Gamechangers in Cardiology: 2018

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Annual Refresher Course for Family Physicians

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Conflict of Disclosure

Speaker has no conflict of interest

Except bad jokes…

Objectives

1. Primary prevention in cardiology: have we taken a step back?

1. MRIs in pacemaker patients?

2. Atrial fibrillation: balance between stroke and bleeding

3. What improvements have been made in heart failure management?

1. Primary Prevention

Aspirin for Primary Prevention

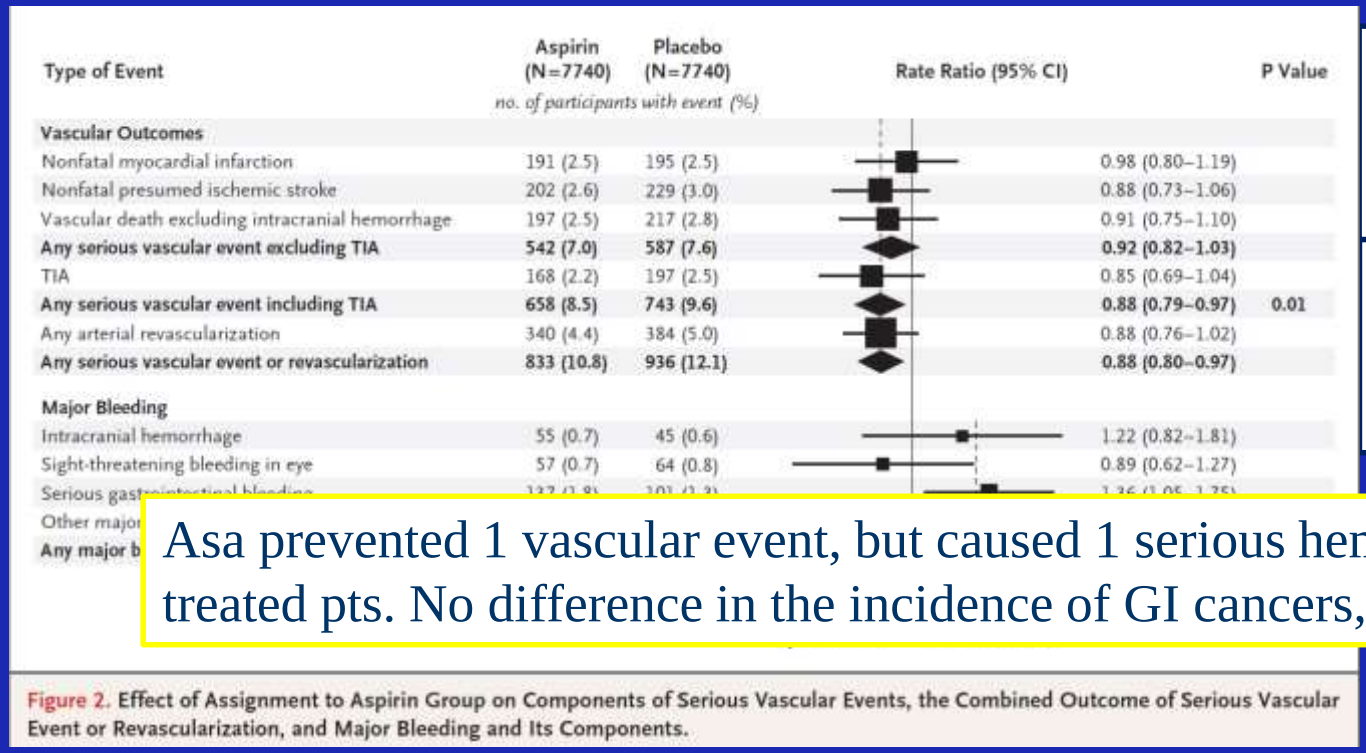
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

ASA 100mg daily vs placebo for primary prevention of cardiovascular disease in 15,000 diabetics (without CV disease)
-F/up 7.4 yrs
-outcome: vascular event (Mi, stroke, TIA, death from vascular cause)
-Mean age 63, 63% male



Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Value
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major				
Any major b				

Figure 2. Effect of Assignment to Aspirin Group on Components of Serious Vascular Events, the Combined Outcome of Serious Vascular Event or Revascularization, and Major Bleeding and Its Components.

Vascular events
8.5% vs 9.6% 95% CI 0.79-0.97, p=0.01

Bleeding events
4.1% vs 3.2% 95% CI 1.09-1.52, p=0.003

Asa prevented 1 vascular event, but caused 1 serious hemorrhage for every 100 treated pts. No difference in the incidence of GI cancers, or all cancers.

In diabetic patients at increased cardiovascular risk (10 year risk > 10%), suggest to continue ASA. If low-moderate risk, ASA on an individual basis.

N Engl J Med 2018;379:1529-39.

ARRIVE study: Lancet. 2018

2007-2016: 12,546 pts randomized to ASA vs placebo
Age: 55+ (male) or 60+ (women) with moderate CV risk
Excluded diabetics and pts at high risk of GI bleeding, other bleeding,
Median 5 year follow-up
Primary endpoint: composite of CV death, Mi, unstable angina, stroke, or TIA
Safety endpoints: hemorrhagic events

Results:
Primary endpoint: 4.39% ASA vs 4.48% placebo (95% CI 0.81-1.13, p=0.60)
GI bleeds: 61 (0.97%) vs 29 (0.46%) (95% CI 1.36-3.28, p=0.0007)
No difference in mortality (2.55% vs 2.57%)

Conclusion: In moderate-risk, nondiabetic patients, many of whom were receiving treatment for hypertension and hyperlipidemia, ASA did not add incremental benefit

The Lancet volume 392, issue 10152, p1036

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 18, 2018 VOL. 379 NO. 16

Effect of Aspirin on Disability-free Survival in the Healthy Elderly

J.J. McNeil, R.L. Woods, M.R. Nelson, C.M. Reid, B. Kirpach, R. Wolfe, E. Storey, R.C. Shah, J.E. Lockery, A.M. Tonkin, A.B. Newman, J.D. Williamson, K.L. Margolis, M.E. Ernst, W.P. Abhayaratna, N. Stocks, S.M. Fitzgerald, S.G. Orchard, R.E. Trevaks, L.J. Beilin, G.A. Donnan, P. Gibbs, C.I. Johnston, J. Ryan, B. Radziszewska, R. Grimm, and A.M. Murray, for the ASPREE Investigator Group*

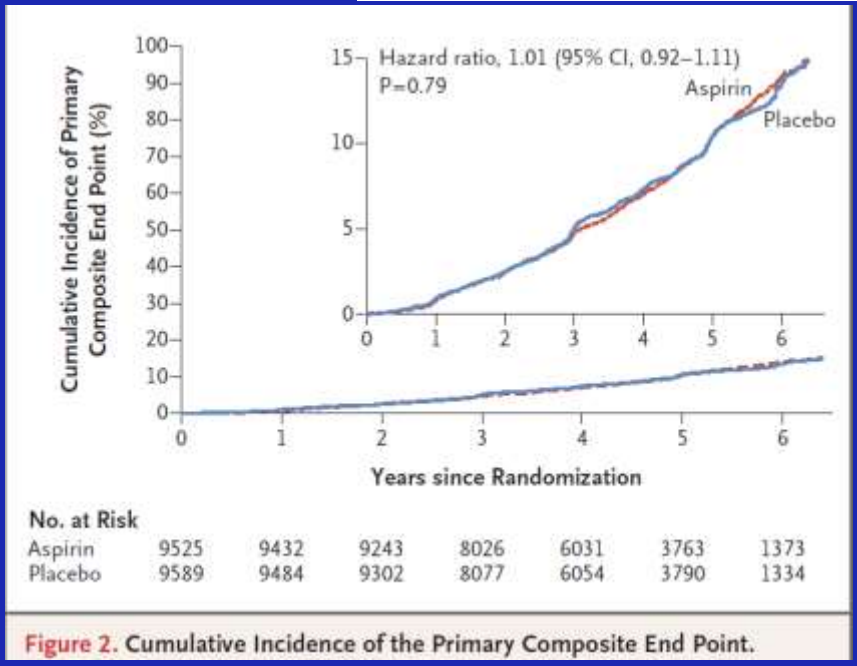


Figure 2. Cumulative Incidence of the Primary Composite End Point.

-19,114 patients (median age 74) randomized to ASA 100mg Qd vs placebo
-No baseline CV disease, dementia or physical disability
-Primary outcome: composite of death, dementia, or persistent physical disability
Results: no significant difference in the outcome. 3.8 vs 2.8% major hemorrhage.

Conclusion: ASA in healthy elderly patients did not prolong disability-free survival over 5 years, but increased the rate of major hemorrhage

N Engl J Med 2018;379:1499-508.

Aspirin in Primary Prevention

Conclusion:

Multiple studies in several moderate risk populations, all demonstrate no reduction in CV events or mortality with ASA.

We are better at preventing heart disease than ever before (managing cholesterol, diabetes and hypertension) which has dramatically reduced the cardiac event rates.

Side note: substudy of the ASPREE trial analyzed the higher all-cause mortality observed in pts who received aspirin. New cancer diagnoses and death were higher in patients on aspirin. Results clearly to be interpreted with caution.

N Engl J Med 2018;379:1499-508.

Who should be screened prior to athletic participation?

- Sudden cardiac death during athletic activity is rare
- These deaths have a devastating impact because athletes are perceived as epitomizing good health
- No Canadian guidelines regarding screening

https://youtu.be/v8fwQCygr4E

Who should be screened prior to athletic participation?

- Sudden cardiac death during athletic activity is rare, but devastating
- No Canadian guidelines

https://youtu.be/v8fwQCygr4E

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2018;379:524-34.

ORIGINAL ARTICLE

Outcomes of Cardiac Screening in Adolescent Soccer Players

1996-2016: 11,168 adolescent athletes screened, mean age 16.4, 95% male. Health questionnaire, physical exam, ECG, and Echo.

23 deaths. 8 (35%) were sudden deaths due to cardiac disease. Cardiomyopathy caused 7/8 deaths. 6/8 (75%) had normal cardiac screening results.

Table 2. Summary of Cardiac Conditions Detected According to Screening Tool.

