2021 Hot Topics in Cardiology

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Disclosure

Speaker has no conflict of interest

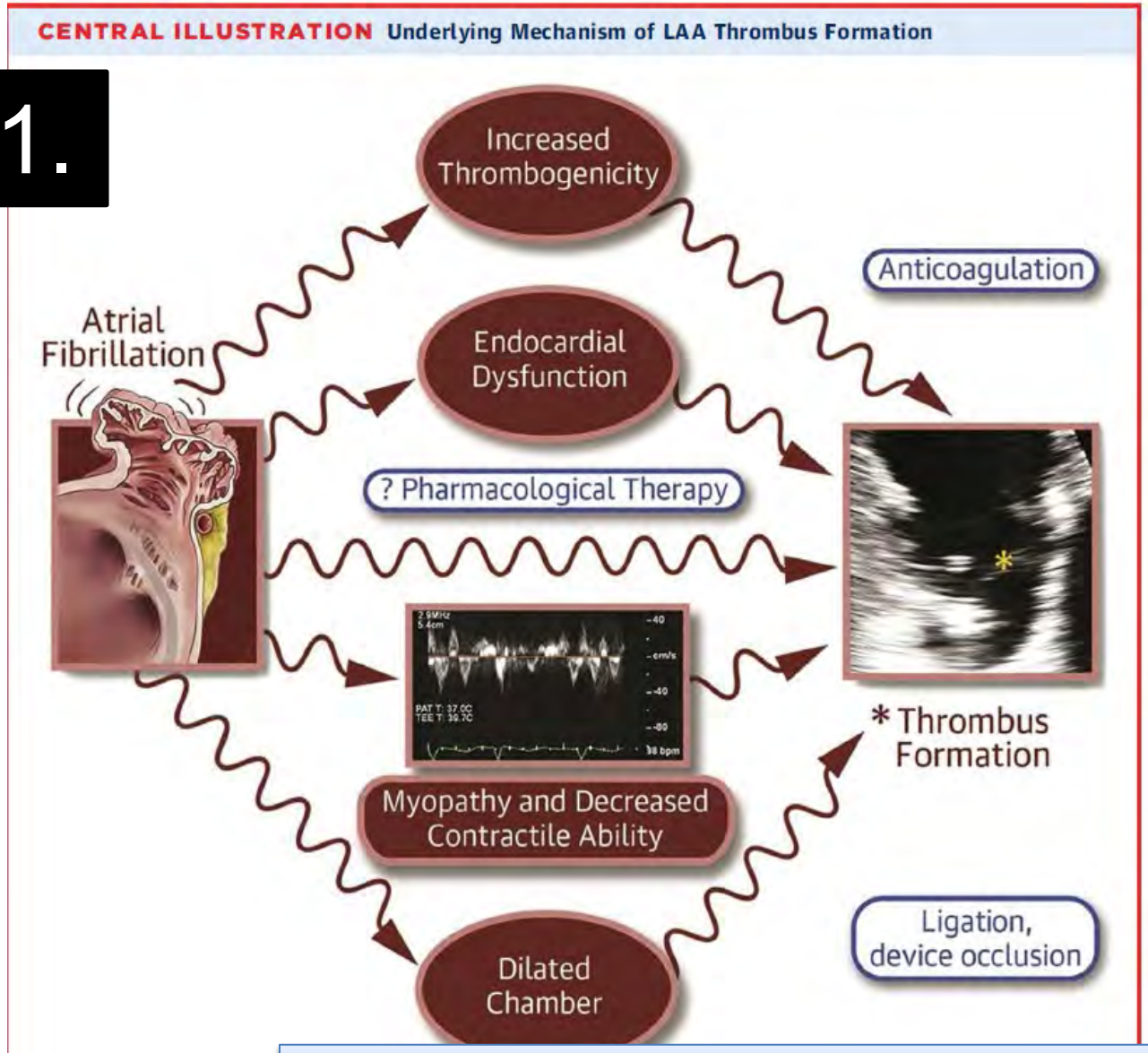
Except bad jokes…

Objectives

- Update your knowledge on several key areas in cardiology
- Reinforce older knowledge
- Learn about upcoming new technologies in cardiology

1. Does closing the left atrial appendage at time of cardiac surgery reduce the risk of stroke in patients with atrial fibrillation?
2. Endocarditis prophylaxis in patients undergoing dental procedures
3. Should we proceed to surgery for asymptomatic patients with severe aortic stenosis?
4. Aspirin 81mg vs 325mg
5. Is caffeine really that bad for our cardiovascular health?
6. Updates in pacing: a look to the future

1.

