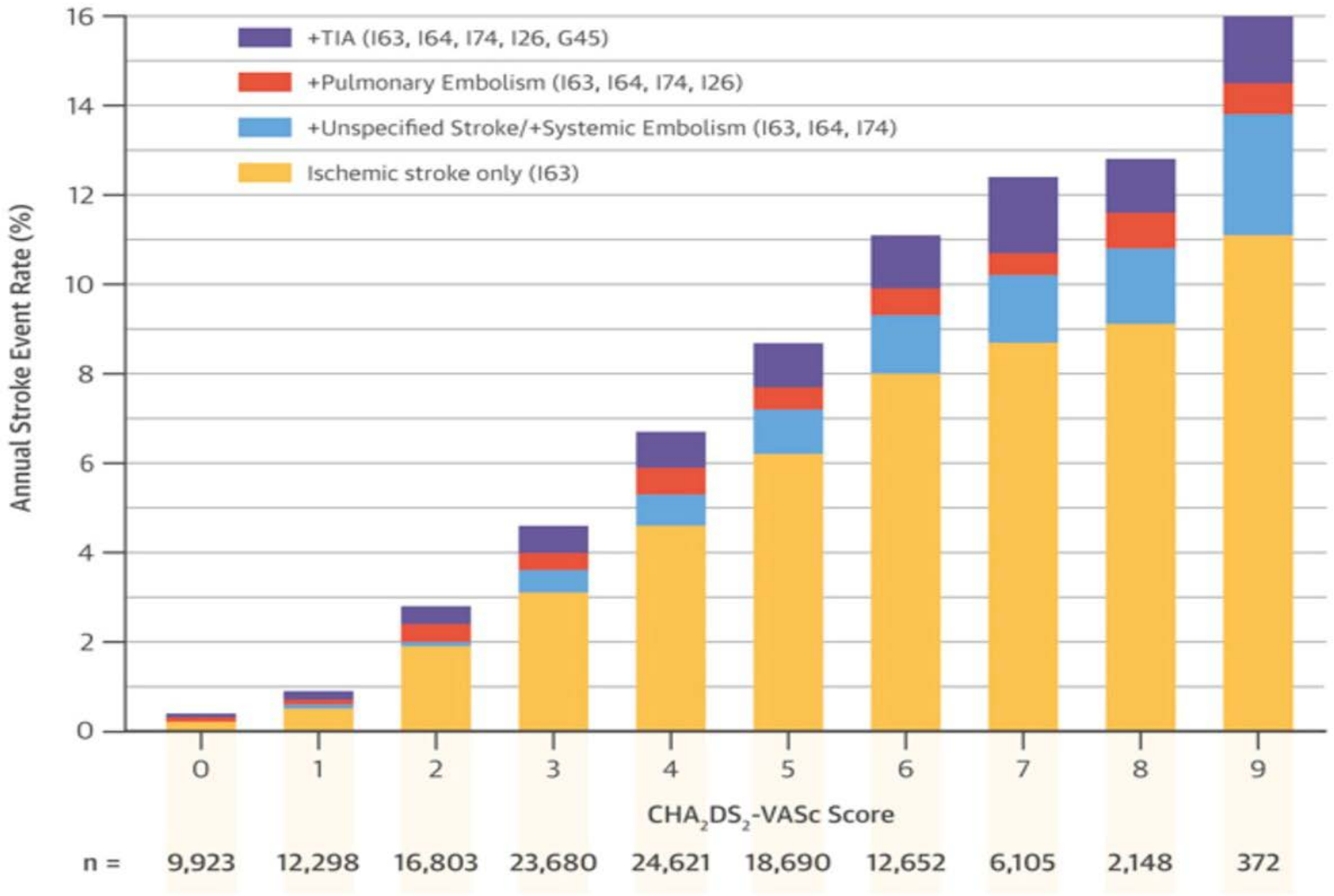
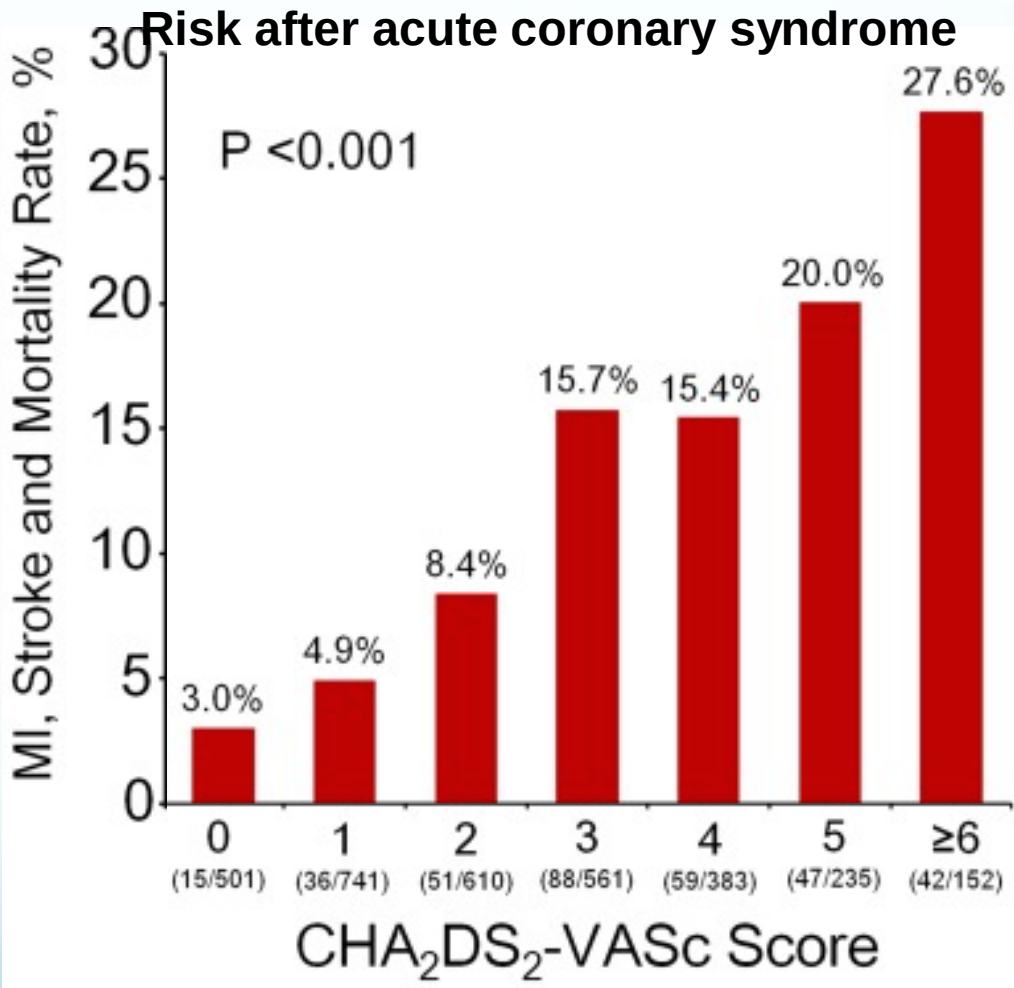


Friberg, L. et al. J Am Coll Cardiol. 2015; 65(3):225-32.

1. Risk of LAA-related stroke CHA_2DS_2-VASc Scores: Not specific

- CHA_2DS_2-VASc predicts risk of ischemic stroke in the ABSENCE of AF. (*Atherosclerosis*. 2014 Dec;237(2):504-13.)
- An assessment of LAA-related risk of stroke is necessary to decide on its closure.



PLoS One. 2014; 9(10): e111167.

When to anticoagulate patients with AF

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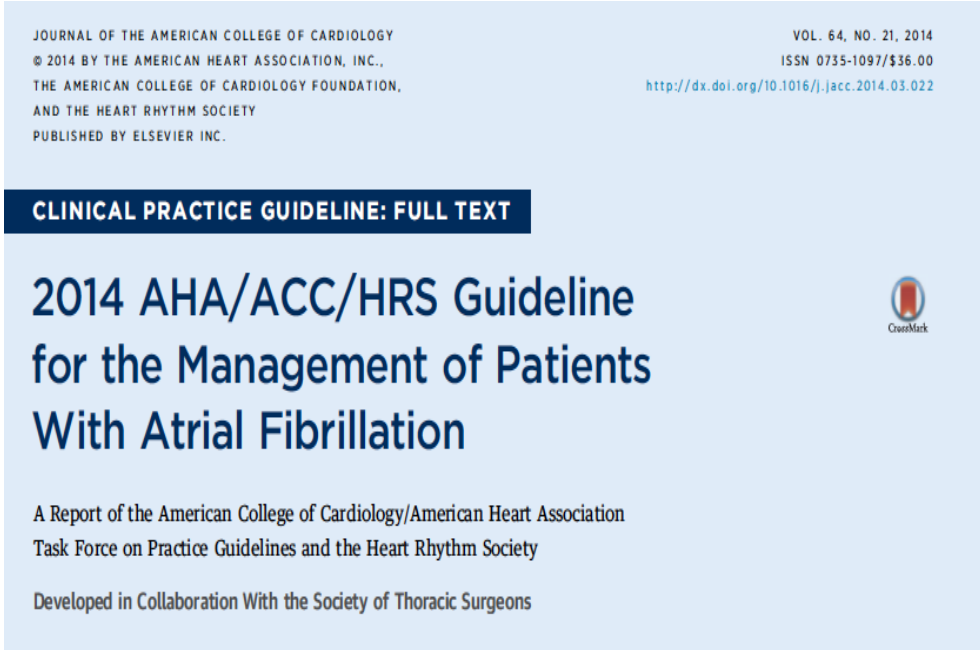
- Benefits of stroke risk reduction must outweigh risks of bleeding.
- CHADS2>1
- CHADS-VASc ≥1 for men and ≥2 for women



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CLINICAL PRACTICE GUIDELINE: FULL TEXT

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Developed in Collaboration With the Society of Thoracic Surgeons

Stroke prevention strategies

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- Systemic anticoagulation
  - Warfarin
  - NOACs
- LAA closure
  - Watchman and other devices
  - Lariat
  - Atri-clip
- Selecting the right strategy requires individualization of risks/benefits!