Condition	No. of Athletes	No. of Athletes with Abnormal Result			
		History	Examination	ECG	Echocardiography
Any cardiac condition	267	6	76	84	237
Condition associated with sudden cardiac death	42	3	2	36	12
Hypertrophic cardiomyopathy	5	0	0	5	5
Arrhythmogenic right ventricular cardiomyopathy	2	1	0	1	2
Dilated cardiomyopathy	1	1	0	1	1
Coronary-artery anomalies	2	0	0	0	2
Bicuspid aortic valve–associated disease*	3	1	2	0	3
Long-QT syndrome	3	0	0	3	0
Wolff–Parkinson–White ECG pattern	26	0	0	26	0
Other cardiac condition	225	3	74	48	225
Bicuspid aortic valve	68	1	32	15	68
Atrial septal defect	62	1	6	26	62
Aortic regurgitation	29	0	16	2	29
Mitral-valve prolapse	24	0	12	3	24
Patent ductus arteriosus	18	0	1	1	18
Ventricular septal defect	13	0	3	1	13
Pulmonary stenosis	9	1	4	0	9
Cor triatriatum	2	0	0	0	2

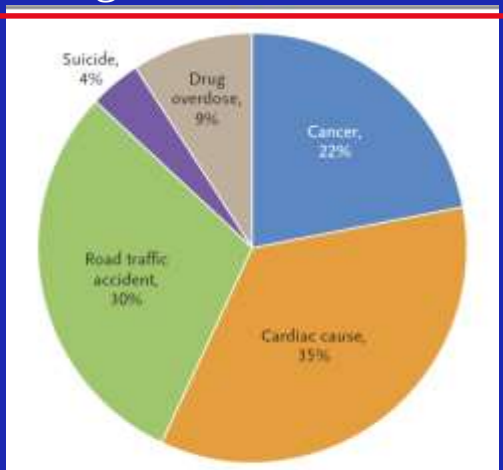


Figure 2. Causes of Death among the 23 Screened Adolescent Soccer Players Who Died.

Who should be screened prior to athletic participation?

Competitive athlete (organized team or individual sport that requires regular competition, places high premium on excellence and achievement, and intense training >10 hrs per week): should be screened (Hx, Physical exam, ECG ±echo ± stress testing)

Young athletes (high school/college, age <35): Personal history, Family history, and Physical exam. (Routine ECG, echo, and/or stress testing not recommended. European guidelines: advocate for ECG).

Masters athletes: (age > 35 in whom cardiac death is due to coronary artery disease; includes many who are ages 50-80). Personal history, Family history, and physical exam ± 12-lead ECG in age >40 (AHA) ± EST if at higher risk of CAD (male >40 or woman >50/postmenopausal with ≥1 RF (dlp, htn, smoker, DM, history of Mi or SCD in 1st degree relative <60). EST if age ≥ 65 in absence of RF or symptoms

Personal history: exertional chest pain/discomfort, unexplained syncope (not vasovagal), excessive exertional dyspnea/fatigue, palpitations, prior heart murmur, elevated BP, prior restriction from participation in sports, prior cardiac testing;

Family history: premature death in one relative – sudden, unexpected <age 50 from heart disease, disability from heart disease in close relative <50, specific disease in family members: hypertrophic cardiomyopathy, dilated cardiomyopathy, long QT syndrome, short QT syndrome, ARVC, Marfan syndrome.

Physical exam: heart murmur in supine/standing/valsalva, femoral pulses to rule out aortic coarctation, features of Marfan, BP.

J Am Coll Cardiol. 2015 Dec;66(21):2356-61

ECG Interpretation in Athletes: who requires further evaluation?

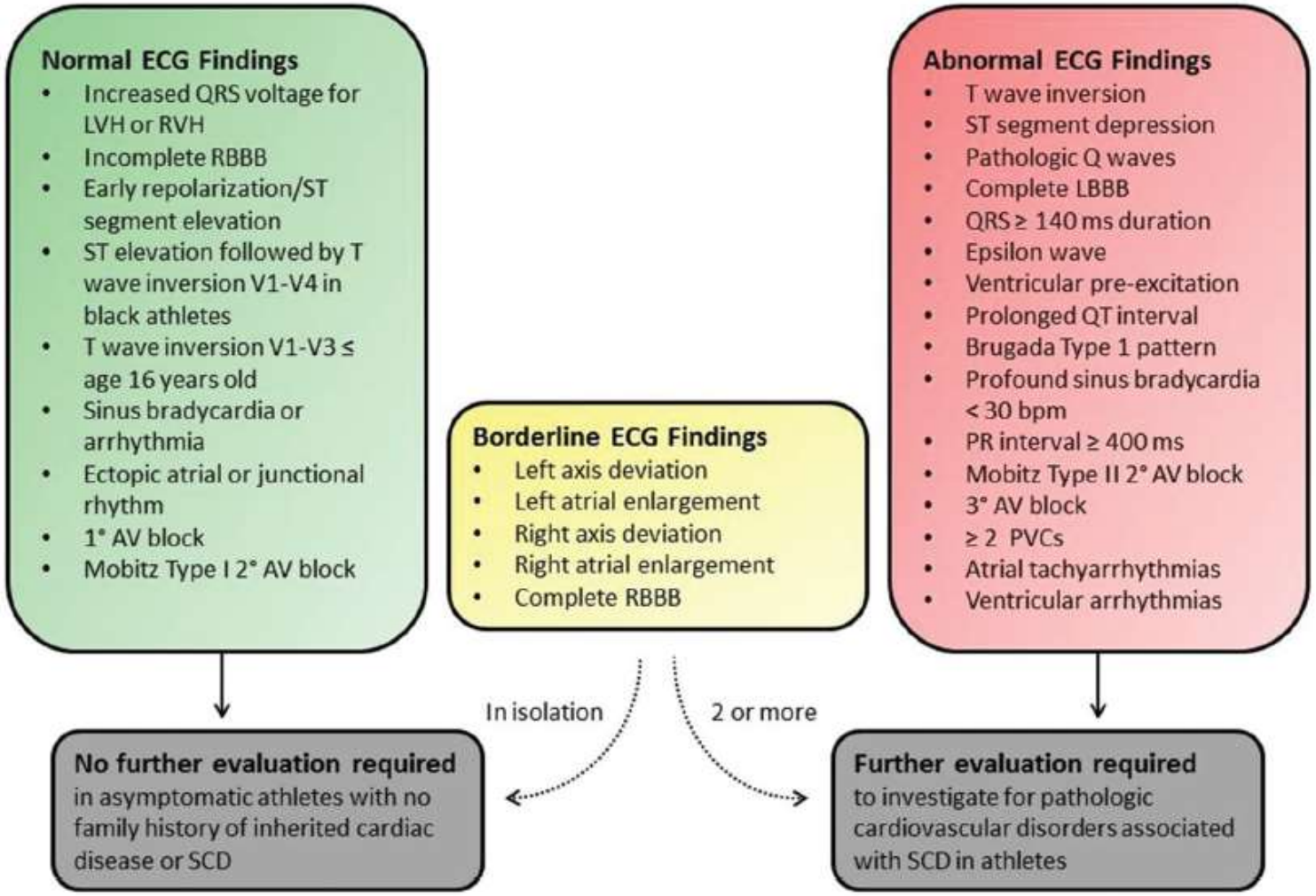


Figure 1 International consensus standards for ECG interpretation in athletes. AV, atrioventricular; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; PVC, premature ventricular contraction; RBBB, right bundle branch block; RVH, right ventricular hypertrophy; SCD, sudden cardiac death.

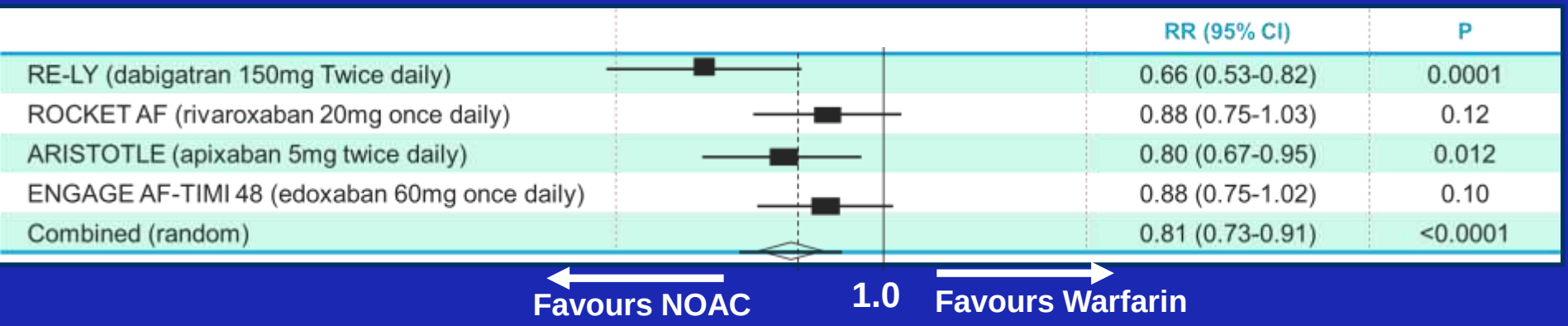
Drezner JA, et al. Br J Sports Med 2017;**51**:704–731.

Anticoagulation and No Anticoagulation

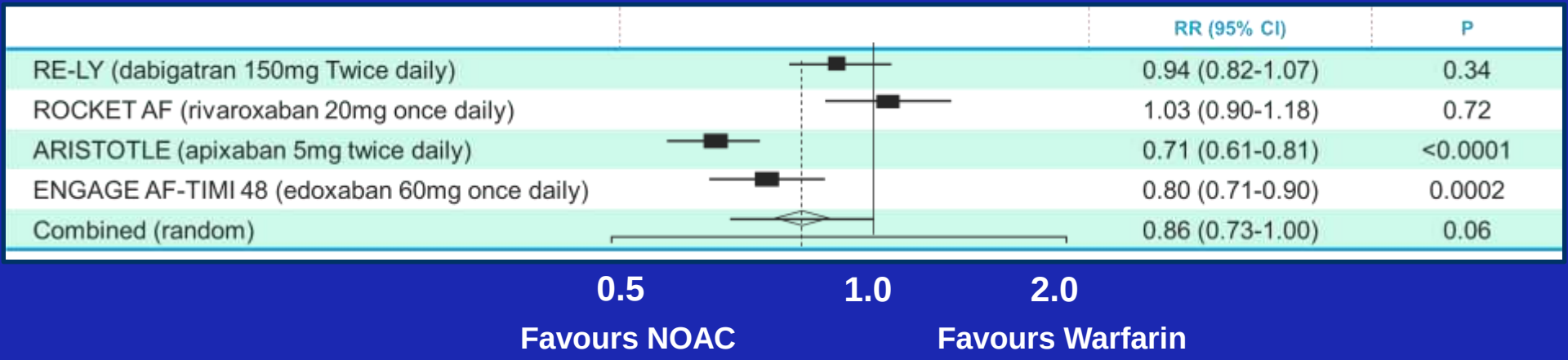
NOACS Currently Available in Canada

	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Mechanism of action	Direct Factor Xa inhibitor	Direct thrombin inhibitor	Direct Factor Xa inhibitor	Direct Factor Xa inhibitor
Oral bioavailability	~50%	~6.5%	62%	80-100% (when taken with food)
Food effect	No	No	No	Yes (needs to be taken with food*)
Pro-drug	No	Yes	No	No
Renal clearance	~27%	85%	50%	36%
Mean half-life ($t_{½}$)	~12 h	11-17 h	10-14 h	5-13 h
T_{max}	3-4 h	0.5-2 h	1-2 h	2-4 h
Standard dosage	5 mg	150 mg	60 mg	20 mg
Dosing frequency	Twice daily	Twice daily	Once daily	Once daily
CYP metabolism	Yes	No	Minimal <4%	Yes