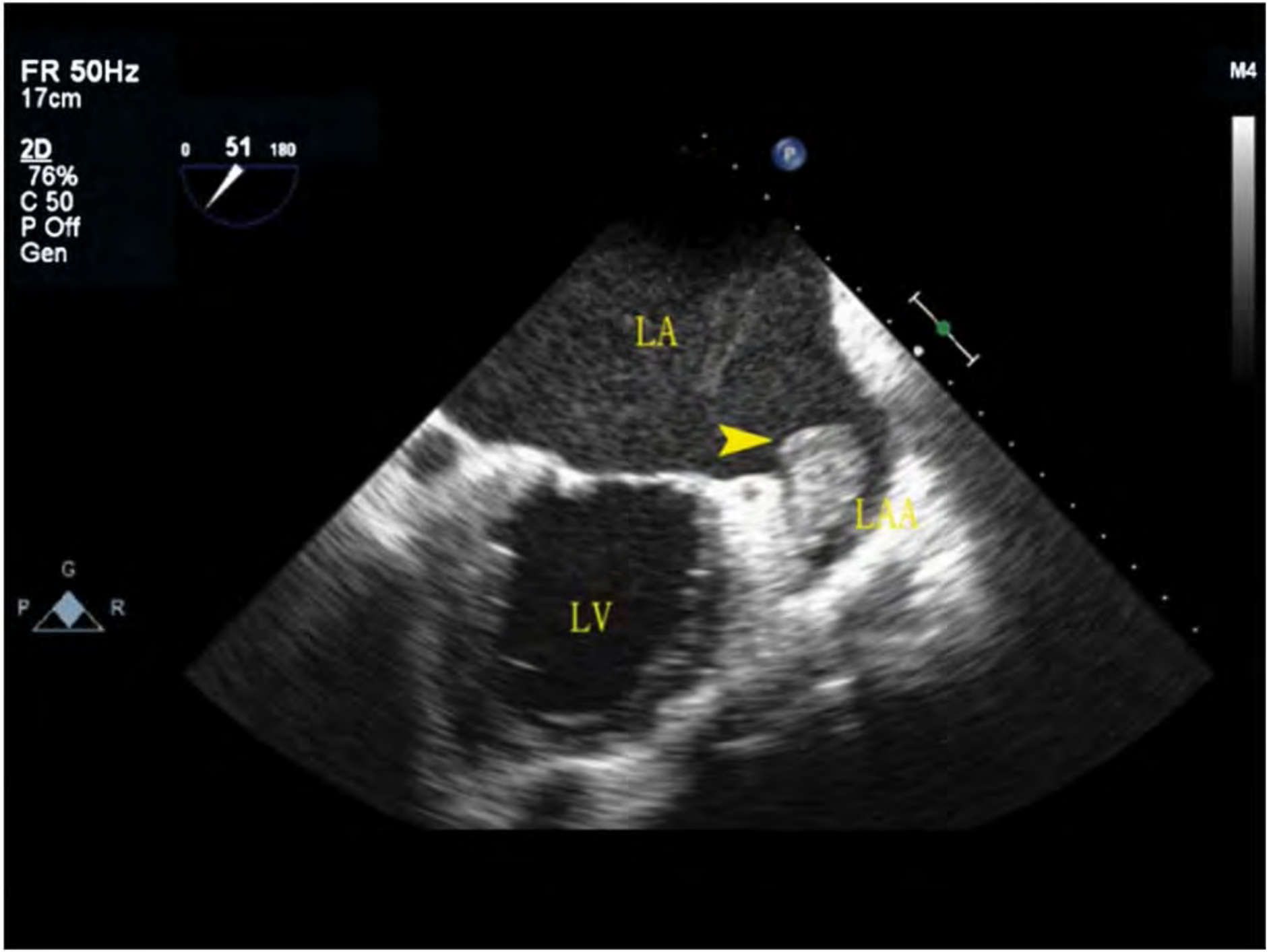


The left atrial appendage (LAA) is the primary source of thromboembolism in patients with atrial fibrillation.

AF causes atrial dilatation, scarring, endocardial dysfunction and low emptying velocity

When patients with AF undergo cardiac surgery, LAA occlusion is sometimes performed with limited evidence

Naksuk, N. et al. J Am Coll Cardiol EP. 2016;2(4):403-12.


FR 50Hz
17cm
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76%
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1.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Left Atrial Appendage Occlusion during Cardiac Surgery to Prevent Stroke

R.P. Whitlock, E.P. Belley-Cote, D. Paparella, J.S. Healey, K. Brady, M. Sharma, W. Reents, P. Budera, A.J. Baddour, P. Fila, P.J. Devereaux, A. Bogachev-Prokophiev, A. Boening, K.H.T. Teoh, G.I. Tagarakis, M.S. Slaughter, A.G. Royse, S. McGuinness, M. Alings, P.P. Punjabi, C.D. Mazer, R.J. Folkeringa, A. Colli, Á. Avezum, J. Nakamya, K. Balasubramanian, J. Vincent, P. Voisine, A. Lamy, S. Yusuf, and S.J. Connolly, for the LAAOS III Investigators*

ABSTRACT

LAAOS III; Peer-reviewed funding sources
Canadian-led trial out of McMaster/PHRI

In addition to anticoagulation, does concomitant occlusion of the LAA prevent ischemic stroke or systemic embolism in patients who continued to receive usual care, including anticoagulation?

Currently, surgical LAA occlusion at time of cardiac surgery is a class IIb indication

Inclusions:

1. ≥ 18 years old scheduled for a cardiac surgery with cardiopulmonary bypass
2. history of AF (CHA_2DS_2 VASc ≥ 2)

Exclusions:

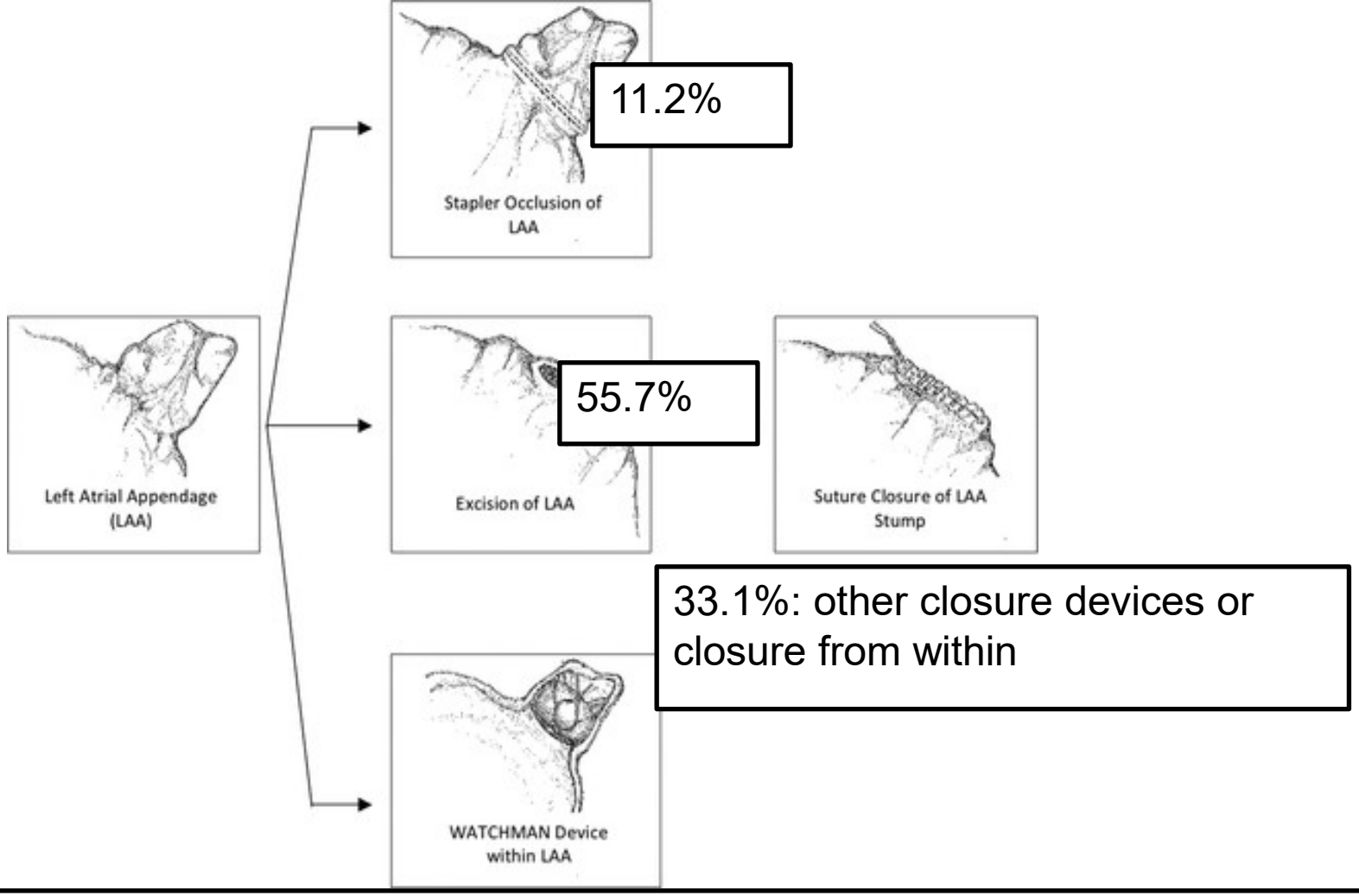
Off-pump surgery
Mechanical valve implantation
Heart transplant surgery
Congenital heart disease surgery
Isolated LVAD implant
Those with prior surgery involving opening the pericardium
Prior LAA closure device

1:1 randomization
Patients, trial personnel, clinicians caring for the patients, were unaware of the trial group assignments

Hypothesis: risk of stroke or systemic embolism would be lower with surgical occlusion compared to no occlusion assuming mean chads-vasc 2.3

Estimated sample size of 4700 patients, median follow up 4 years for 80% power to detect a 25% RRR

LAAOS III



This study strongly encouraged amputation and primary closure.