Novel Oral Anticoagulants (NOACS)

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	Dadigatran[1]	Rivaroxaban[2]	Apixaban[3]	Edoxaban[4]
Comparator	Warfarin	Warfarin	Warfarin	Warfarin
Total enrolled subjects	18,113	14,264	18,201	21,105
Trial design	Randomized, controlled, non-inferiority (doses of dabigatran were blinded)	Randomized, controlled, double-blind, non-inferiority	Randomized, controlled, double-blind, non-inferiority	Randomized, double-blind, double-dummy
Median duration of follow-up	2 years	1.94 years	1.8 years	2.8 years
Average $CHADS_2$ score	2.1	3.5	2.1	2.8
Results (primary outcome = stroke or systemic embolism)	Reduction in primary outcome compared with warfarin	Reduction in primary outcome compared with warfarin	Reduction in primary outcome compared with warfarin	Noninferior to warfarin

Preventing Strokes in AF patients
Individualizing Risk: 4 questions

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- **1. What are the causes of stroke risk in this patient?**
  - AF-related vs AF unrelated stroke
  - LAA-related vs LAA unrelated
- **2. What are the risks of stroke prevention strategies?**
  - Bleeding risk
  - Hemorrhagic stroke risk
  - Procedural risk
- **3. Are there benefits of anticoagulation besides preventing LAA thrombus in AF?**
- **4. What is the prior patient's experience on anticoagulation?**

1. Risk of LAA-related stroke
CHA_2DS_2-VASc Scores: Not specific

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CHA_2DS_2-VASc score **5**

- Sixty-six year-old (1)
- Female (1)
- Diabetic (1)
- Hypertensive (1)
- Ca score of 450 (1)
- Persistent AF for 2 years
- TEE prior to cardioversion showing LAA thrombus, resolved 1 month later

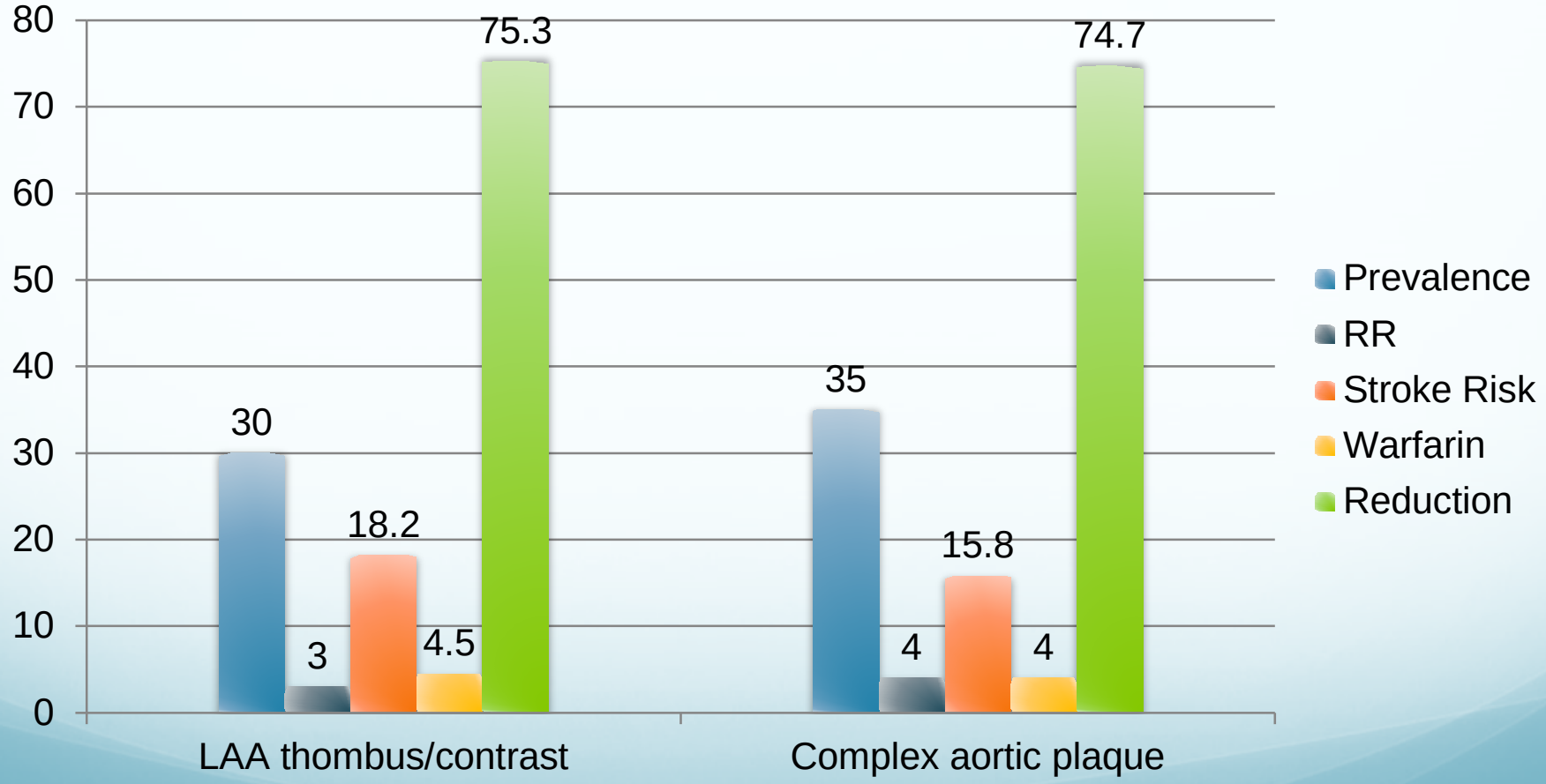
CHA_2DS_2-VASc score **5**

- Sixty-six year-old (1)
- Prior strokes (2)
- Ischemic cardiomyopathy with CHF (1)
- Extensive, mobile atheromatous plaque in the aortic arch (1)
- Persistent AF post CABG, cardioverted without recurrence

Only patients with high LAA-related risk of stroke would benefit from closure

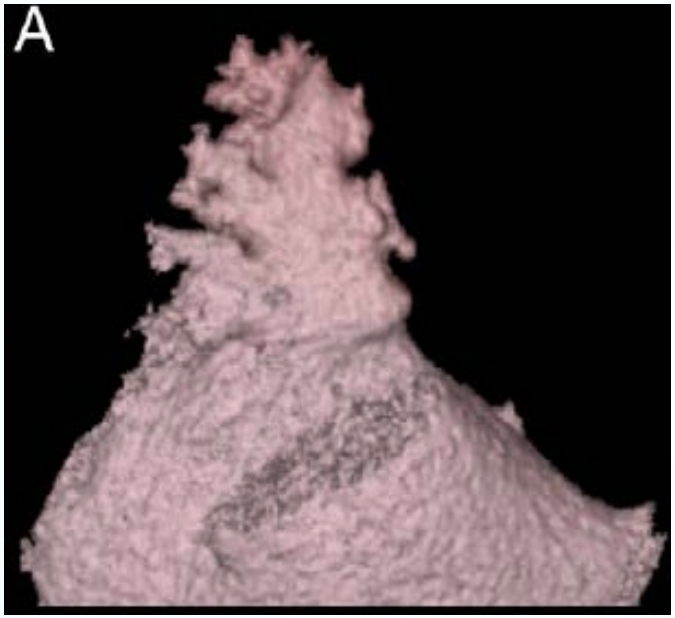
1. Risk of LAA-related stroke CHA_2DS_2-VASc Scores: LAA vs Aortic plaque

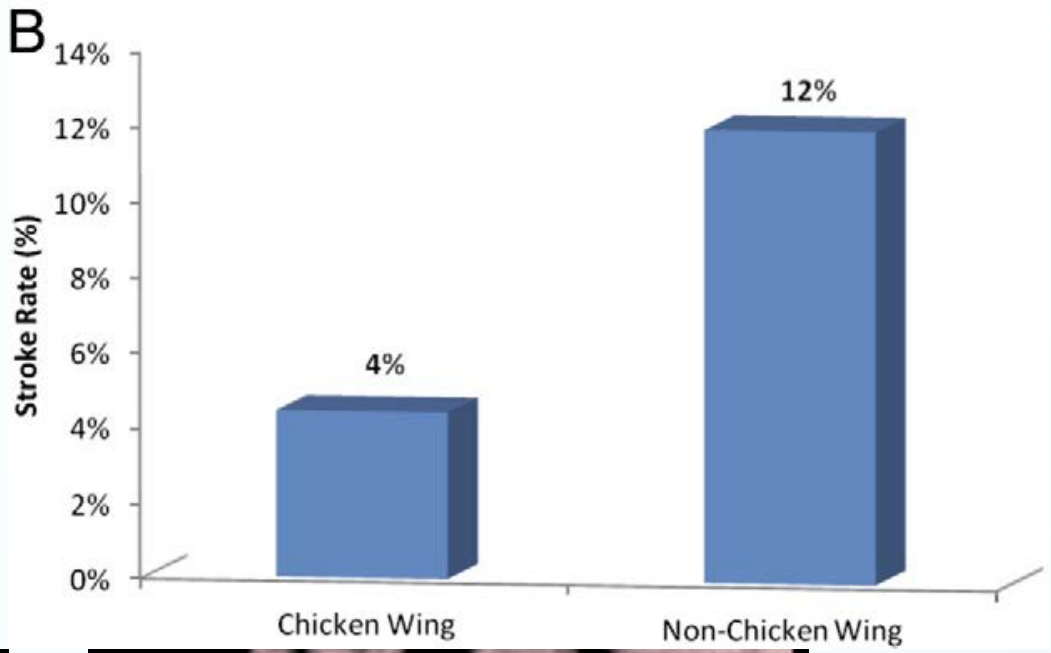
- SPAF-TEE study: Of 332 High-risk AF patients with CHF, prior stroke, female sex, Age >75. (One or more)

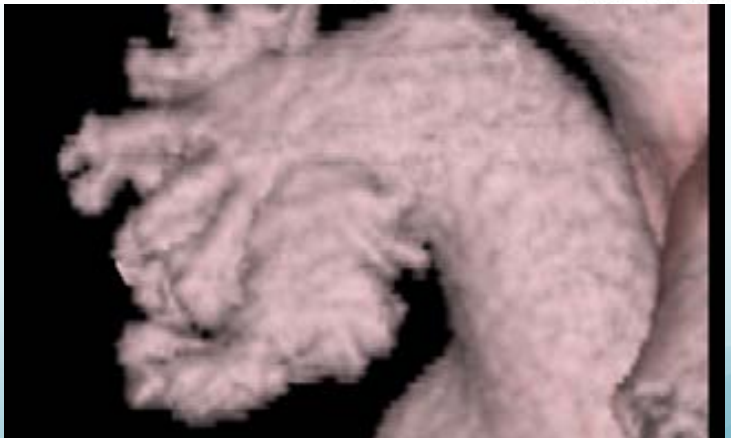


SPAF investigators. *Ann Intern Med*. 1998 Apr 15;128(8):639-47.