Stroke or Systemic Embolic Event

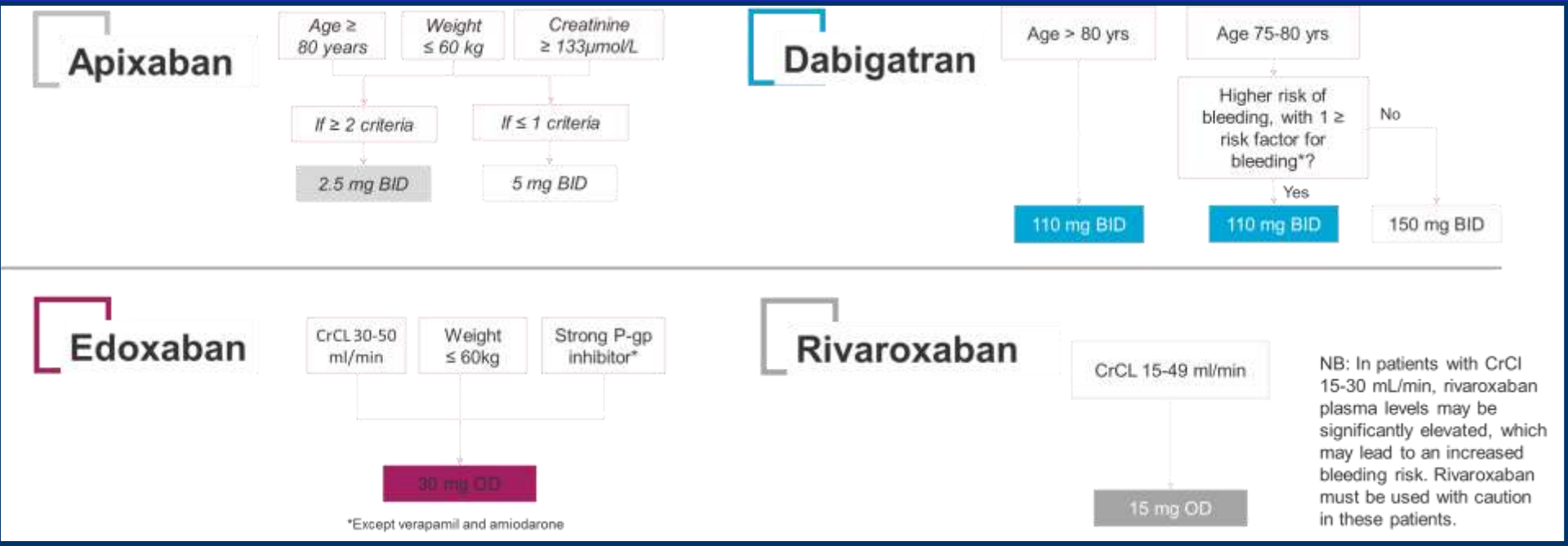


Major Bleeding



Ruff CT, et *al*. *Lancet* 2014;383:955-62

Dosing for the Various NOACs



CrCl: creatinine clearance; P-gp: P-glycoprotein

*e.g. Renal impairment, extensive cerebral infarction (haemorrhagic or ischemic) within the last 6 months, active peptic ulcer disease with recent bleeding

Edoxaban:

-Increased INR can be seen, the INR is not valid in interpreting level of anticoagulation

-limited data in patients with severe renal impairment (CrCl<30 mL/min) or on dialysis

-The absorption of edoxaban is mediated by P-glycoprotein (P-gp). P-gp inhibitors can increase the absorption of edoxaban. Conversely, P-gp inducers can reduce the absorption of edoxaban

No anticoagulation

Case: 46M

Medical history:

GI bleeding s/p right anterior hemicolectomy from infectious CMV colitis

DM-1 on insulin, htn, glaucoma, chronic renal failure

Medications: ASA 80mg Qd, rosuvastatin 10mg Qd, candesartan 8mg Qd, sevalamer, pantoprazole

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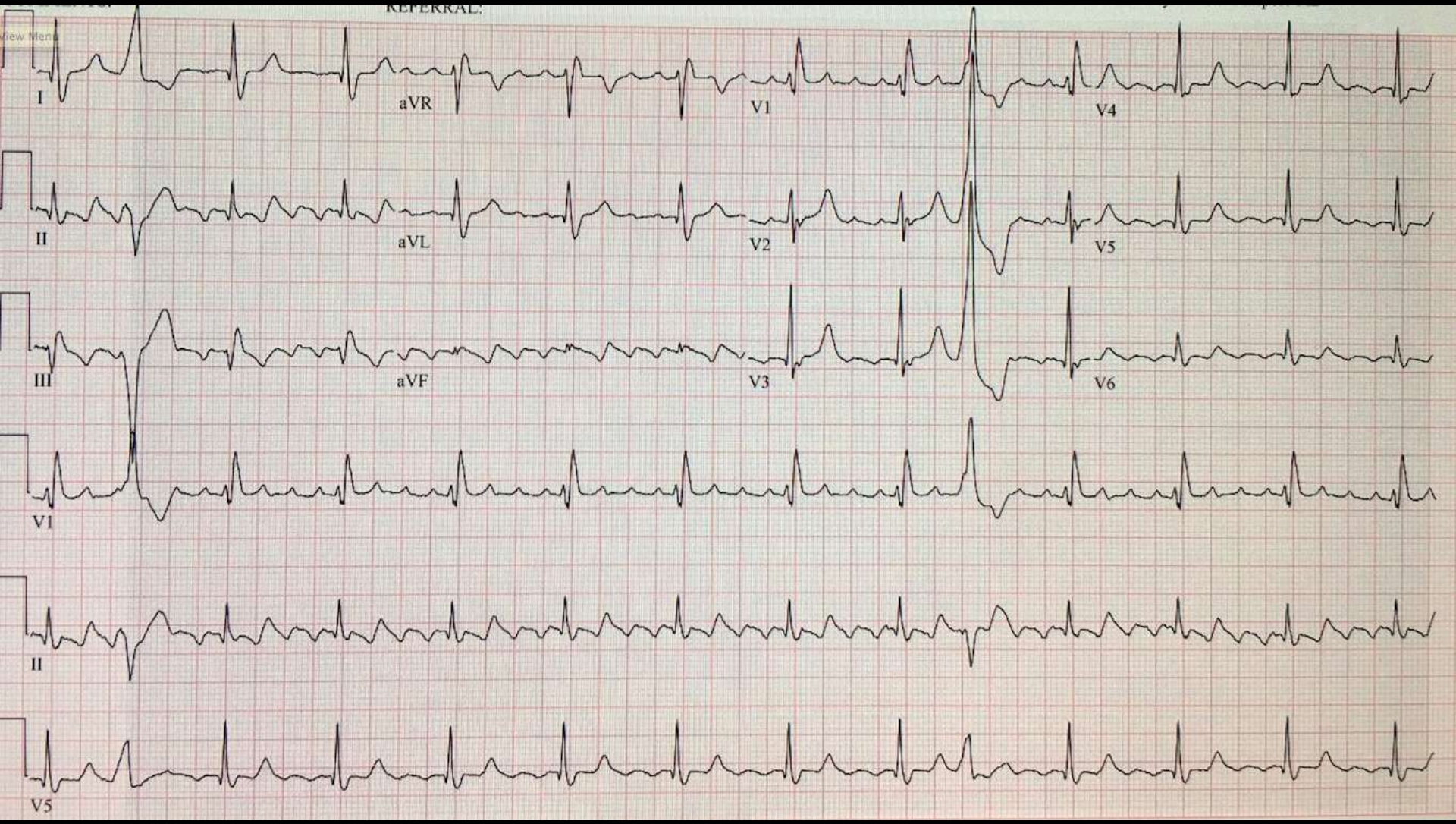
Present history:

Increasing fatigue and dyspnea on exertion over the last month

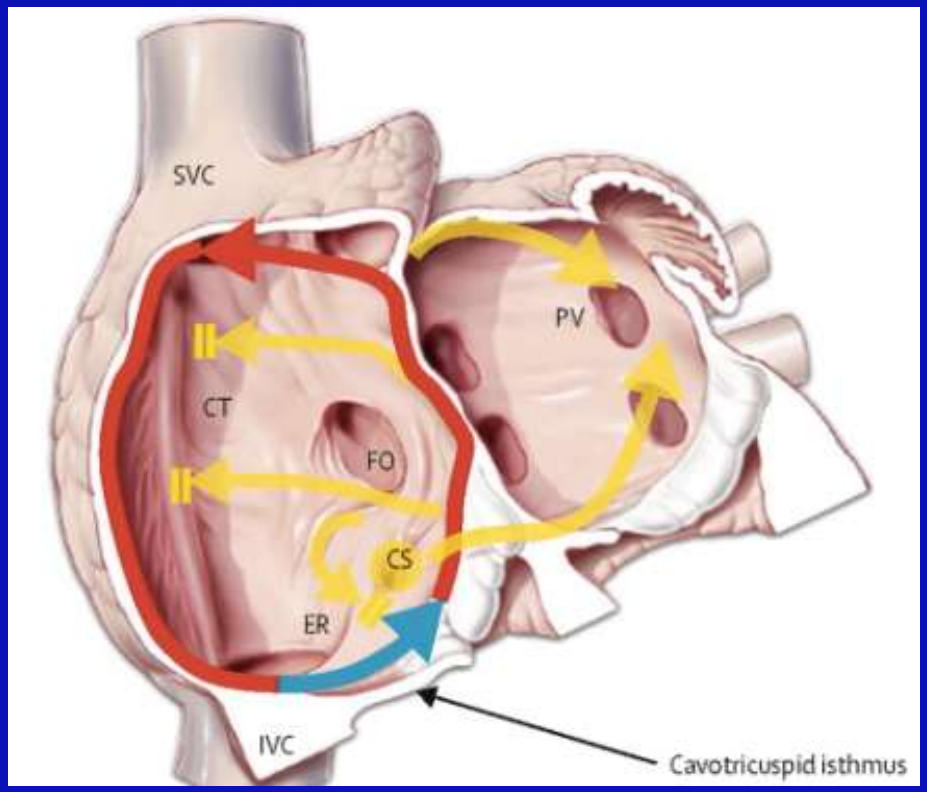
Patient has a high risk of bleeding! What next?