Stapler and closure devices were allowed. NO percutaneous closure or purse-string closure

Intra-op TEE was recommended

Whitlock et al Circulation 2009

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline, Antithrombotic Therapy, and Surgical Treatments.*

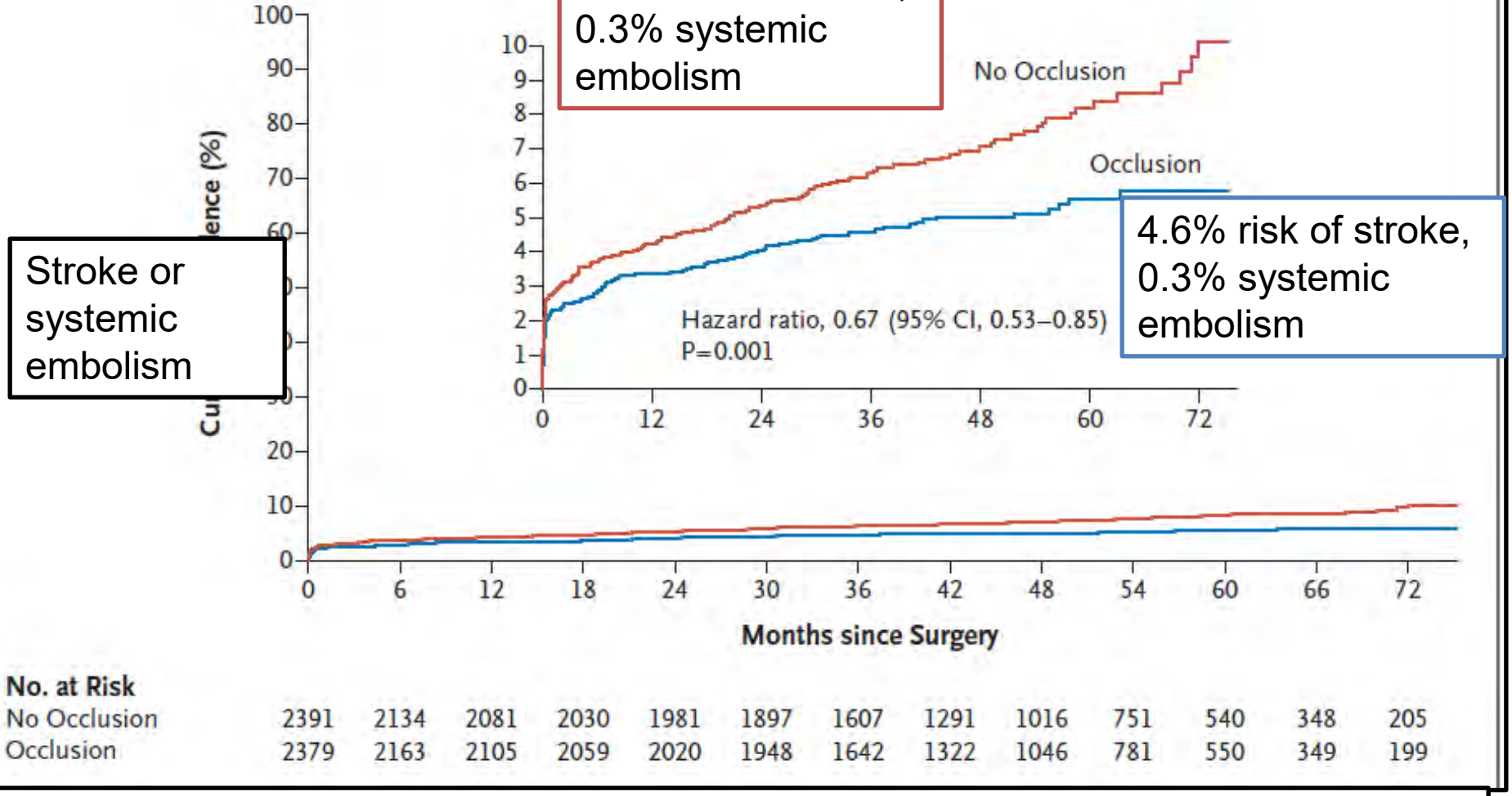
Variable	Occlusion (N=2379)	No Occlusion (N=2391)
Participants		
Age — yr	71.3±8.4	71.1±8.3
Male sex — no. (%)	1617 (68.0)	1601 (67.0)
Type of atrial fibrillation — no. (%)		
Permanent	692 (29.1)	707 (29.6)
Persistent	577 (24.3)	508 (21.3)
Paroxysmal	1110 (46.7)	1176 (49.2)
Medical history — no. (%)		
Hypertension	1960 (82.4)	1941 (81.2)
CHA_2DS_2-VASc score†		
Mean	4.2±1.5	4.2±1.5
Median (interquartile range)	4 (3–5)	4 (3–5)

6 **Table S1: Anticoagulation during follow-up.**

	Left Atrial Appendage Occlusion			No Left Atrial Appendage Occlusion		
	Any anticoagulation	Vitamin K antagonist	Direct oral anticoagulant	Any anticoagulation	Vitamin K antagonist	Direct oral anticoagulant
Discharge	83.4%	64.8%	18.6%	81.0%	62.6%	18.4%
One Year	79.6%	44.6%	35.0%	78.9%	43.2%	35.6%
Two Years	77.1%	39.2%	37.9%	77.7%	39.7%	38.0%
Three Years	75.3%	38.3%	37.0%	78.2%	39.4%	38.8%