LAA-related stroke risk?

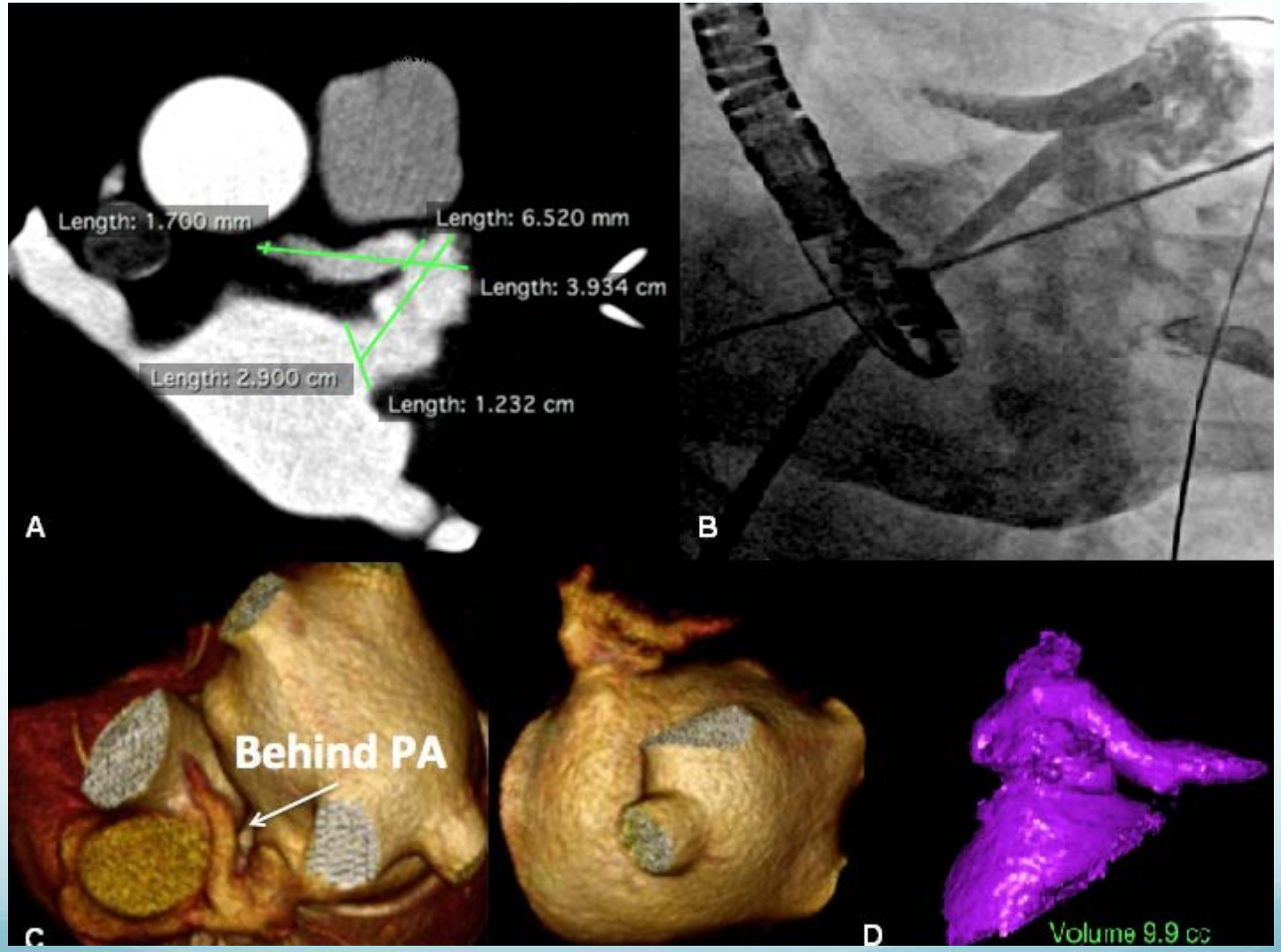






DiBiase *J Am Coll Cardiol.* 2012; 60(6):531-538. doi: 10.1016/j.jacc.2012.04.032

Extreme LAA Features

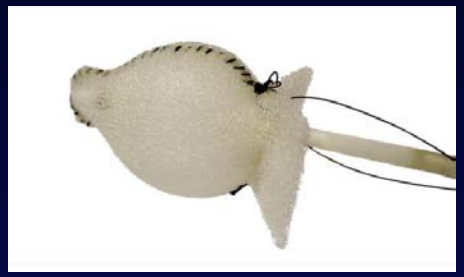
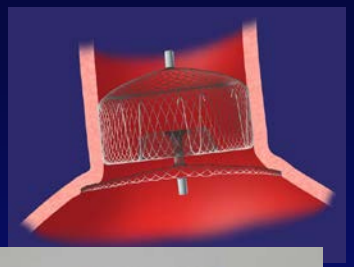


Kreideh B, Valderrábano M *HeartRhythm Case Rep*. 2015;1(6): 406-410

LA appendage closure

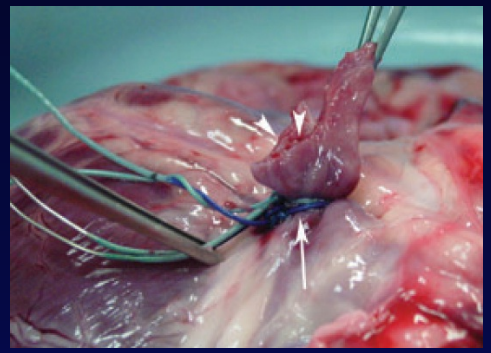
Endovascular



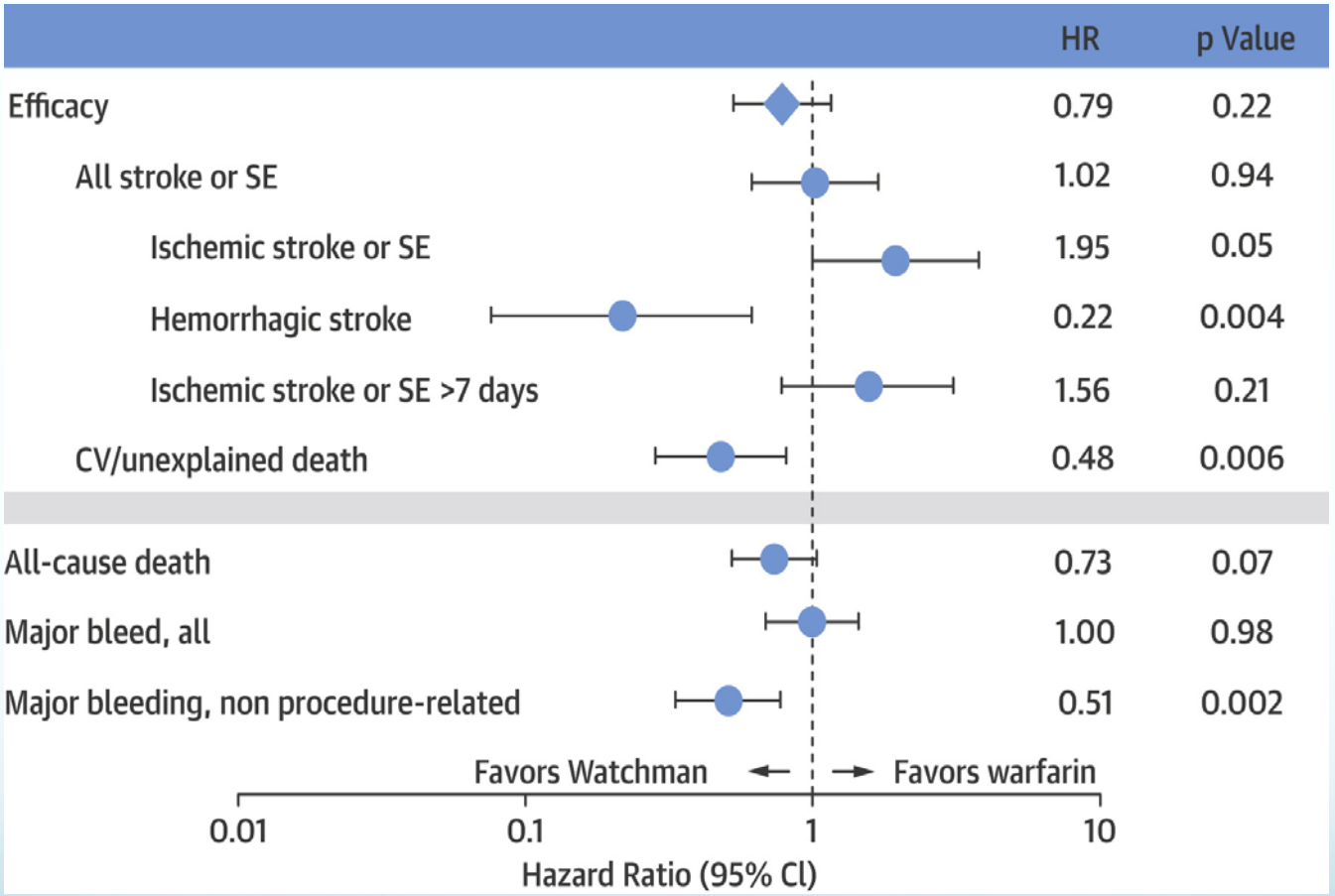

Epicardial





Courtesy of Randall Lee, MD

Risks of Stroke Prevention Warfarin vs Watchman



Reddy et al *JAMA.* 2014;312(19):1988-1998.