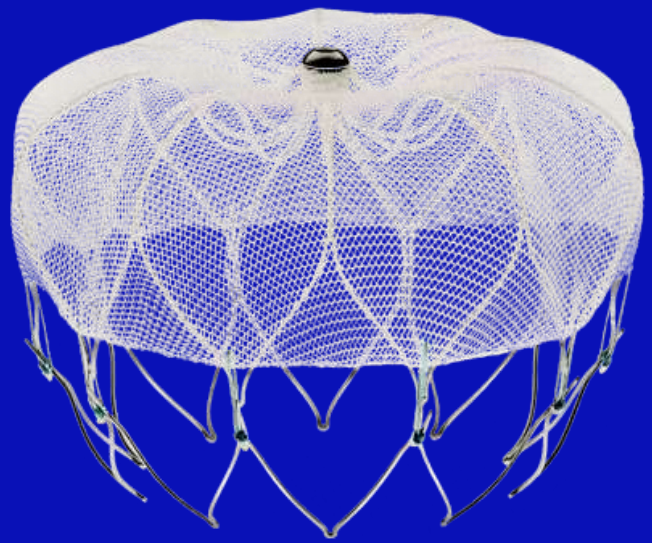

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

Case: 46M

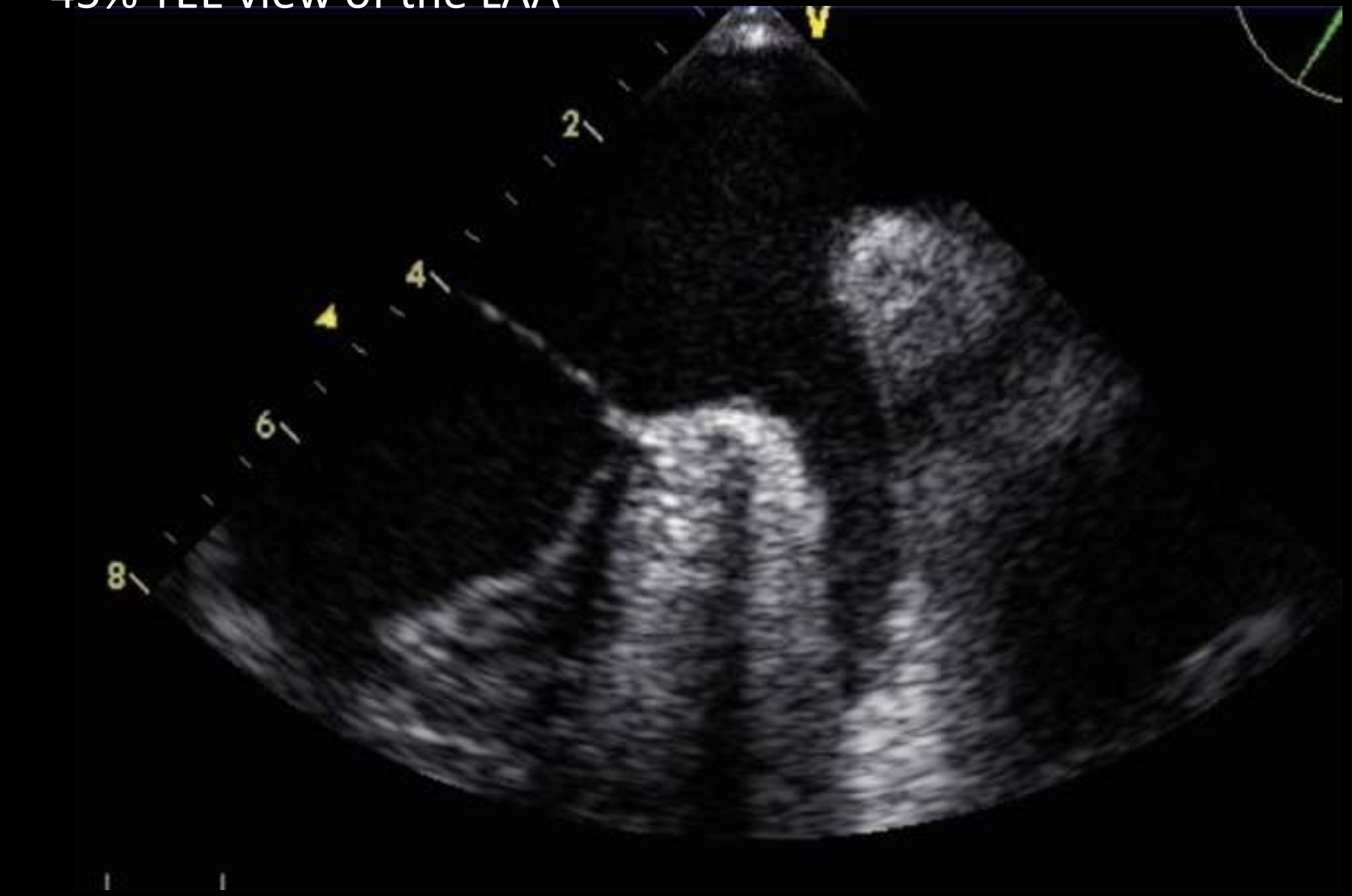
PLAN:

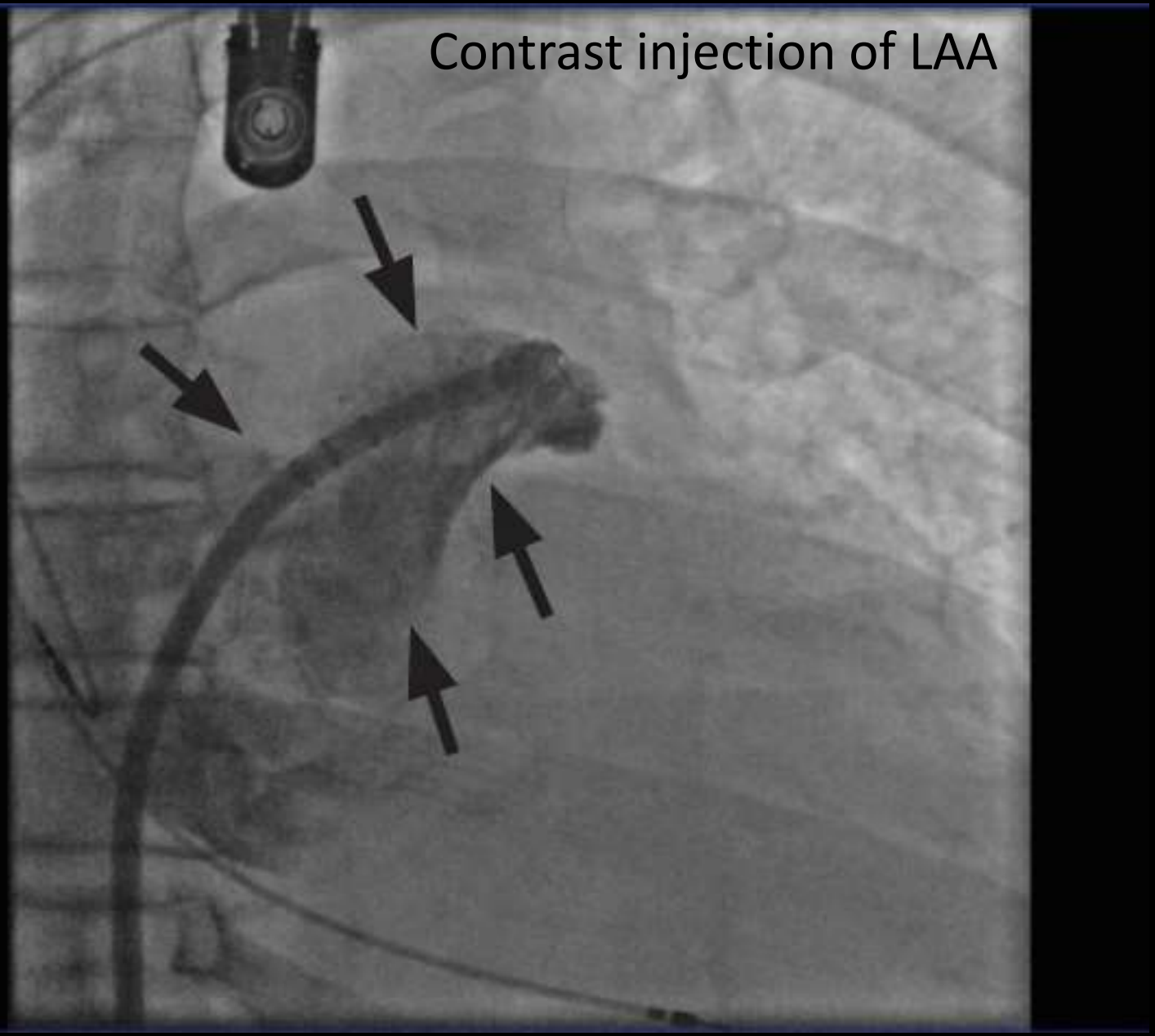
Typical Flutter ablation + Watchman Implant during same procedure