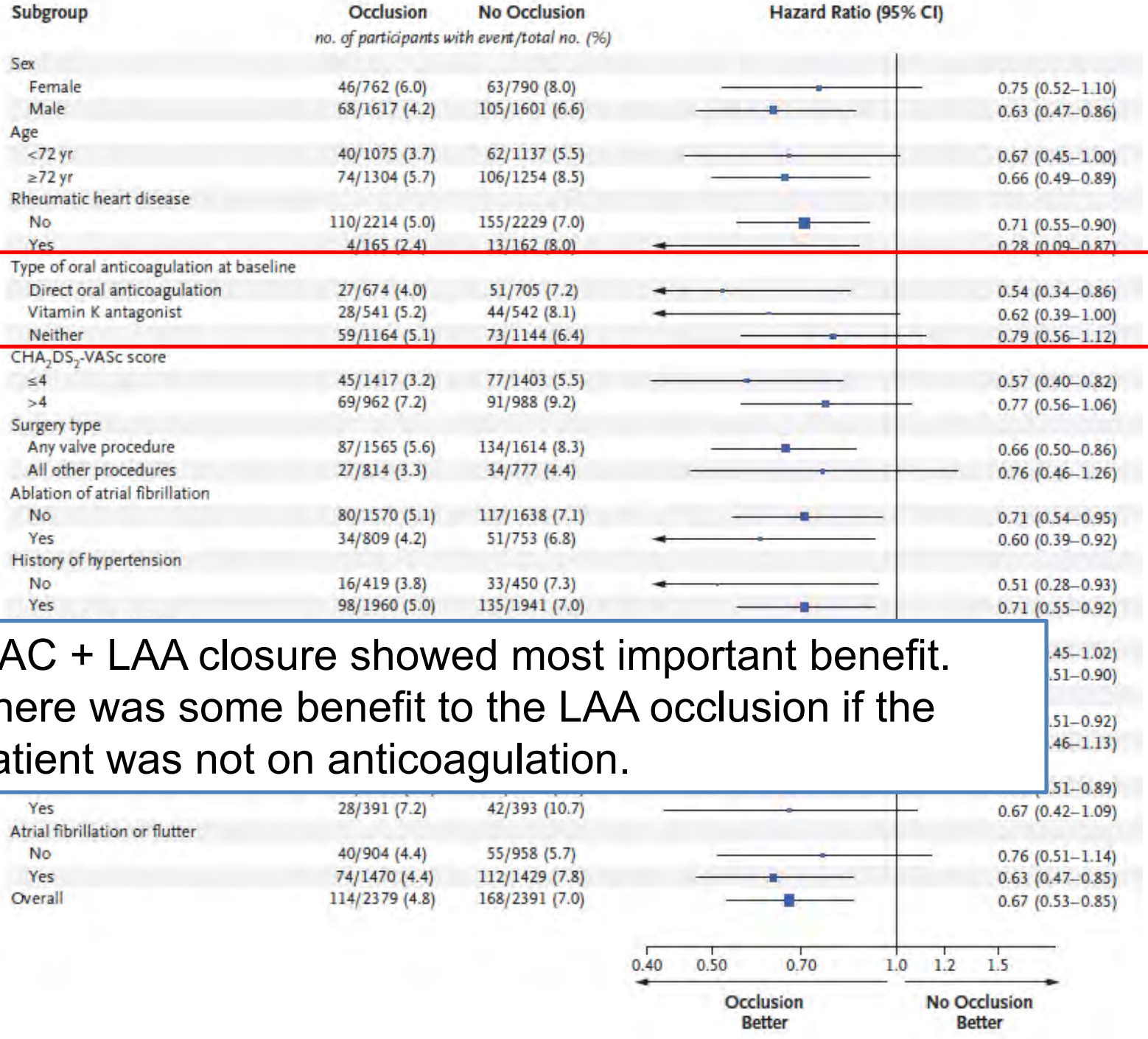
LAAOS III

6.9% risk of stroke, 0.3% systemic embolism



These results were consistent with the per-protocol, as-treated, and intention-to-treat analyses, and with that of the analysis that considered death as a competing risk.

NNT = 37 to prevent 1 stroke over a 5 year period



OAC + LAA closure showed most important benefit. There was some benefit to the LAA occlusion if the patient was not on anticoagulation.

Messages

1. These results support the use of surgical LAA **occlusion as an adjunct to long-term anticoagulation** for patients undergoing cardiac surgery for another indication who have AF and a CHA_2DS_2-Vasc risk score of at least 2.

2. These results do not apply to endovascular devices (Amplatz/Watchman): the benefit from these devices will come from the prevention of major bleeding…

3. This trial **did not compare LAA occlusion with oral anticoagulation**

4. This study will likely change guidelines. Currently surgical occlusion at time of cardiac surgery is a class IIb indication

2. Infective Endocarditis (IE) Prophylaxis in 2021

Minor changes to the 2007 guidelines for the prevention of viridans group streptococcal infective endocarditis:

i) no more clindamycin
ii) doxycycline is now another option for those allergic to penicillin

Otherwise the type of high-risk cardiac patients requiring antibiotic prophylaxis remains the same.

Circulation. 2021;143:e963–e978

Endocarditis Prophylaxis in 2021

IE is more likely to develop from routine activities: chewing food, brushing teeth etc. Therefore, antibiotic prophylaxis is suggested for patients with the highest risk of an adverse outcome from IE:

Includes pts with percutaneous aortic valve replacements pts! (TAVR)

1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts. Mortality rate: >20% (vs <5% in pts with native valve IE)
2. Prosthetic material used for heart valve repair, such as annuloplasty rings, chords or clips.
3. Previous IE.
4. Unrepaired cyanotic congenital heart defect (birth defects with oxygen levels lower than normal) or repaired congenital heart defect, with residual shunts or valvular regurgitation at the site adjacent to the site of a prosthetic patch or prosthetic device.
5. Cardiac transplant with valve regurgitation due to a structurally abnormal valve.

Prophylaxis NOT recommended for complete septal closure devices, pacemakers/ICDs, peripheral vascular grafts including those used for hemodialysis, coronary or other vascular stens, IVC filters because infections are rare, and most are caused by staphylococci.

Endocarditis Prophylaxis in 2021

2021 AHA statement – Table 5[1]

Situation	Agent	Adults	Children
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin	2 g IM or IV	50 mg/kg IM or IV
	OR cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillin or ampicillin—oral	Cephalexin*	2 g	50 mg/kg
	OR azithromycin or clarithromycin	500 mg	15 mg/kg
	OR doxycycline	100 mg	<45 kg, 4.4mg/kg >45 kg, 100 mg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone†	1 g IM or IV	50 mg/kg IM or IV

3.

10.1161/CIRCULATIONAHA.121.057639

_A_ortic _V_alve Repl_A_cemen_T_ versus Conservative Treatment in _A_symptomatic Seve_R_e Aortic Stenosis: The AVATAR Trial

Running Title: *Banovic et al.; Intervention in asymptomatic aortic stenosis*

Current Recommendations: watchful waiting and delaying aortic valve replacement until the onset of aortic stenosis-related symptoms or left ventricular dysfunction (decreased EF).

Is early aortic valve replacement beneficial at preventing adverse outcomes in patients who have severe aortic stenosis, but who are asymptomatic?