Holmes et al. *J Am Coll Cardiol*. 2015;65(24):2614-2623.

Risks of Stroke Prevention Bleeding on Warfarin vs Watchman

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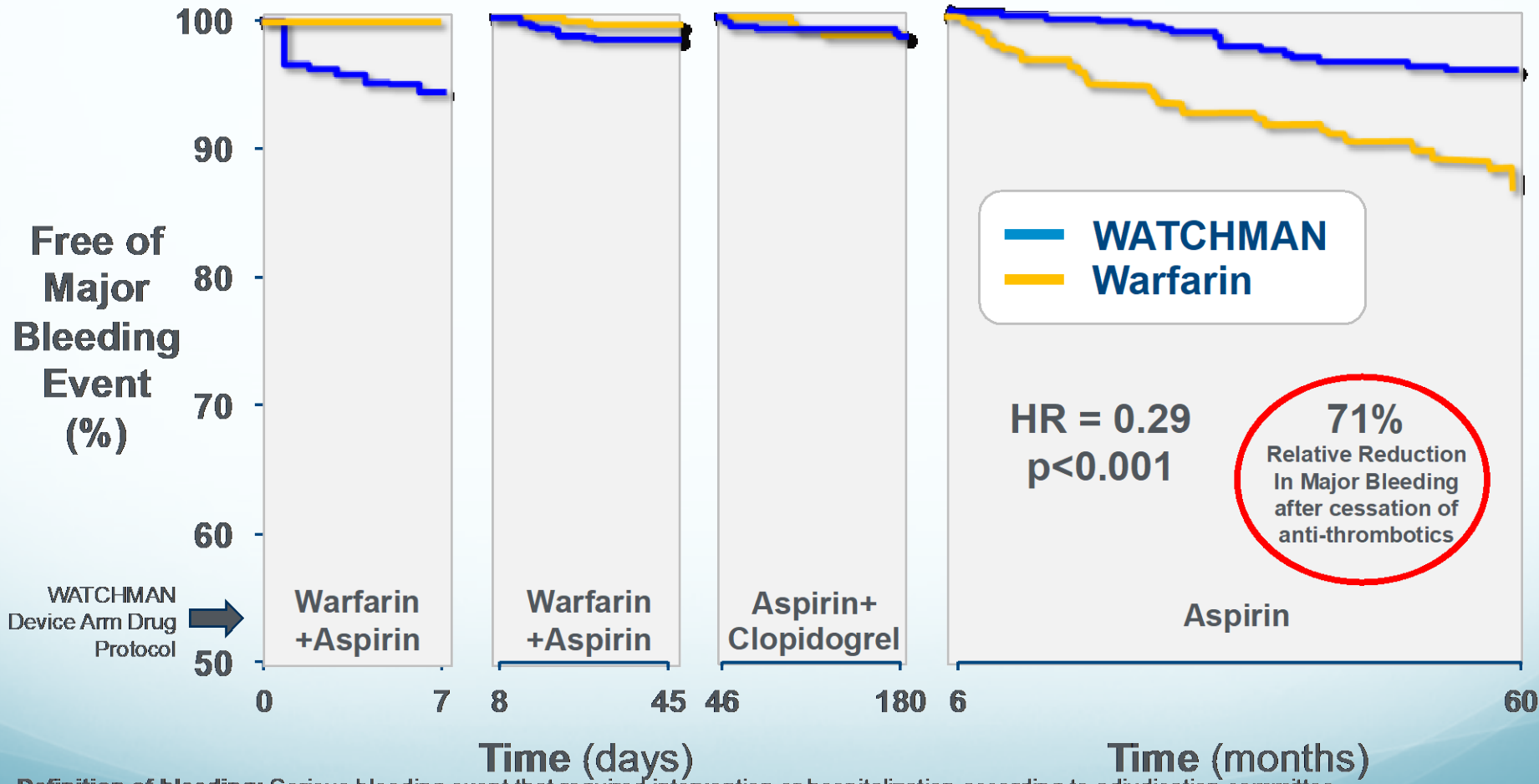

Definition of bleeding: Serious bleeding event that required intervention or hospitalization according to adjudication committee

Price et al. *JACC Cardiovasc Interv.* 2015 Dec 28;8(15):1925-32

Are there benefits of anticoagulation beyond the LAA?

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- SPAF study (*Neurology*. 1993; 43: 32–6) :
  - 65 % of strokes in atrial fibrillation classified as cardioembolic.
  - Up to 25% of strokes can be related to intrinsic cerebrovascular disease
- AF associations “procoagulant systemic state”:
  - Myocardial infarction. Internal and Emergency Medicine. April 2010, Volume 5, Issue 2, pp 91-94
  - Complex aortic atherosclerotic plaque. Ann Intern Med. 1998 Apr 15;128(8):639-47.
  - Abnormal carotid IMT in patients with AF. Atherosclerosis. 2015 Feb;238(2):350-5.
  - AF in patients with carotid atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2013 Nov;33(11):2660-5.
- **4. Are there other diagnoses: DVT, PE**

Making decisions

- Extreme risk: LAA thrombus, other diagnoses requiring anticoagulation

- First choice

- Financial constraints
- Stable INRs
- No bleeding
- Good tolerance

- Bleeding
- Stroke on anticoagulation
- Poor tolerance
- Hemorrhagic stroke
- Procedural candidacy
- High LAA-risk

NOACs | Warfarin | Watchman

Role of LAA in atrial fibrillation

- Source of thromboembolic events
- Source of atrial fibrillation triggers/substrate
  - Autonomic innervation
  - **Reentrant circuits**
  - **AF Triggers**
- Source of atrial natriuretic peptide
  - Potential role in fluid retention post-ligation or post-ablation

LAA automaticity

Yamada *Heart Rhythm* 2008 5:766-767

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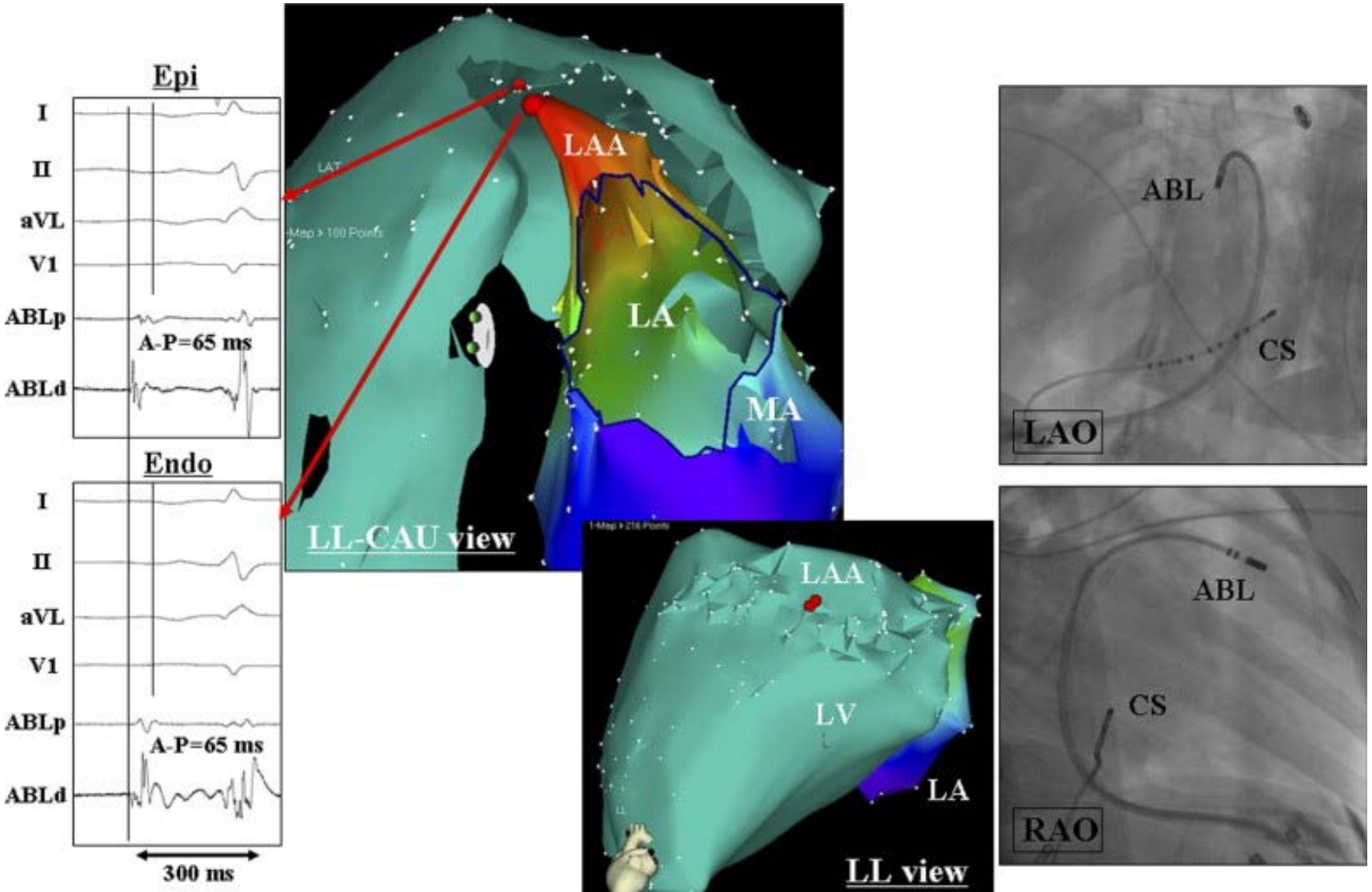