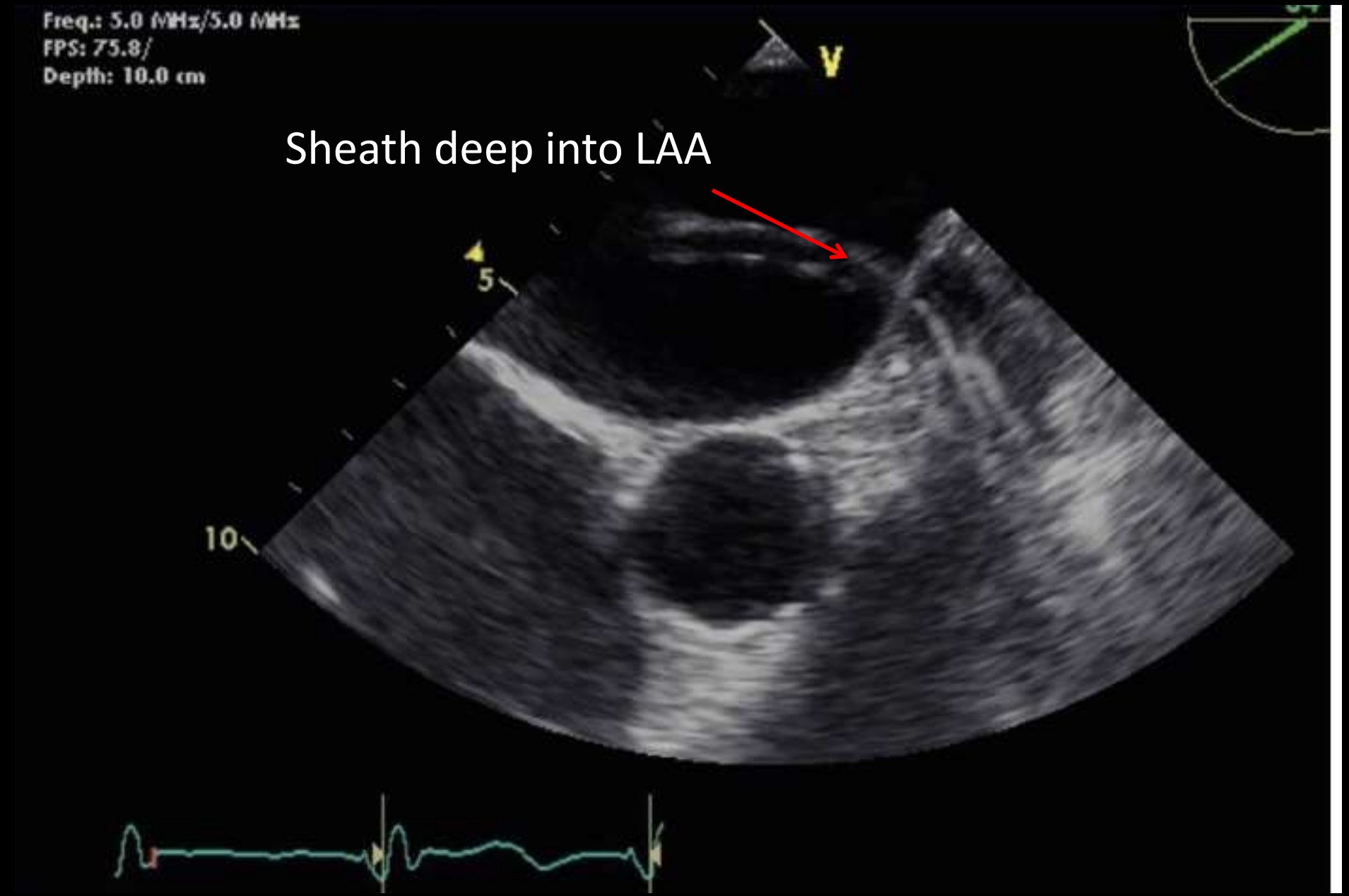


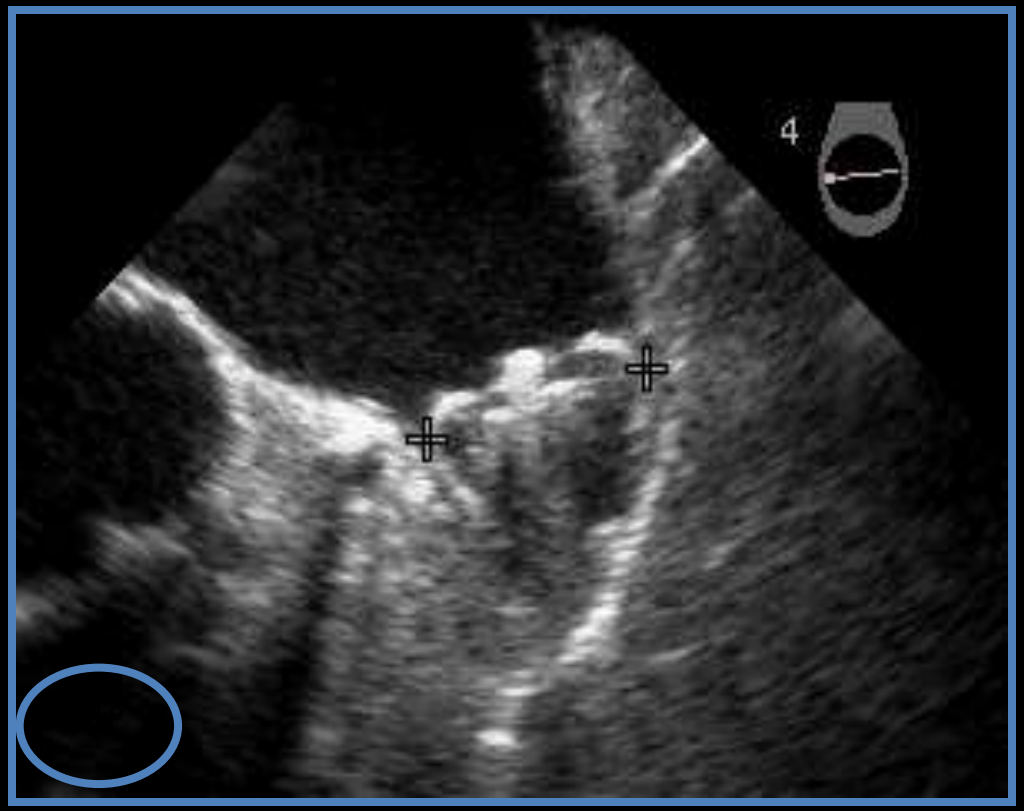


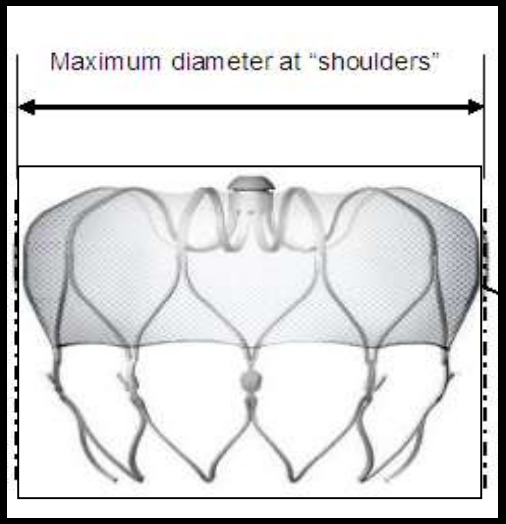
45% TEE view of the LAA




Contrast injection of LAA


Freq.: 5.0 MHz/5.0 MHz
FPS: 75.8/
Depth: 10.0 cm
Sheath deep into LAA
5
10





Device Compression Table

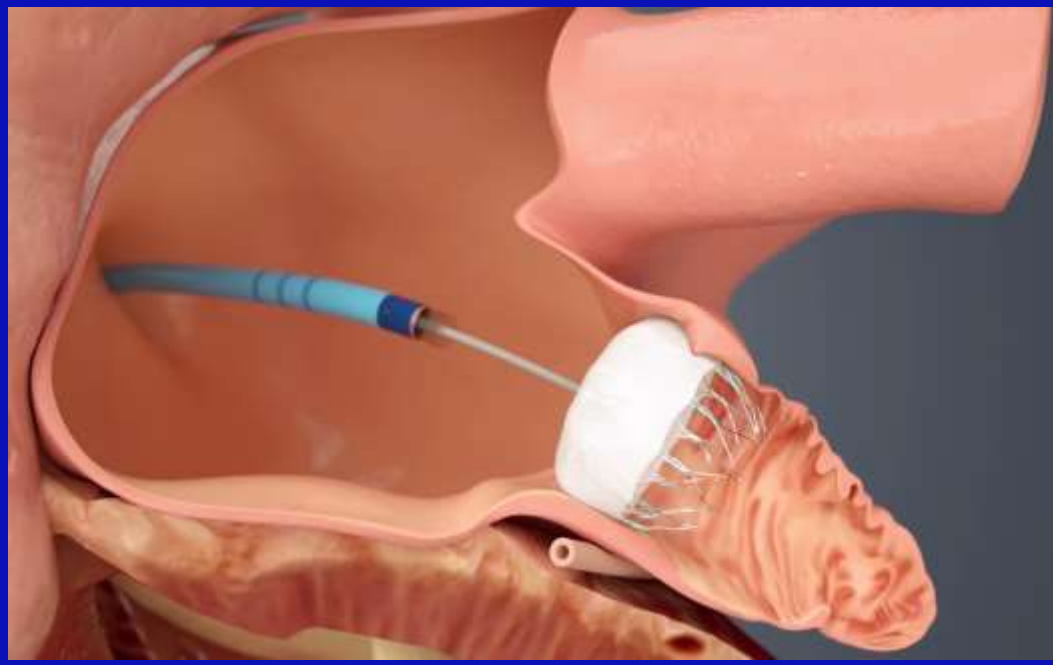
8 – 20% of original device size selected

Device Size *(uncompressed diameter)*	**Maximum (20%)** Compression Measured Diameter*	**Minimum (8%)** Compression Measured Diameter*
21	16.8 mm	19.3 mm
24	19.2 mm	22.1 mm
27	21.6 mm	24.8 mm
30	24.0 mm	27.6 mm
33	26.4 mm	30.4 mm

WATCHMAN™ Left Atrial Appendage Closure (LAAC) Device Procedure

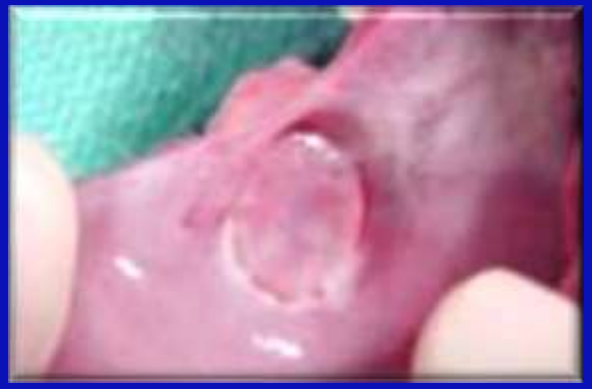
- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite
- Performed by a Team
  - IC/EP or IC&EP, TEE, General Anesthesia, Surgical Back- up, WATCHMAN Clinical Specialist
- Transfemoral Access: Catheter advanced to the LAA via the femoral vein
  (Does not require open heart surgery)