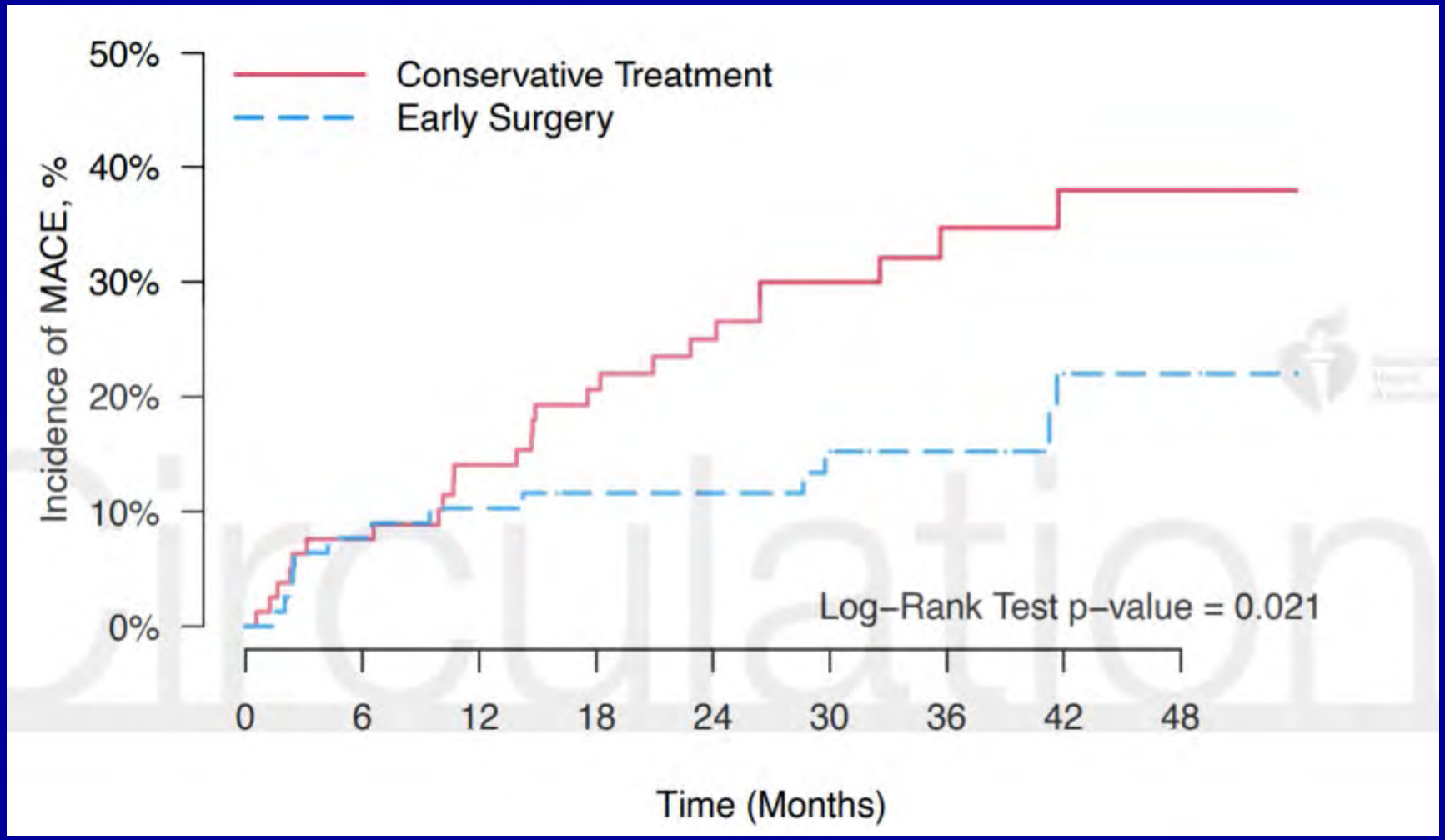
Asymptomatic severe Aortic Stenosis:
-asymptomatic status confirmed by exercise testing
-Mortality risk score (STS-PROM) < 8%

Early AVR Surgery
n=78

Conservative therapy
n=79

Followed for 32 months
Mean age 67, 43% female, 23% diabetic

Primary outcome: composite of all-cause death, heart failure, acute myocardial infarction or stroke



30-day mortality was not significant, however KM curves separate after 1 year where primary outcome becomes statistically significant

Early Surgery | Conservative

Table 3. Primary and secondary outcomes.

Primary outcome: Time to first MACE			
Outcome	Early surgery group 3-Year KM estimate (%)	Conservative treatment group 3-Year KM estimate (%)	Hazard Ratio [95% CI]
Primary endpoint	15.22%	34.70%	0.46 [0.23, 0.90]
Time-to-Event secondary outcomes			
HF hospitalization	9.54%	20.11%	0.32 [0.08, 1.19]
All cause death rate (median + IQR)	4.01%	12.94%	0.56 [0.24, 1.27]
SAE	17.31%	27.50%	0.57 [0.28, 1.12]
Cardiovascular death	9.54%	9.09%	1.02 [0.40, 2.58]

Operative mortality in early surgery group: 1 patient (1.4%)
Conservative group: 1 death within 30 days of OR

A Few Concerns..

1. Primary endpoint was driven by all-cause death (16 vs 9). However, cardiovascular deaths were not different: 9% in both arms. 3 patients in the conservative arm died of COVID..

2. Small number of patients

3. Generalizability: the average age in this trial was 67. These were young, mobile patients with aortic stenosis.

-Most of our patients are older and come with comorbidities, and therefore have a much harder time with surgery.
-Cannot apply this to the TAVR (percutaneous aortic valve replacement) group: need a separate trial

Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease

W. Schuyler Jones, M.D., Hillary Mulder, M.S., Lisa M. Wruck, Ph.D., Michael J. Pencina, Ph.D., Sunil Kripalani, M.D., Daniel Muñoz, M.D., David L. Crenshaw, L.M.S.W., Mark B. Effron, M.D., Richard N. Re, M.D., Kamal Gupta, M.D., R. David Anderson, M.D., Carl J. Pepine, M.D., et al., for the ADAPTABLE Team*

4.

Virtual trial with 15, 076 patients: May 2015-2021 randomized to 81mg or 325mg with known or existing heart disease to prevent death or another heart attack or stroke.

About ADAPTABLE

The purpose of ADAPTABLE is to find the best dose of aspirin, 81 mg or 325 mg, for people with known or existing heart disease to prevent death or another heart attack or stroke.

81 mg 325 mg

There were no differences in rates of death, hospitalization for a heart attack or stroke, and bleeding between participants who took 81 mg and those who took 325 mg.

Over the course of the trial, participants who were assigned to 325 mg of aspirin were more likely to switch doses or stop taking aspirin than people assigned to 81 mg.

NEJM May 2021; 384:1981

5.

Influenza Vaccination After Myocardial Infarction: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial

Ole Fröbert, Matthias Götberg, David Erlinge, Zubair Akhtar, Evald H. Christiansen, Chandini R. MacIntyre, Keith G. Oldroyd, Zuzana Motovska, Andrejs Erglis, Rasmus Moer, ... See all authors

Originally published 30 Aug 2021 |
https://doi.org/10.1161/CIRCULATIONAHA.121.057042 |
Circulation. 2021;144:1476–1484

Double-blind, RCT testing whether influenza vaccination early after admission with myocardial infarction or high risk CAD reduces cardiovascular events at 1 year