Localized LAA reentry

Hocini et al *Heart Rhythm*, 8 (2011), pp. 1853-1861

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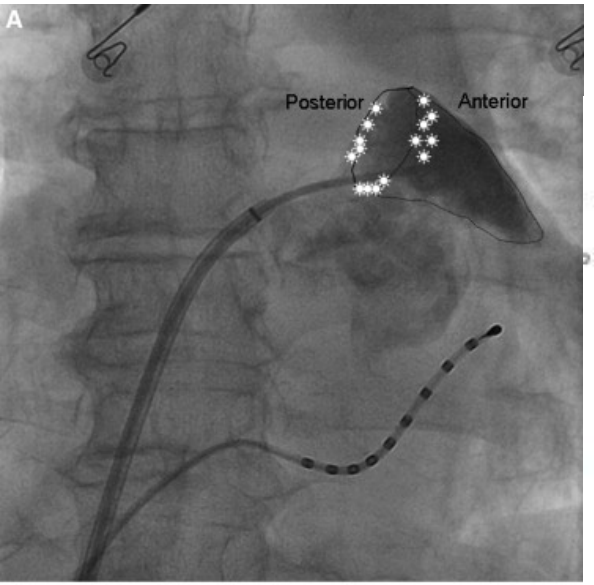

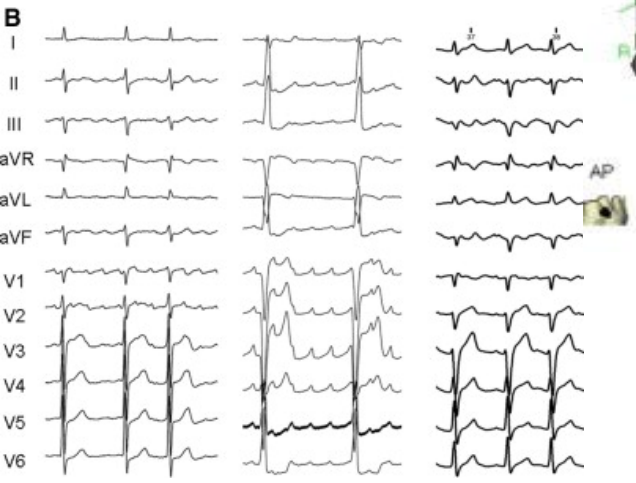

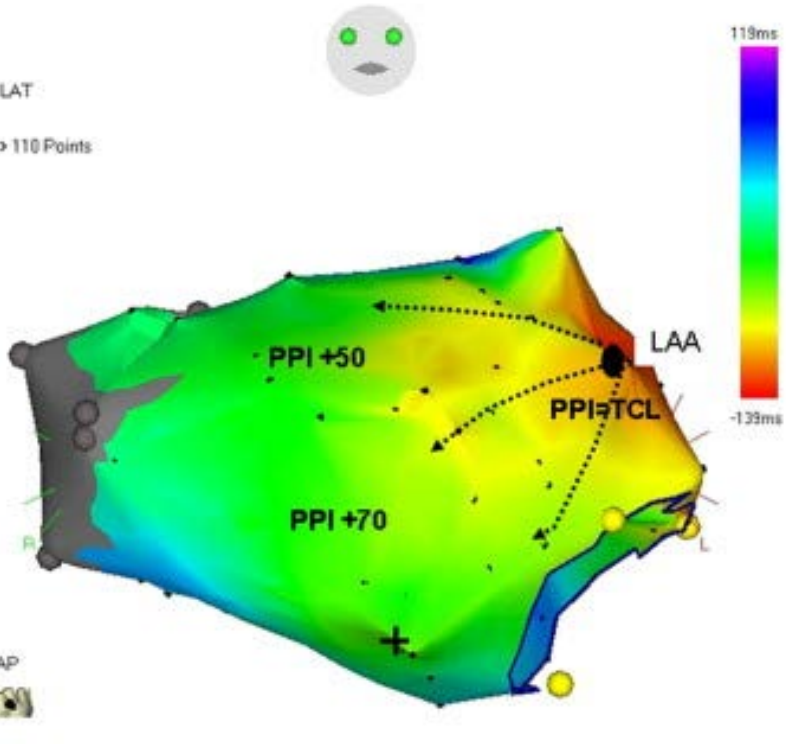

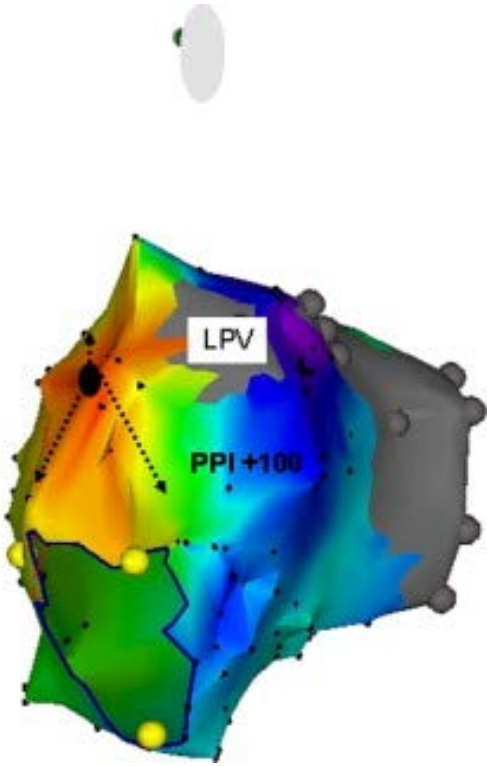

VOM bypassing Mitral Isthmus

Briceño D, Valderrábano M. *Circ Arrhythmia Electrophysiol* 2014

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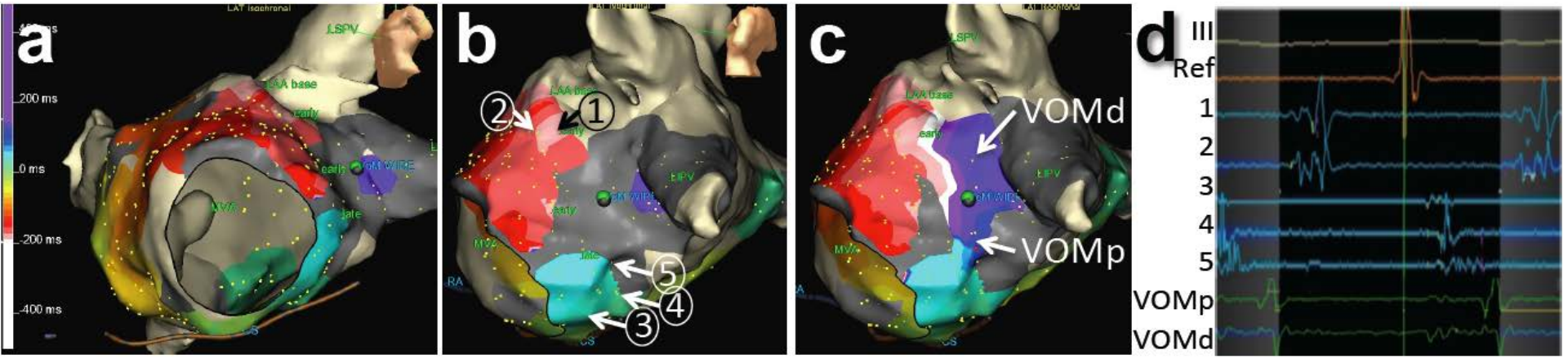