- +- General anesthesia
- 1-2 hour procedure
- 1-2 day hospital stay

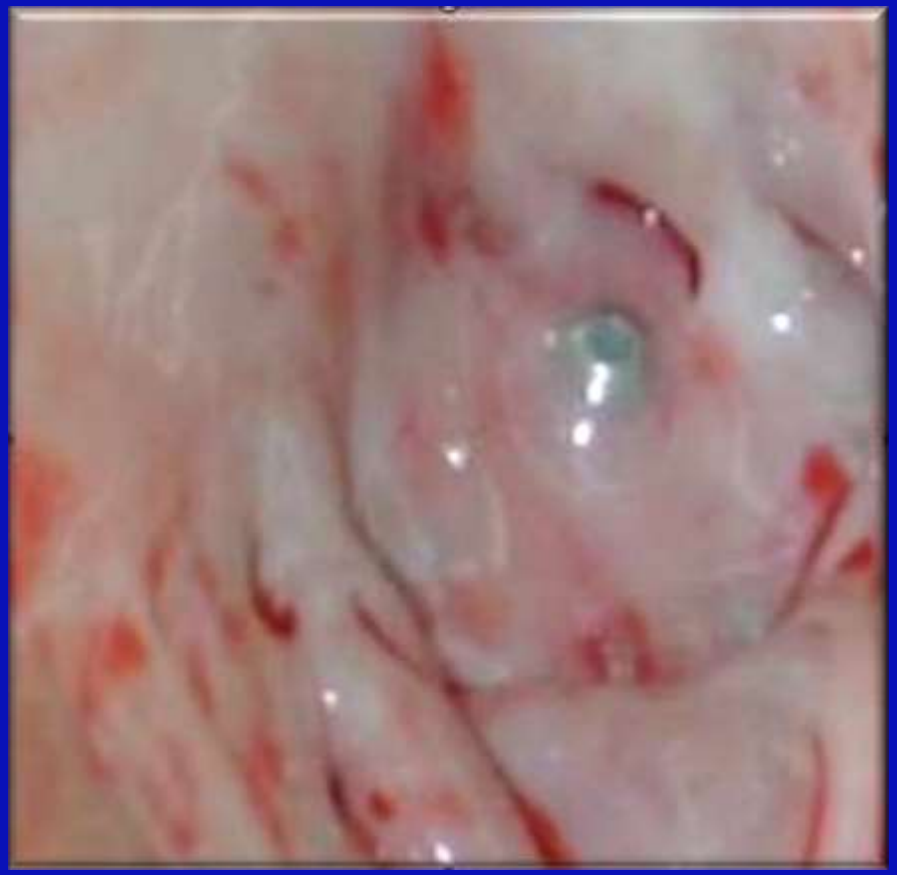


WATCHMAN™ Device Endothelialization

Canine Model – 30 Day



Canine Model – 45 Day



Human Pathology – 9 Months Post-implant
(Non-device related death)

Images on file at Boston Scientific Corporation.
Results in animal models may not necessarily be indicative of clinical outcomes.

Watchman Warfarin

Table 2. Intention-to-Treat Primary Efficacy and Safety Outcomes According to Treatment Group by Bayesian Model

Event	Device Group (n = 463)		Warfarin Group (n = 244)		Device/Warfarin Rate Ratio (95% Credible Interval)	Posterior Probabilities, %	
	Events/Patient-Years	Observed Rate[a]	Events/Patient-Years	Observed Rate[a]		Noninferiority	Superiority
Primary efficacy end point[b]	39/1720.2	2.3 (1.7-3.2)	34/900.8	3.8 (2.5-4.9)	0.60 (0.41-1.05)	>99	96
Stroke	26/1720.7	1.5 (1.0-2.2)	20/900.9	2.2 (1.3-3.1)	0.68 (0.42-1.37)	>99	83
Ischemic	24/1720.8	1.4 (0.9-2.1)	10/904.2	1.1 (0.5-1.7)	1.26 (0.72-3.28)	78	15
Hemorrhagic	3/1774.2	0.2 (0.0-0.4)	10/916.2	1.1 (0.5-1.8)	0.15 (0.03-0.49)	>99	99
Disabling[c]	8/1771.3	0.5 (0.2-0.8)	11/912.7	1.2 (0.6-1.9)	0.37 (0.15-1.00)	>99	98
Nondisabling[c]	18/1723.7	1.0 (0.7-1.7)	9/907.7	1.0 (0.4-1.7)	1.05 (0.54-2.80)	89	34
Systemic embolization	3/1773.6	0.2 (0.0-0.4)	0/919.5	0	NA		
Cardiovascular or unexplained death	17/1774.3	1.0 (0.6-1.5)	22/919.4	2.4 (1.4-3.4)	0.40 (0.23-0.82)	>99	99
Primary safety end point[d]	60/1666.2	3.6 (2.8-4.6)	27/878.2	3.1 (2.0-4.3)	1.17 (0.78-1.95)	98	20

- At 5 years: 40% fewer events with the Watchman
  - 85% fewer hemorrhagic strokes
  - 65% fewer cardiovascular deaths
- OR of 1.26 for ischemic stroke favouring warfarin
- Secondary endpoint: all-cause mortality: 34% fewer deaths in Watchman compared to warfarin.

Circulation 2013; 127: 720-729

TABLE 1. COMPARISON OF OUTCOMES IN DEVICE PATIENTS IN PROTECT AF, CAP, AND PREVAIL				
	Protect AF (%)	**CAP (%)**	**PREVAIL (%)**	***P* Value**
Implant success	90.9	94.3	95.1	.04
All 7 days procedural complications	8.7	4.2	4.5	.004
Pericardial effusion requiring surgery	1.6	0.2	0.4	.03
Pericardiocentesis	2.4	1.2	1.5	.318
Procedure-related stroke	1.1	0	0.7	.02
Device embolization	0.4	0.2	0.7	.368

Reprinted from J Am Col Cardiol., Vol. 61, Holmes DR, et al, Prospective randomized evaluation of the Watchman left atrial appendage closure device in patients with atrial fibrillation vs long-term warfarin therapy, pp. 1–12, 2014, with permission from Elsevier.[19]

TABLE 2. AVERAGE DISCOUNTED LIFETIME COST OF STROKE PREVENTION TREATMENTS IN AF	
Warfarin	$21,429
Dabigatran	$25,760
LAA occlusion	$27,003

Note: Analysis performed from perspective of Ontario Ministry of Health and Long Term Care, the third-party payer for insured health services in Ontario, Canada.

Singh SM, Micieli A, Wijeysundera HC. Economic evaluation of percutaneous left atrial appendage occlusion, dabigatran, and warfarin for stroke prevention in patients with nonvalvular atrial fibrillation. Circulation. 2013;127:2414-2423.

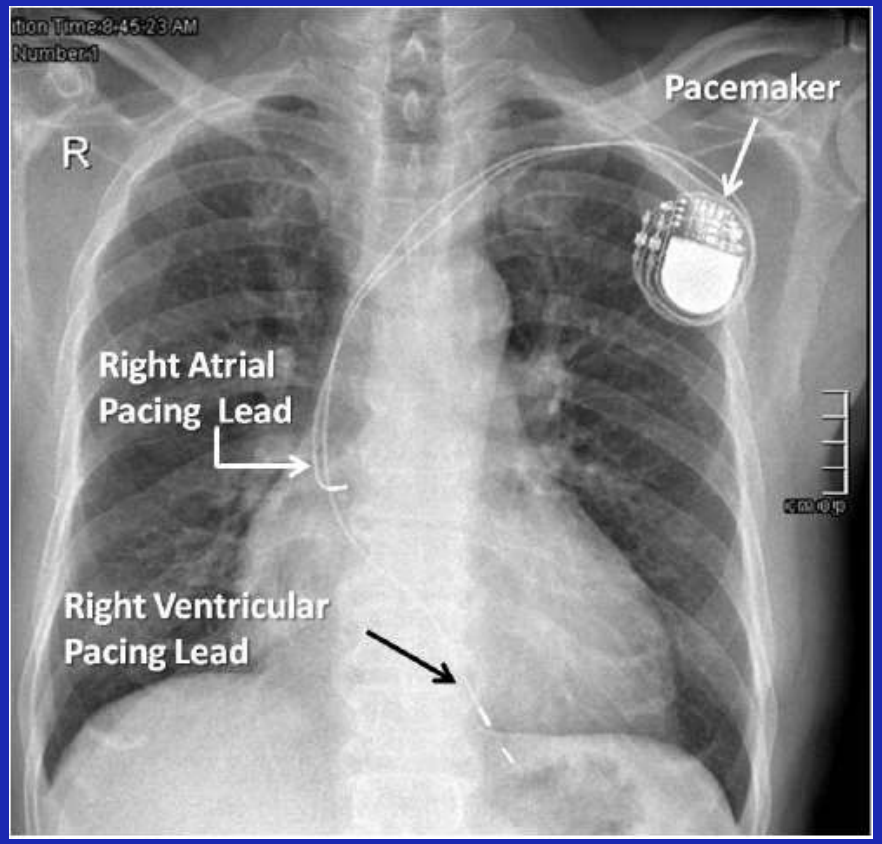
MRI safety

Case

72F presents with intermittent blurry vision and headache associated with alterations in LH/FSH and TSH.

Past medical history: Dual-chamber pacemaker implanted 10 years ago.

You would like to order an MRI of her brain as you suspect a pituitary adenoma, but the patient has a pacemaker.



Can an MRI be performed in a patient with a pacemaker?

The presence of a cardiac device (pacemaker or defibrillator) has long been a contraindication to perform MRIs.
Device companies have been actively ensuring that new wires and devices are ‘MRI compatible’, however many ‘old’ devices are present, or non-MRI devices still implanted


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Assessing the Risks Associated with MRI in Patients with a Pacemaker or Defibrillator

Robert J. Russo, M.D., Ph.D., Heather S. Costa, Ph.D., Patricia D. Silva, M.S., Jeffrey L. Anderson, M.D., Aysha Arshad, M.D., Robert W.W. Biederman, M.D., Noel G. Boyle, M.D., Ph.D., Jennifer V. Frabizzio, M.D., Ulrika Birgersdotter-Green, M.D., Steven L. Higgins, M.D., Rachel Lampert, M.D., Christian E. Machado, M.D., Edward T. Martin, M.D., Andrew L. Rivard, M.D., Jason C. Rubenstein, M.D., Raymond H.M. Schaerf, M.D., Jennifer D. Schwartz, M.D., Dipan J. Shah, M.D., Gery F. Tomassoni, M.D., Gail T. Tominaga, M.D., Allison E. Tonkin, M.D., Seth Uretsky, M.D., and Steven D. Wolff, M.D., Ph.D.

-1000 pacemaker patients and 500 ICD patients.
-No deaths, lead failures, losses of capture, or ventricular arrhythmias occurred
-Minor effects: 6 cases of self-terminating atrial fibrillation/flutter and 6 cases of partial electrical reset.
-Repeat MRI did not increase the number of adverse events.