2571 participants: 1272 assigned to vaccine; 1260 placebo

All-cause death, Mi, or stent thrombosis at 12 months

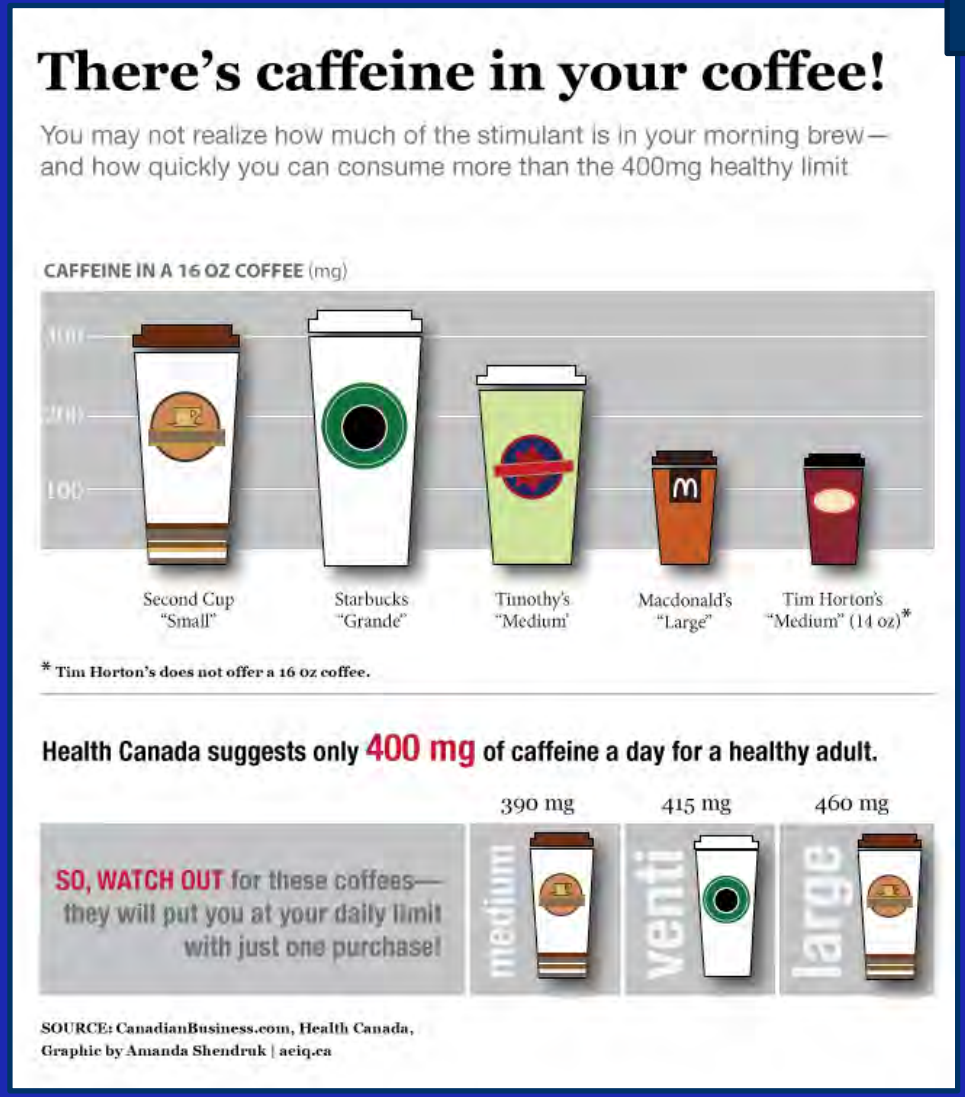
	Influenza vaccine n= 1272	Placebo n=1260	HR
Primary outcome (death, CV death, Mi, stent thrombosis)	67 (5.3%)	91 (7.2%)	0.72 CI 0.52-0.99
CV death	34 (2.7%)	56 (4.5%)	0.59 CI 0.39-0.9
All-cause death	37 (2.9%)	61 (4.9%)	0.59 CI 0.39-0.89
Myocardial infarction	25 (2%)	29 (2.4%)	0.86 CI 0.5-1.46

The mechanism of benefit is not entirely clear, but likely in a potential anti-inflammatory effect of the vaccine. Alternatively, could be that contracting the influenza infection may lead to cardiovascular events, however only 6% of patients reported a URI. Similar results in other studies.

6.

How Much Coffee do you Drink in a Day?

Health Canada suggests you limit your caffeine intake to 400mg/d

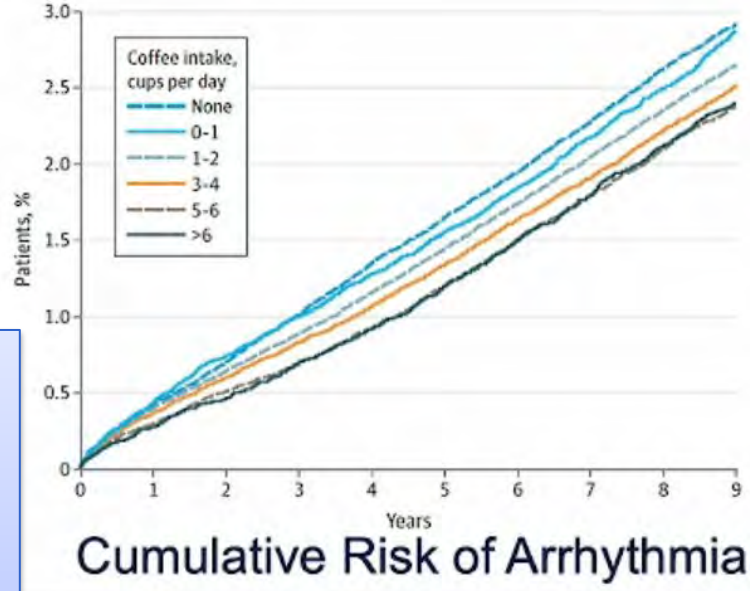


JAMA Internal Medicine | Original Investigation

Coffee Consumption and Incident Tachyarrhythmias

Reported Behavior, Mendelian Randomization, and Their Interactions

Eun-jeong Kim, MD; Thomas J. Hoffmann, PhD; Gregory Nah, MA; Eric Vittinghoff, PhD; Francesca Delling, MD; Gregory M. Marcus, MD, MAS



Prospective cohort study analyzing data from the UK Biobank. 386, 256 individuals.

Exposure: Daily coffee intake and genetic polymorphisms that affect caffeine metabolism
Outcome: any cardiac arrhythmia

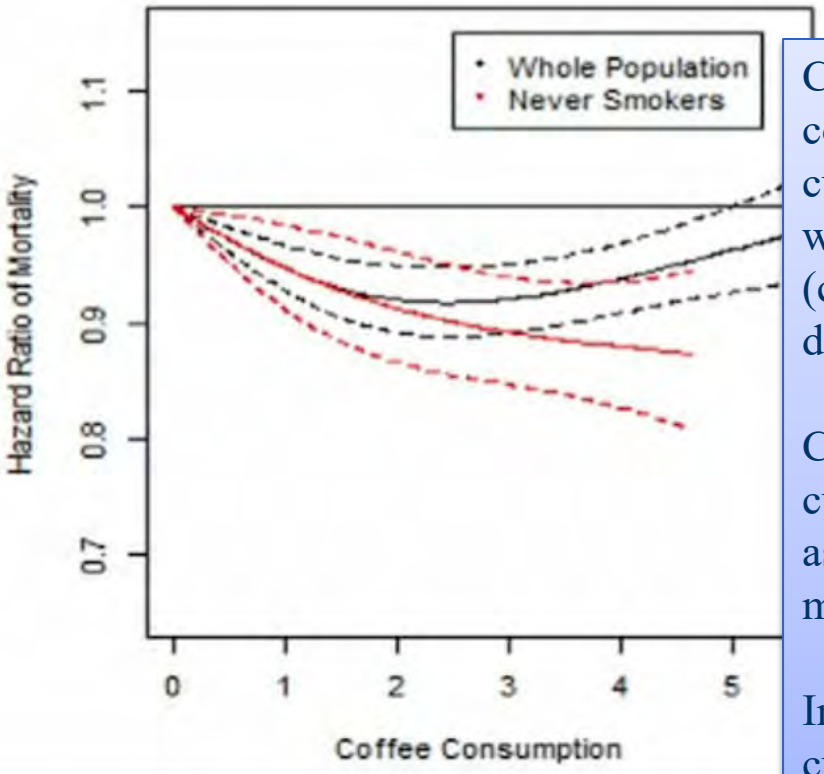
Mean f/up of 4.5 years, 17, 000 developed an arrhythmia.