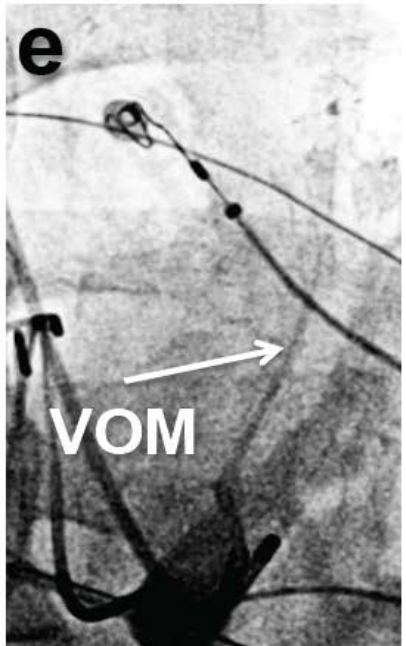

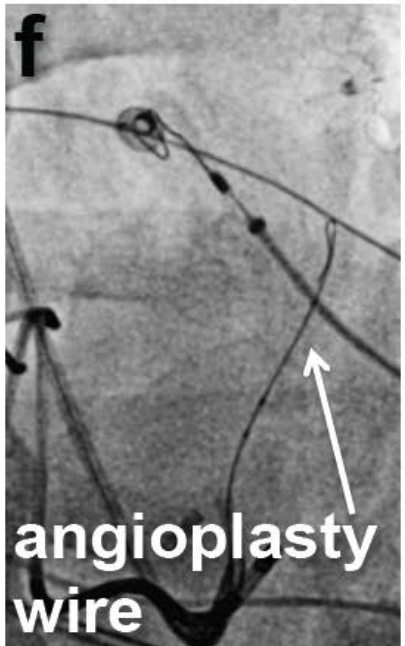

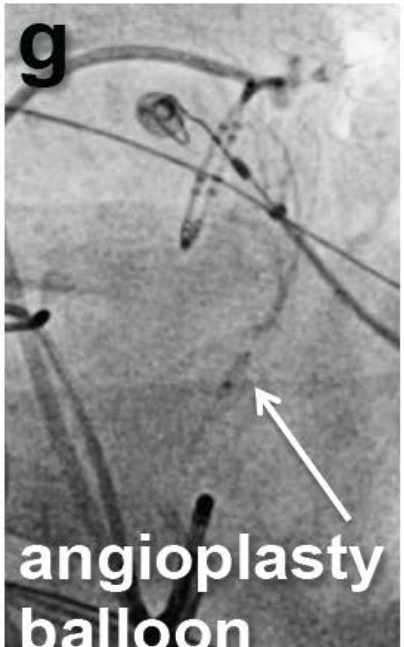

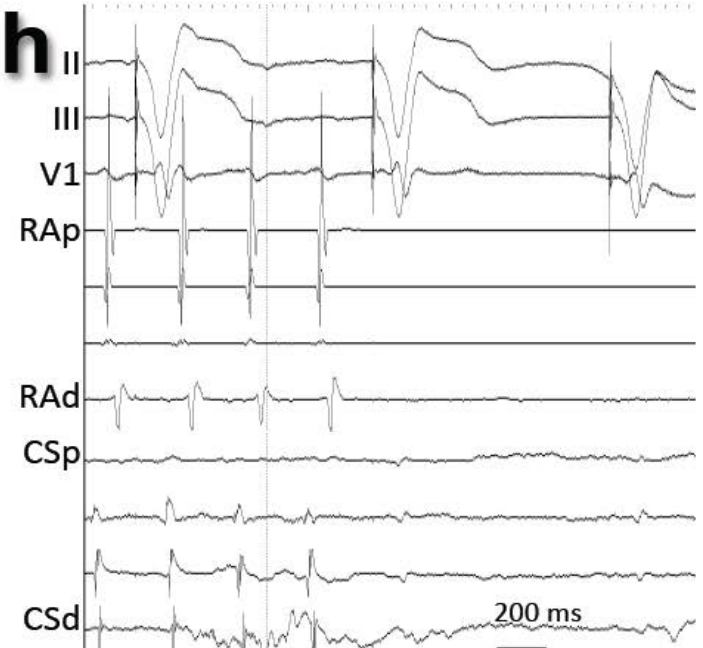

LAA AF triggers

Circulation. 2009;120:S690–S691

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- Up to 30 % of recurrent AF patients with persistent AF had LAA triggers
- LAA isolation –but not focal ablation- effective.

LAA AF triggers

Al Rawahi et al JACC: Clinical Electrophysiology
Volume 6, Issue 1, January 2020, Pages 21-30

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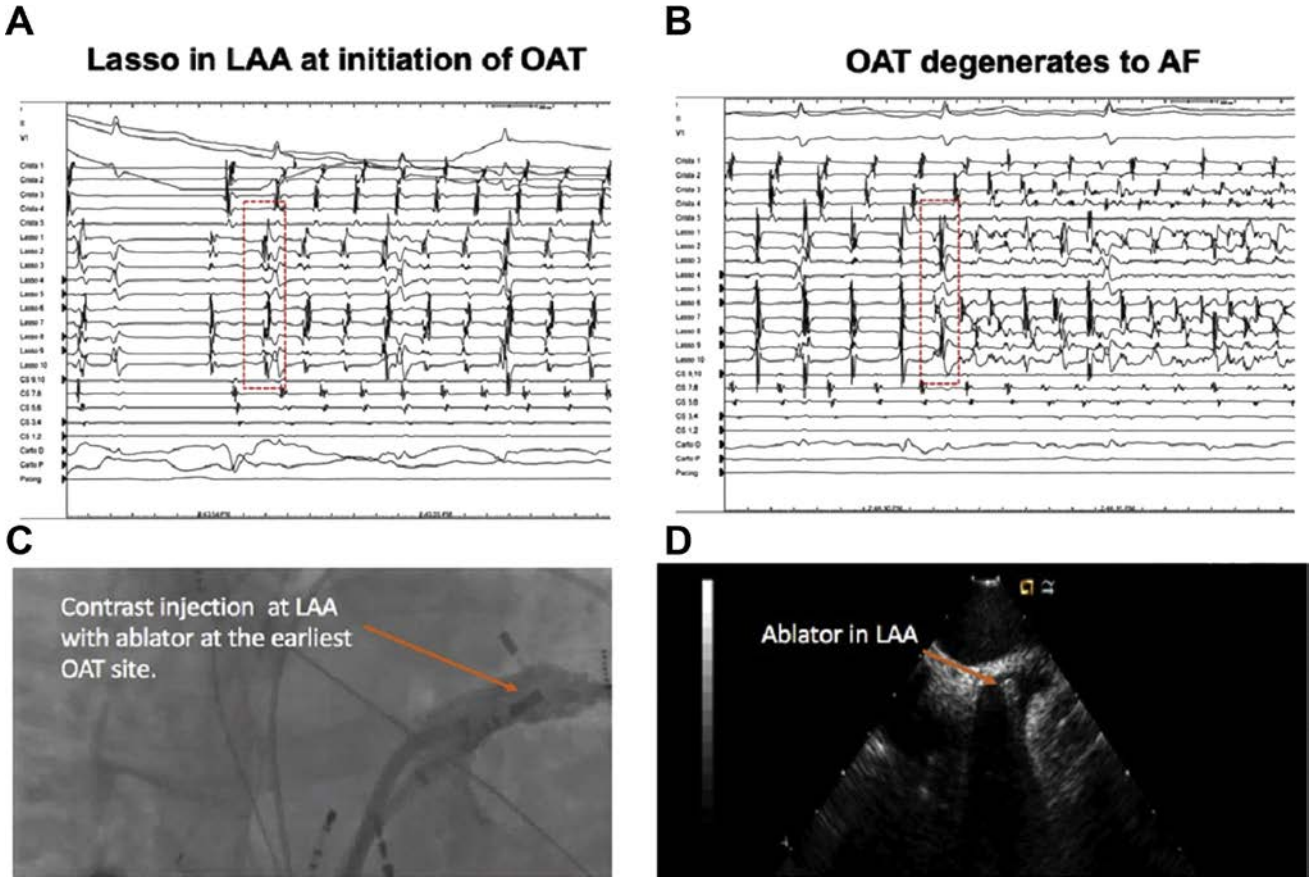

- LAA triggers were observed in 21 (0.3%) subjects (age 60 ± 9 years; 57% males; 52% persistent AF). Twenty (95%) patients were undergoing repeat ablation. The LAA was the only nonpulmonary vein trigger in 3 patients; the remaining 18 patients had both LAA and other nonpulmonary vein triggers.

Longstanding Persistent AF: Left atrial appendage isolation?

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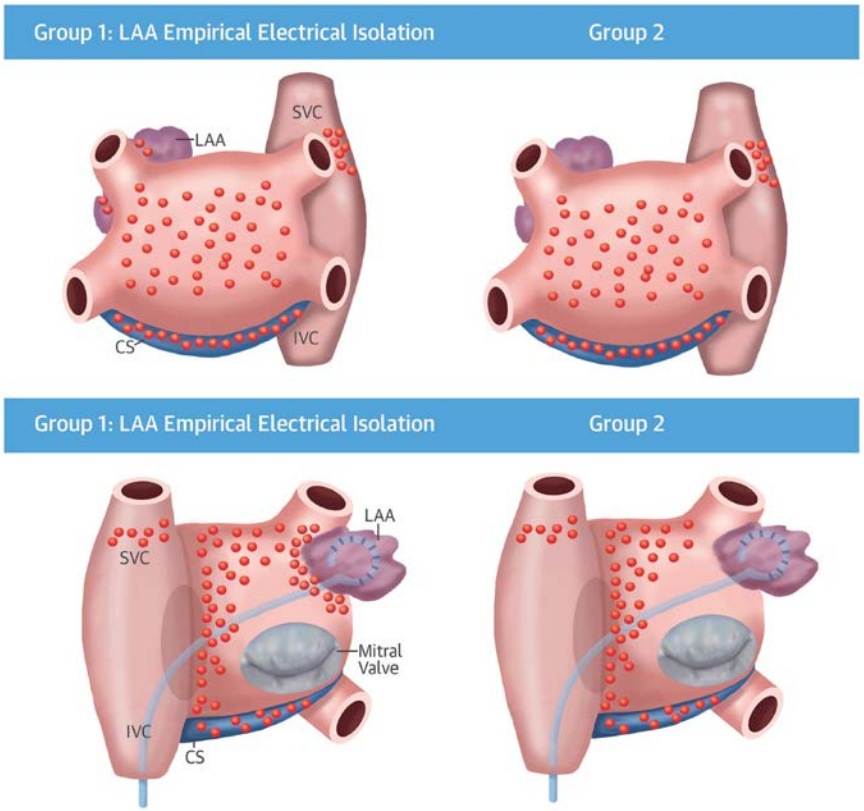
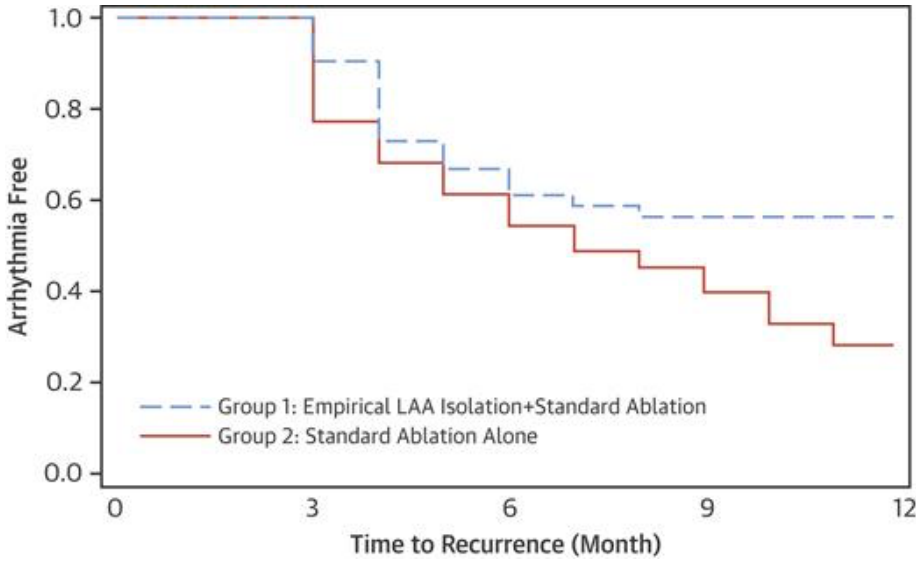
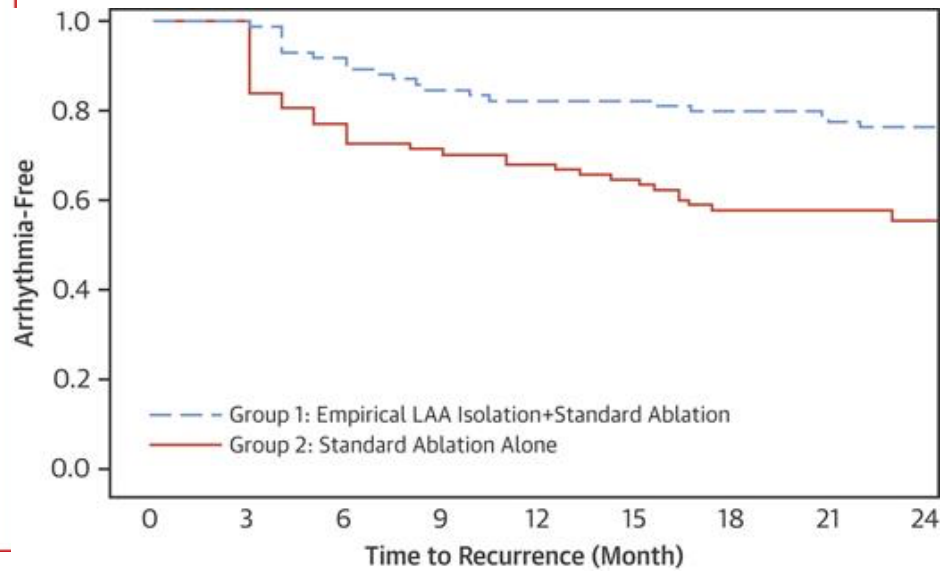
CENTRAL ILLUSTRATION: Lesion Set With and Without Empirical LAA Electrical Isolation