N Engl J Med 2017;376:755-64

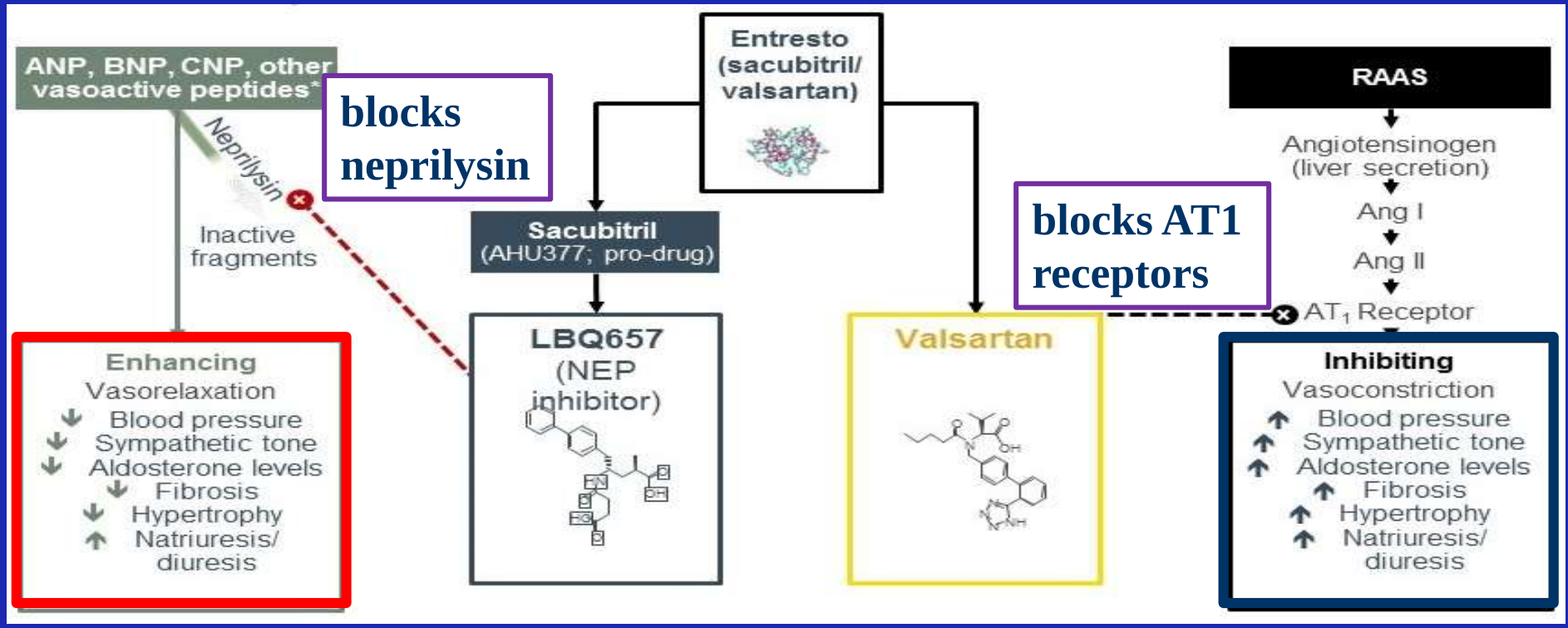
Conclusion:

We should not withhold the MRI from patients with cardiac devices.

Caveat: these MRIs should only be performed in a setting where an electrophysiology service is present, to appropriate program the device before and after the MRI

Heart Failure

1. Entresto (sacubitril/valsartan)



- Paradigm-HF (RCT 2014): entresto 200mg BID vs enalapril 10mg BID
- 27 months follow-up
- Death from CV cause or first hospitalization for HF: 21.8% Entresto vs 26.5% Enalapril (HR 0.8; CI 0.73-0.87).
- Number needed to treat to prevent 1 primary event: 21 compared to usual care

McMurray *et al. N Engl J Med* 2014;371:993–1004

1. Entresto (sacubitril/valsartan).

Table 3. Adverse Events during Randomized Treatment.*

Event	LCZ696 (N=4187)	Enalapril (N=4212)	P Value
	no. (%)		
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<0.001
Symptomatic with systolic blood pressure <90 mm Hg	112 (2.7)	59 (1.4)	<0.001
Elevated serum creatinine			
≥2.5 mg/dl	139 (3.3)	188 (4.5)	0.007
≥3.0 mg/dl	63 (1.5)	83 (2.0)	0.10
Elevated serum potassium			
>5.5 mmol/liter	674 (16.1)	727 (17.3)	0.15
>6.0 mmol/liter	181 (4.3)	236 (5.6)	0.007
Cough	474 (11.3)	601 (14.3)	<0.001
Angioedema†			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	0.19
Use of catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	0.52
Hospitalization without airway compromise	3 (0.1)	1 (<0.1)	0.31
Airway compromise	0	0	—

Safety profile

Overall fewer pts in the Entresto group stopped their study med due to an adverse event (10.7 vs 12.3%, p=0.03) or due to revan impairment (0.7% vs 1.4%, p=0.002)

Indicated for: NYHA class II-IV chronic HF AND those already taking a stable dose of ACEI or ARB, AND LVEF ≤ 35%

McMurray *et al. N Engl J Med* 2014;371:993–1004

2. Ivabridine

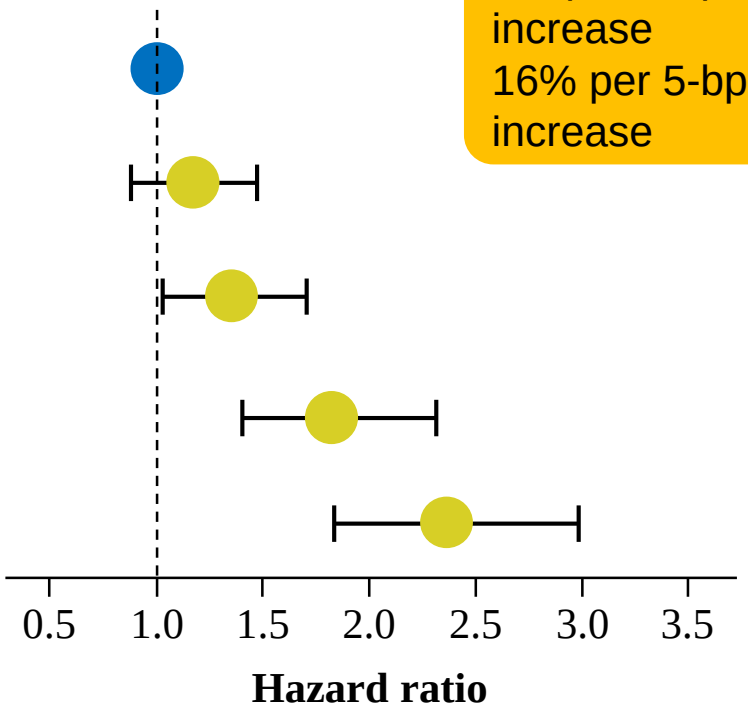
The higher the Heart Rate, the higher the risk of CV mortality and HF hospitalization

CV mortality and HF hospitalization

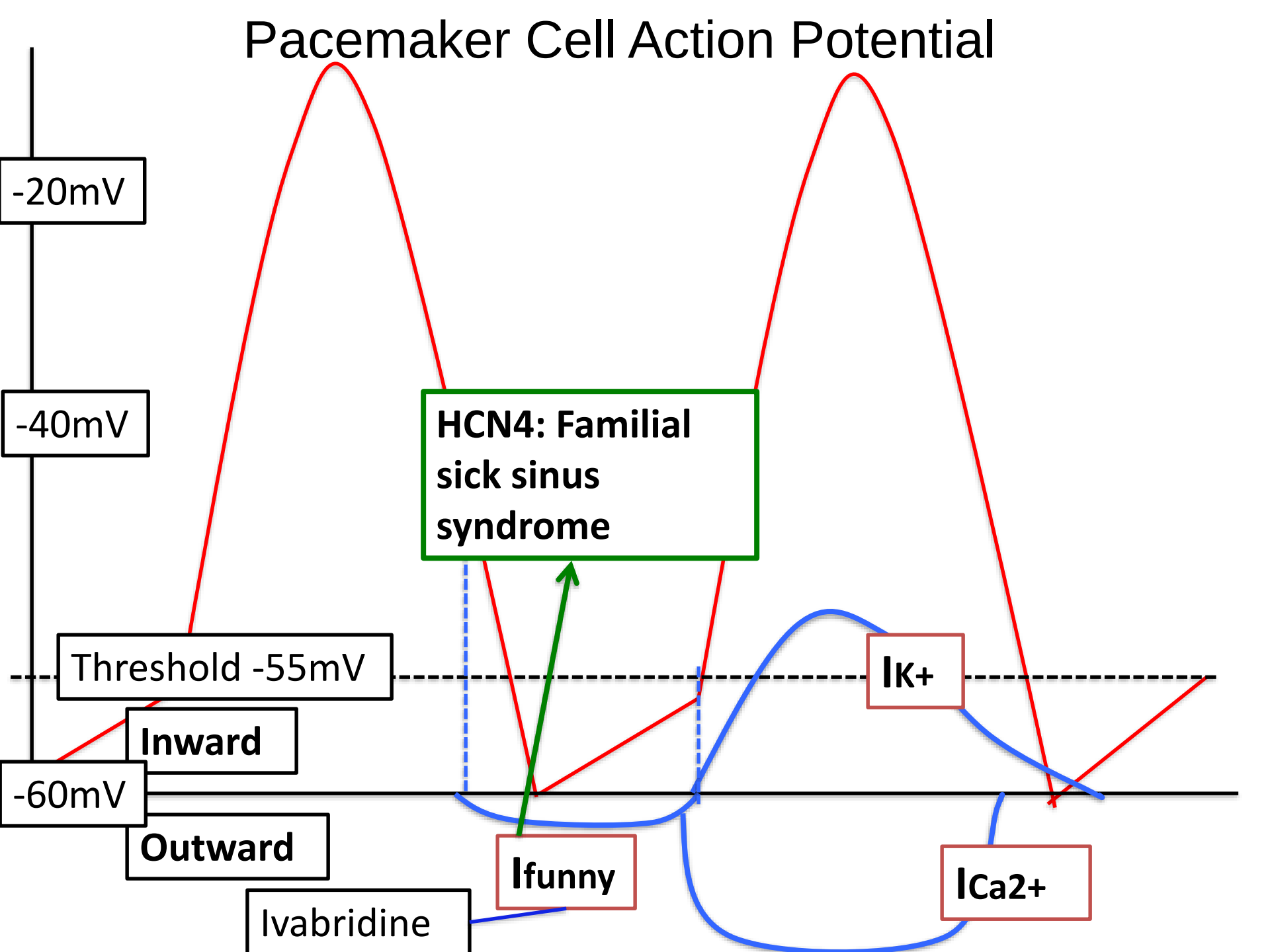
Risk increases by

3% per 1-bpm increase
16% per 5-bpm increase

HR at baseline (bpm)	HR
70 – <70	1.00
72 – <75	1.15
75 – <80	1.33
80 – <87	1.80
≥87	2.34



Böhm et al. *Lancet* 2010; 376: 886-94 (Shift placebo group).