Each additional cup of coffee was associated with a 3% lower risk of incident arrhythmia.

No evidence that genetically mediated caffeine metabolism affected the association.

Nurses' Health study I and II and men from the Health Professionals Follow-up Study:
4, 690 072 person years of follow-up

Overall Mortality



Compared to non-drinkers, coffee consumption of 1-5 cups per day was associated with a lower risk of mortality (caffeinated and decaffeinated)

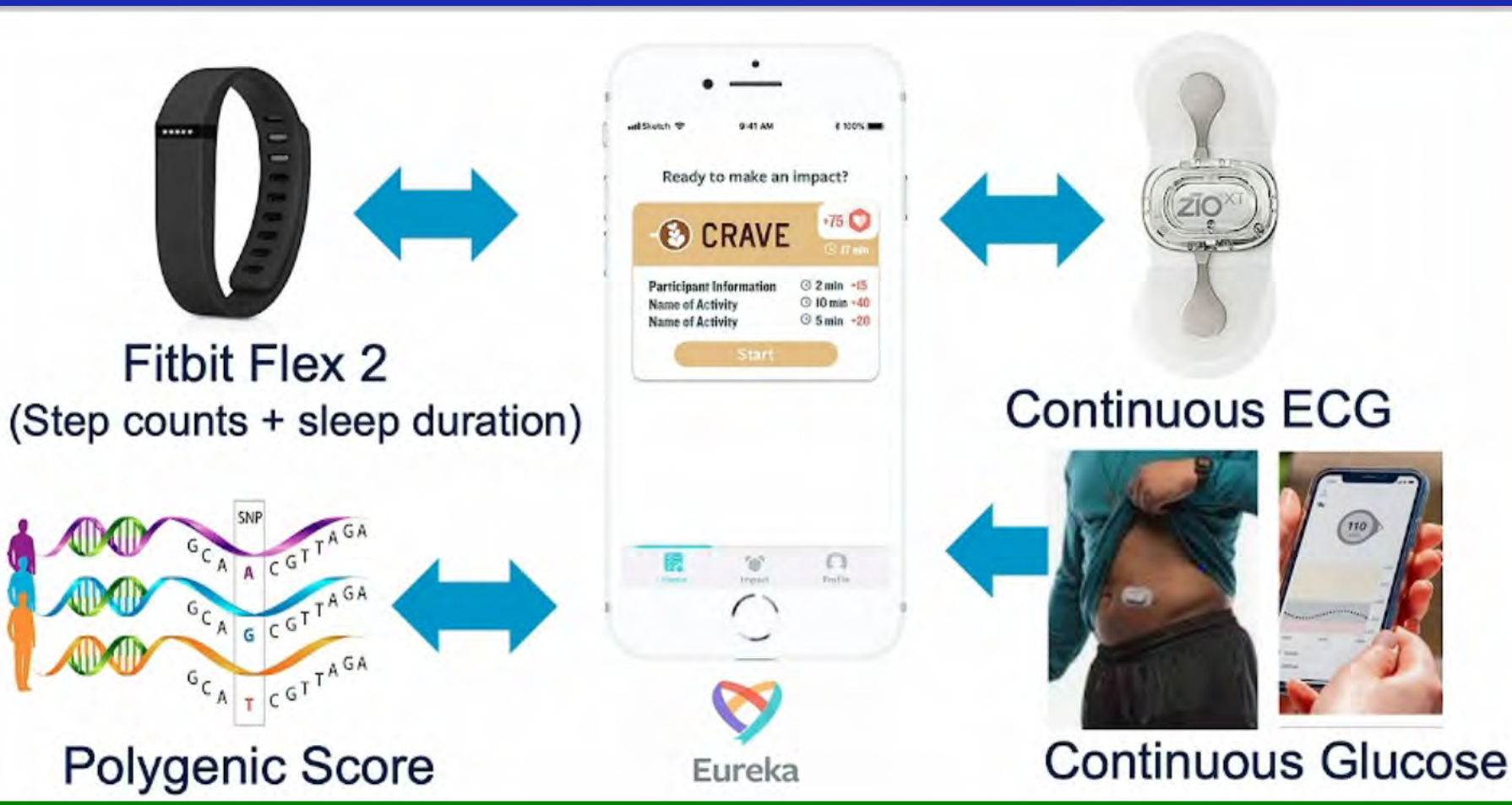
Coffee consumption of > 5 cups per day was **not** associated with risk of mortality.

In never smokers: increasing cups of coffee translated into increasingly lower mortality (CV disease, neurologic disease and suicide).

- Purpose:
  - To assess real-time relationships between random assignment to consume versus avoid coffee and cardiac ectopy, physical activity, sleep, and glucose levels

Inclusion Criteria: Healthy volunteer adults who consumed coffee
-Willing to go without coffee for no more than 2 consecutive days
-Owned a smart-phone

Exclusion Criteria: History of AF, heart failure, ICD/pacemaker, treated with beta blockers/Ca-channel blockers, or class 1 or 3 AAD



Daily Randomization: coffee vs avoidance of coffee
During the 2 weeks of CRAVE, the participants would receive a text to either consume caffeine for 1 day, and avoid caffeine the following day, or vice-versa

Results: Zio Patch

- Median 13.3 days (IQR 12.2-13.8)

	Median	Interquartile Range
	Daily Median	
PACs	12.8	4.0-29.5
PVCs	7.5	3.0-37.0
Non-sustained SVT episodes*	1	1-2
Non-sustained VT episodes†	1	1-1

*At least one SVT episode observed in 55 participants (range 1-176)
†At least one VT episode observed in 13 participants (range 1-14)

UCSF

Results: Zio Patch

- Premature Atrial Contractions

	RR*	95% CI	P value
Intention to Treat	1.09	0.98-1.20	0.10
Per real-time coffee drink	0.91	0.80-1.03	0.12
Number of drinks			
0	Reference		
1	0.76	0.41-1.40	0.38
>1	0.81	0.51-1.29	0.38

*Adjusted for day of the week

No relationship between coffee consumption and daily PAC counts

Results: Zio Patch

- Premature Ventricular Contractions

	RR*	95% CI	P value
Intention to Treat	1.54	1.19-2.00	0.001
Per real-time coffee drink	1.10	0.82-1.47	0.54
Number of drinks			
0	Reference		
1	2.31	0.57-9.40	0.24
>1	2.20	1.24-3.92	0.007

*Adjusted for day of the week

54% more PVCs on days randomized to coffee
Those consuming > 2 cups/day had a doubling of PVCs: RR 2.2