Di Biase, L. et al. J Am Coll Cardiol. 2016;68(18):1929-40.





Fate of LAA contractility

J Am Coll Cardiol. 2016 Nov 1;68(18):1929-1940

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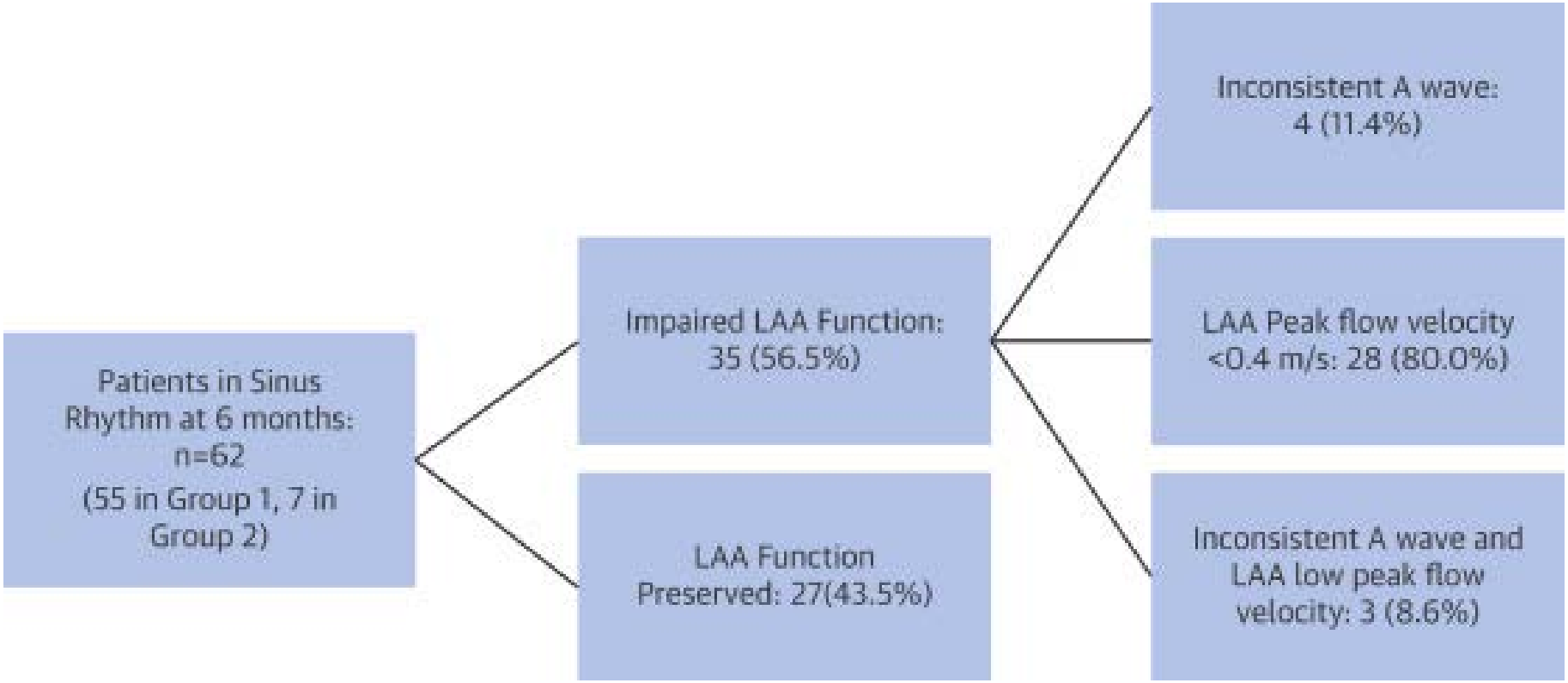

- Of the 93 patients who had transesophageal echocardiography (TEE), preserved left atrial appendage (LAA) function was reported in 45 (48.4%) patients, whereas an impaired contractile pattern was observed in 48 (51.6%).

Unexpectedly High Incidence of Stroke and Left Atrial Appendage Thrombus Formation After Electrical Isolation of the Left Atrial Appendage for the Treatment of Atrial Tachyarrhythmias

Andreas Rillig, MD*; Roland R. Tilz, MD, FHRS*; Tina Lin, MBBS, BMedSci, FRACP; Thomas Fink, MD; Christian-H. Heeger, MD; Anita Arya, PhD, MBBS; Andreas Metzner, MD; Shibu Mathew, MD; Erik Wissner, MD, FHRS; Hisaki Makimoto, MD, PhD; Peter Wohlmuth, PhD; Karl-Heinz Kuck, MD, FESC, FHRS; Feifan Ouyang, MD

Background—Electric left atrial appendage (LAA) isolation (LAAI) may occur during catheter ablation of atrial tachyarrhythmias. Data regarding the risk of thromboembolic events and stroke after LAAI are sparse. This study evaluated the incidence of LAA thrombus formation and thromboembolic events after LAAI.

Methods and Results—Fifty patients had LAAI (age=71 years; female=56%; CHA_2DS_2-VASc score before ablation =3 [2;3]). LAAI patients were compared with matched patients with comparable baseline characteristics who underwent atrial fibrillation ablation without LAAI (n=50). Ablation strategies in the LAAI group included pulmonary vein isolation in 50 (100%), left atrial isthmus line in 47 (94%), anterior line in 45 (90%), complex atrial fractionated potentials in 24 (48%), and roofline in 14 (28%) patients. Transesophageal echocardiography was performed during follow-up in 47/50 (94%) patients in the LAAI group and in all patients of the control group. Oral anticoagulation (OAC) independent of CHA_2DS_2-VASc score was strongly recommended in all patients. During a median follow-up of 6.5 (4–12) months, stroke occurred in 2 patients on OAC and transient ischemic attack in one without OAC in the LAAI group. In the remaining 47 patients, LAA thrombus was identified on transesophageal echocardiography in 10 (21%) patients (OAC=9; no OAC=1). In the control group, no LAA thrombus was detected and no stroke occurred (P<0.001). Stable sinus rhythm was maintained in 32 patients (64%) of the LAAI group after a median follow-up of 6.5 months (4–12), including 17/32 patients on antiarrhythmic drugs.