Pacemaker Cell Action Potential
-20mV
-40mV
-60mV
HCN4: Familial sick sinus syndrome
Threshold -55mV
Inward
Outward
Ifunny
Ivabridine
IK+
ICa2+

Ivabradine significantly reduced mortality

The higher the HR at baseline, the greater the benefits

- Patients with baseline HR ≥ 70 and ≥ 77 bpm

	Significant reduction	
	≥ 70 bpm	**≥ 77 bpm**
Primary endpoints		
CV death or hospital admission for worsening HF	18% (p<0.0001)	25% (p<0.0001)
Mortality endpoints		
All-cause mortality	10% (*p*=0.092)	19% (p=0.0074)
Cardiovascular mortality	9% (*p*=0.128)	19% (p=0.0137)
Death from HF	26% (p=0.014)	39% (p=0.0017)
Other endpoints		
All-cause hospital admission	11% (p=0.003)	18% (p=0.0002)
Any CV hospital admission	15% (p=0.0002)	21% (p<0.0001)
Hospital admission for worsening of HF	26% (p<0.0001)	31% (p<0.0001)

Swedberg et al. *Lancet* 2010; 376: 875-85; Krum & Sindone. *Heart Lung Circ* 2013; 22: s87-8.

Absolute effect (NNT) for prevention of recurrent hospitalizations in HF patients

	Estimated treatment effect*	95% CI	*P* value	NNT
Primary endpoint	0.82	0.75-0.90	< 0.0001	26
Heart failure hospitalizations				
First hospitalization	0.75	0.66-0.84	< 0.0001	27
Recurrent hospitalizations	0.71	0.62-0.82	< 0.0001	14
All-cause hospitalizations				
First hospitalization	0.89	0.83-0.96	0.0036	37
Recurrent hospitalizations	0.83	0.72-0.95	< 0.0001	10

Estimated treatment effects are hazard ratios (calculated using Cox proportional hazards models) for time to rst event analyses and rate ratios for recurrent event analyses (calculated using the negative binomial)

Rogers et al. *Curr Med Res Opin* 2015; 31 (10): 1903–9.

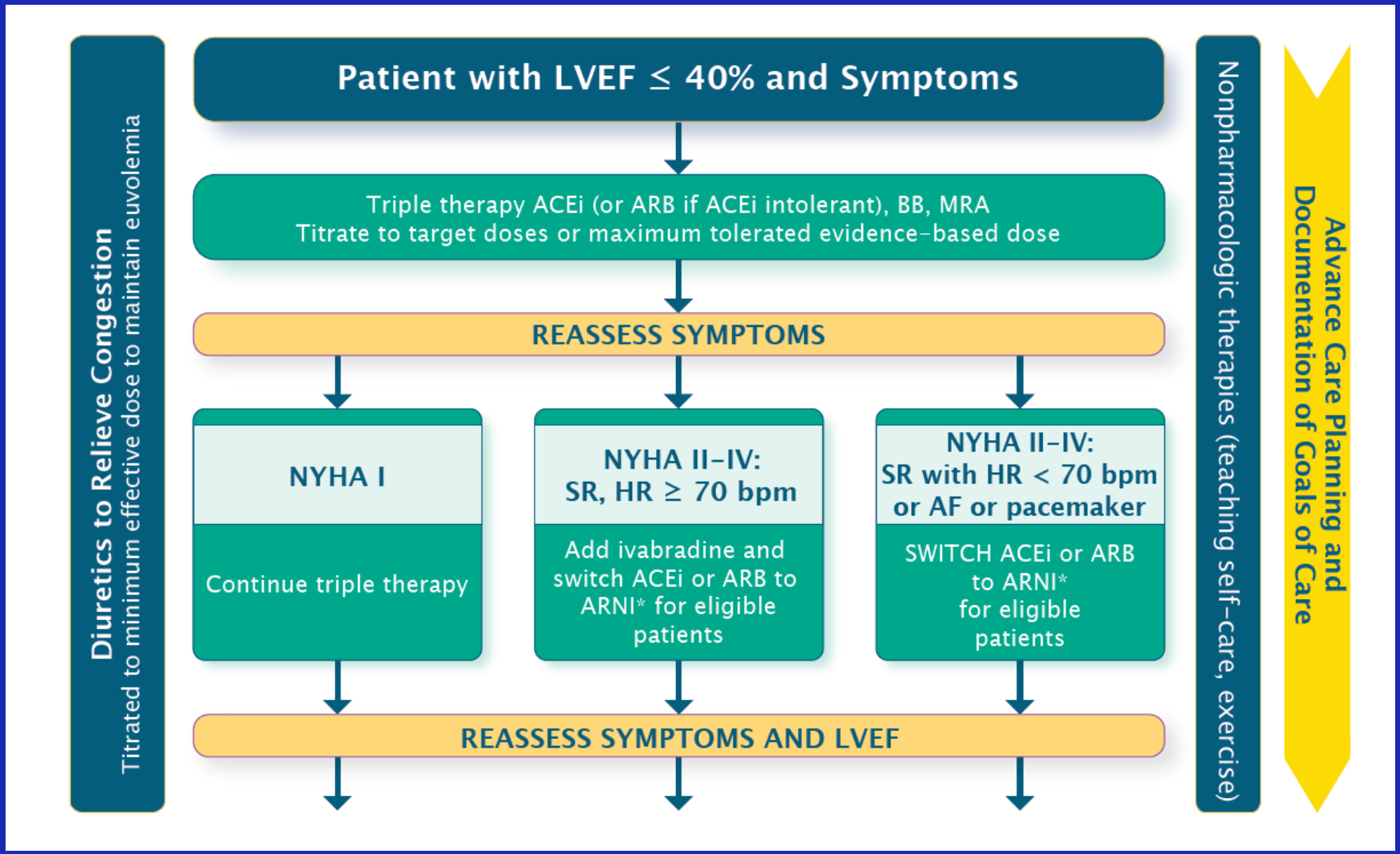
Ikf inhibitor (Ivabridine) and ARNi (Entresto)

Characteristic	Ivabradine (Ikf inhibitor)	Sacubitril/Valsartan (ARNi)
Usage	Add On	Switch from ACE/ARB
Care setting	Chronic HFrEF	Chronic HFrEF
Contraindications	Strong CYP 3A4 inhibitor*	ACE inhibitors
Major indication	NSR, Elevated HR	HFrEF on ACE/ARB
Low BP	**No effect**	**Major limitation**
K+, Renal function	**No effect**	**Less**
Low HR	Major limitation	No effect
Use if AF?	No	Yes
Duration titration	**2 weeks**	**6-12 weeks**
Follow up?	12 lead ECG	Renal function, 'Lytes

*Or moderate CYP3A4 inhibitors with HR-reducing properties, e.g. Verapamil or diltiazem

Ezekowitz JA, et al. Can J Cardiol 2017;33:1342-33;

Therapeutic Approach to Patients With HFrEF



NODE-1: Simple Nasal Spray May Short-circuit Acute PSVT

Patrice Wendling

May 16, 2017

FOR AVNRT AND AVRT

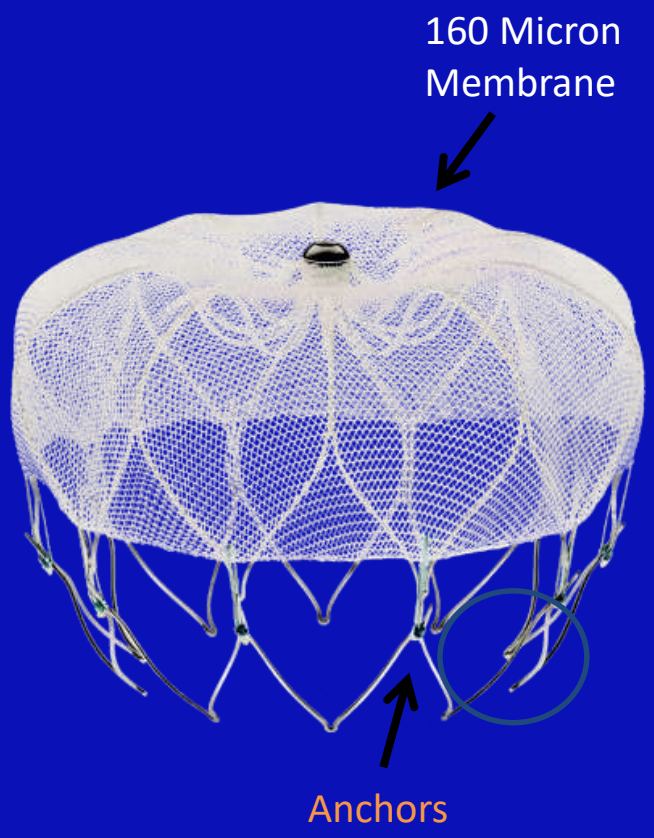
CHICAGO, IL — A nasal spray containing the calcium-channel blocker etripamil could allow patients to convert acute paroxysmal supraventricular tachycardia (PSVT) outside the hospital, phase 2 data from the Intranasal Etripamil for the Conversion of PSVT to Sinus Rhythm (NODE-1) trial suggest[1].

Patients with PSVT awaiting ablation treated with 35-, 70-, 105-, and 140-mg intranasal etripamil returned to normal sinus rhythm in a median of 2 to 3 minutes, with 65%, 87%, 75%, and 95%, respectively, converting within 15 minutes compared with 35% given placebo ($P<0.05$ for the 70-, 105-, and 140-mg doses).

Conclusions

1. Primary prevention: no effect with ASA in moderate CV risk populations
2. Athlete screening: differing protocols based on type of competition, and age.
3. DOACs: Know the dosing and interactions with Edoxaban
4. Consider left atrial appendage occlusion in patients who have high risk of stroke but also have a high risk of bleeding.
5. New drugs in heart Failure: Entresto and Ivabridine

WATCHMAN™ LAAC Closure Device



Minimally Invasive, Local Solution
- Available sizes: 21, 24, 27, 30, 33 mm diameter

Intra-LAA design
- Avoids contact with left atrial wall to help prevent complications

Nitinol Frame
- Conforms to unique anatomy of the LAA to reduce embolization risk
- 10 active fixation anchors - designed to engage tissue for stability

Proximal Face
- Minimizes surface area facing the left atrium to reduce post-implant thrombus formation
- 160 micron membrane PET cap designed to block emboli and promote healing

Warfarin Cessation
- 92% after 45 days, >99% after 12 months[1]
- 95% implant success rate[1]

1. Holmes, DR et al. JACC 2014; Vol. 64, No. 1