Conclusions—After LAAI, an unexpectedly high incidence of LAA thrombus formation and stroke was observed despite OAC therapy. **(*Circ Arrhythm Electrophysiol*. 2016;9:e003461. DOI: 10.1161/CIRCEP.115.003461.)**

The price of LAA isolation

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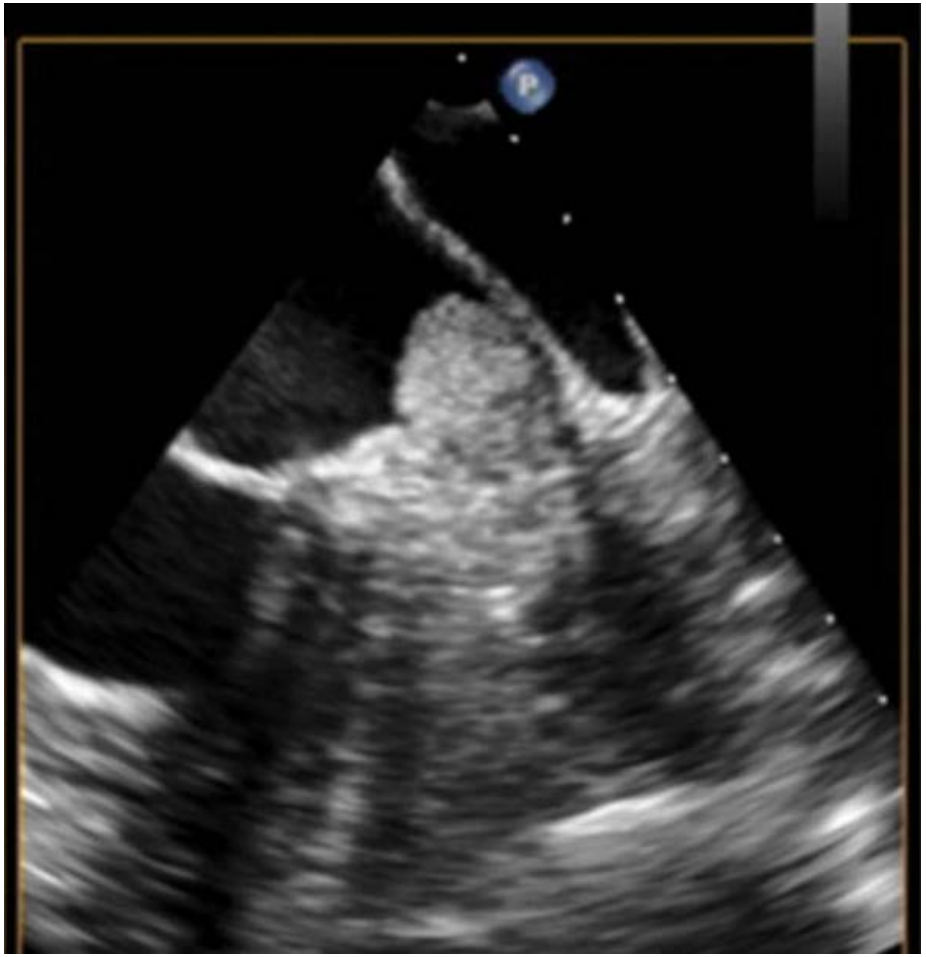
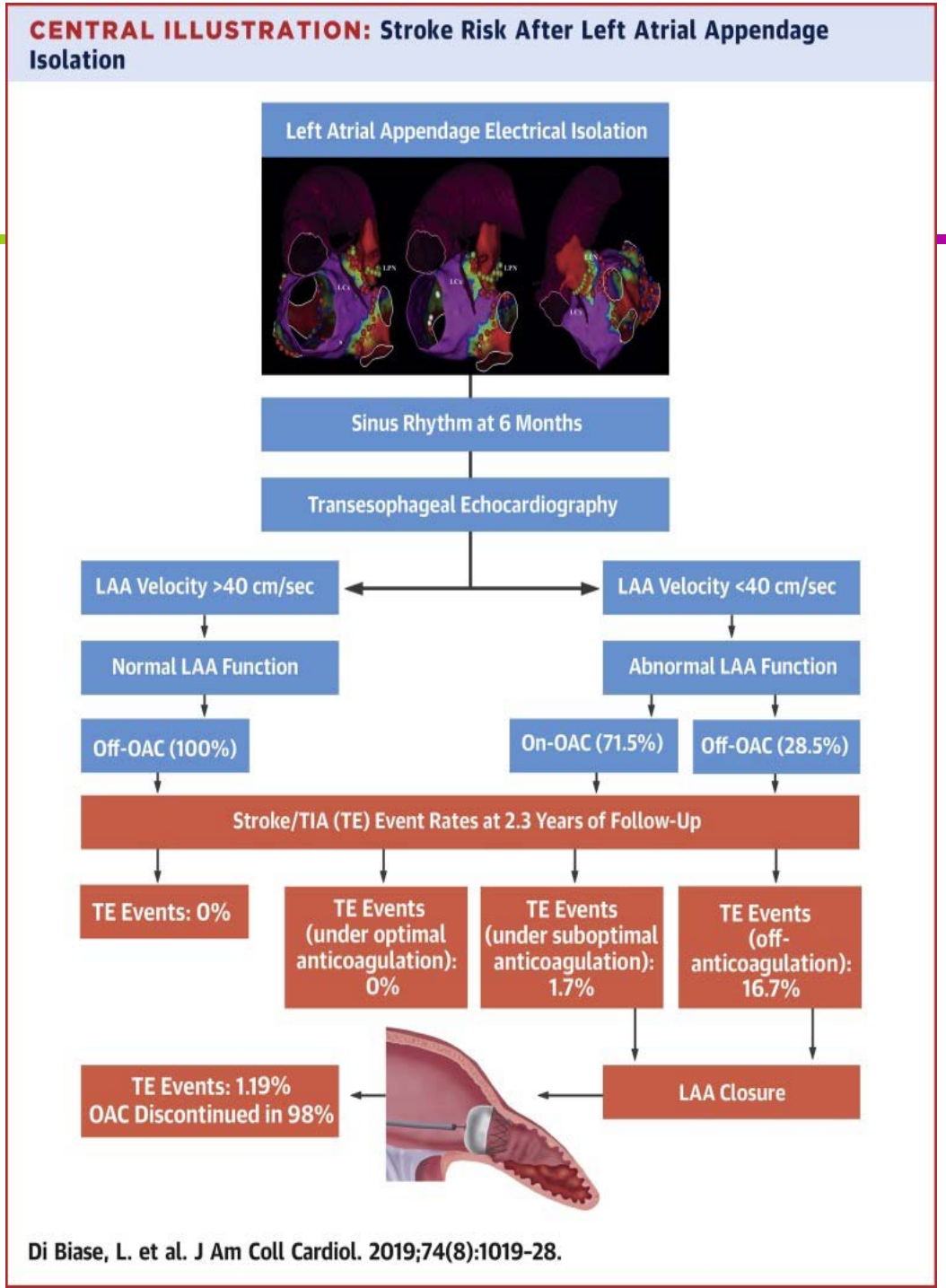
- 50 patients with LAA isolation
- 2 CVA, 1 TIA
- In remainder 47 patients, LAA thrombus was identified on transesophageal echocardiography in 10 (21%) patients (OAC=9; no OAC=1).



After LAA isolation

- If TEE shows LAA velocity >40 cm/s
  - No CVA
- If LAA velocity< 40
  - Off anticoagulation CVA risk 16.7%
  - Reduced by LAA closure

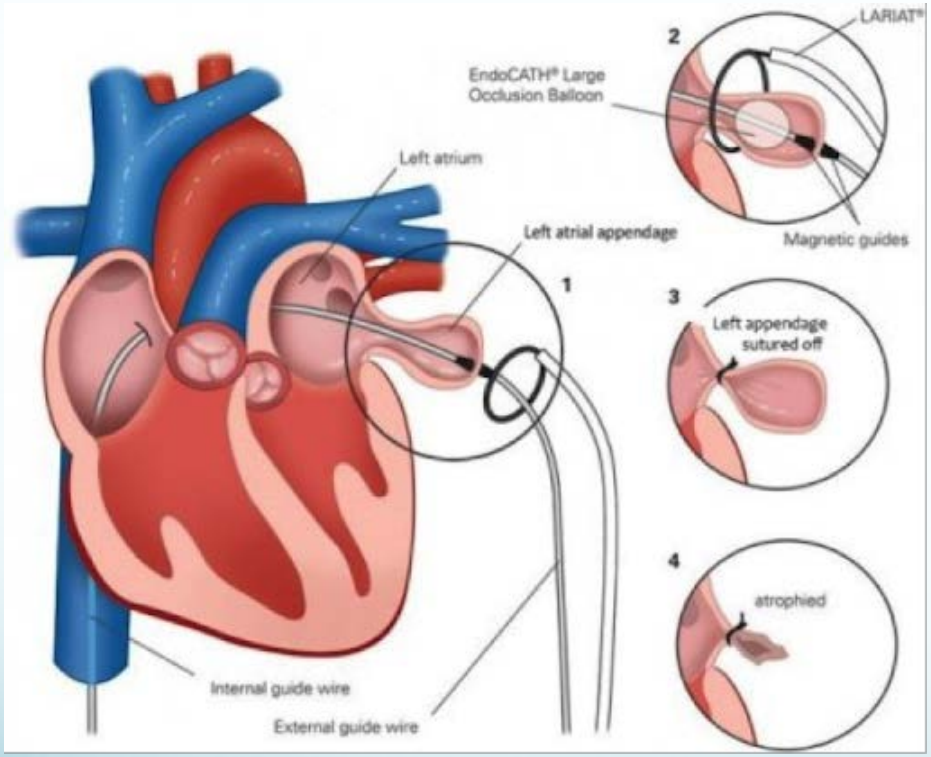


Does ablation reduce stroke?

	Death	Disabling Stroke*	Any Stroke
Ablation Group (n=1108)			
≤30 days after ablation	0	0	4
>30 days after ablation	51	3	22
Never ablated (n=102)	7	0	1
Total	**58**	**3**	**27**
Drug Therapy Group (n=1096)			
≤30 days after initiating drug	0	1	3
>30 days after initiating drug	67	6	35
Never started drug therapy (n=4)	0	0	1
Total	**67**	**7**	**39**
Drug Group Patients Who Crossed Over to Ablation (n=301) **			
Patients with event prior to crossover	--	0	5
Patients with event after crossover	7	0	7

Packer et al *JAMA*. 2019;321(13):1261-1274

Amaze trial


LARIAT®
2
EndoCATH® Large Occlusion Balloon
Left atrium
Left atrial appendage
Magnetic guides
1
3
Left appendage sutured off
4
atrophied
Internal guide wire
External guide wire


PVI + LARIAT
PVI

Conclusions

- The LAA is a critical structure in atrial fibrillation
  - As a source of thromboembolism
    - Not the only one
    - Treated with OAC
    - Treated with LAA exclusion
  - As a source of AF maintenance
    - Triggers
    - Reentry
    - Innervation
    - Treated with LAA isolation
      - Increased risk of OAC dependence
      - Requires LAA occlusion