Results: Zio Patch

- SVT episodes

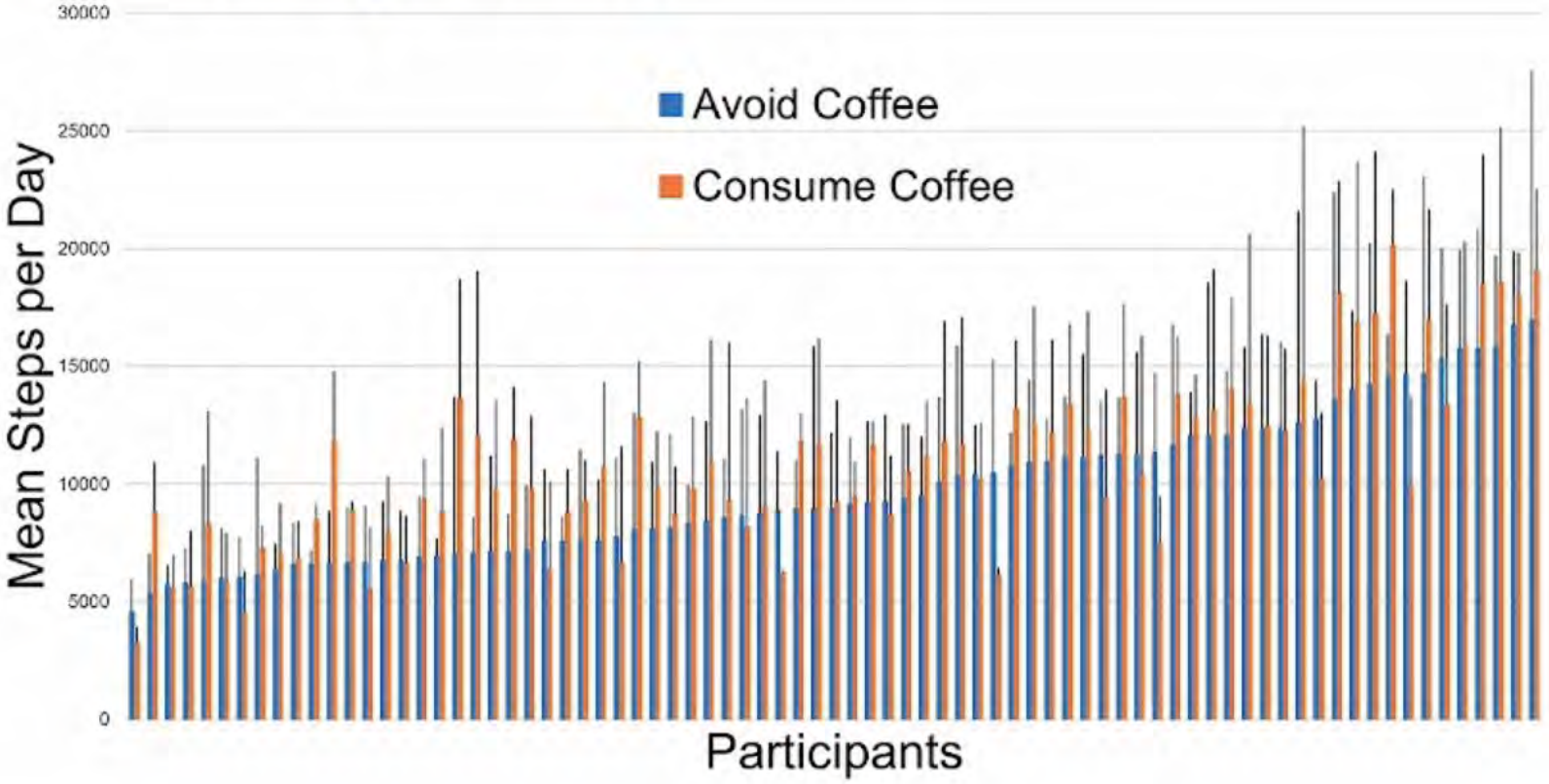
	RR*	95% CI	P value
Intention to Treat	0.84	0.69-1.03	0.10
Per real-time coffee drink	0.88	0.79-0.99	0.028
Number of drinks			
0	Reference		
1	0.59	0.27-1.25	0.17
>1	0.83	0.63-1.10	0.19

*Adjusted for day of the week

No relationship between coffee consumption and SVT episodes in ITT

Per protocol: every additional coffee drink was associated with a 12% **lower** risk for an SVT episode

Results: Step Counts

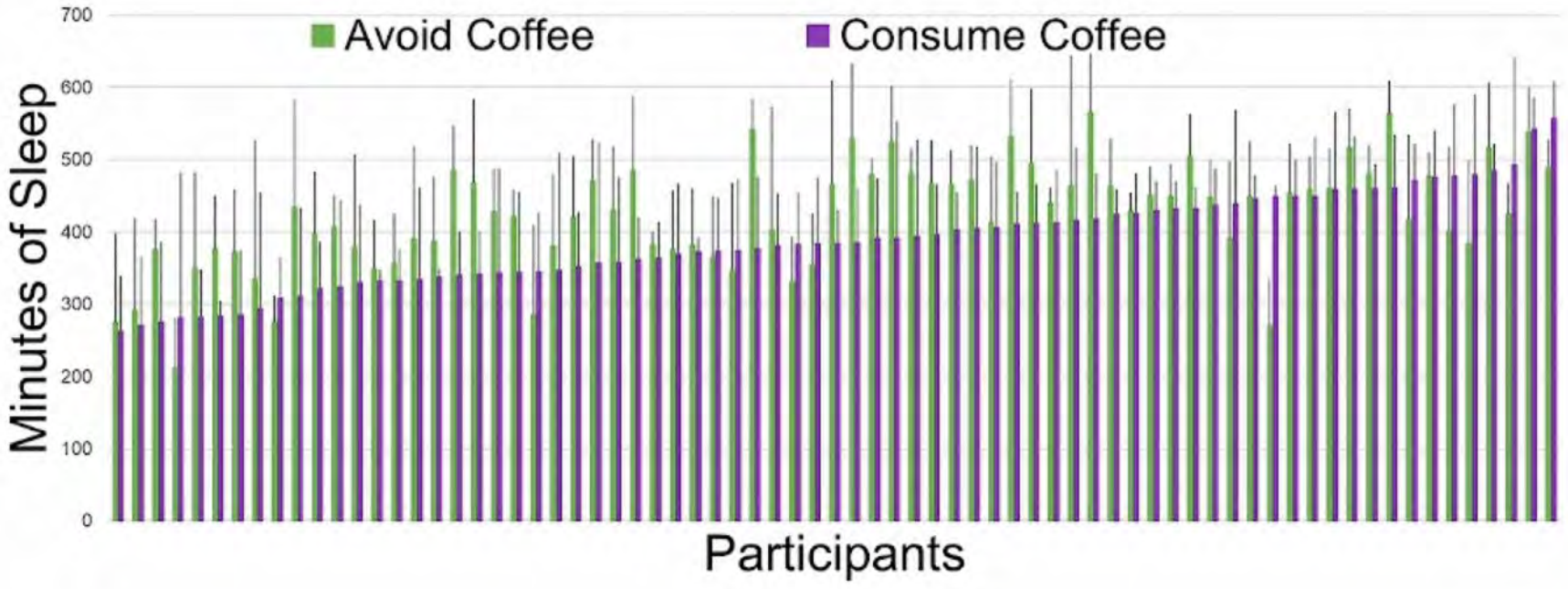


UCSF

ITT: 1058 more steps on days they drank coffee

Per protocol: 587 more steps per day CI 355-830 p <0.01)

Results: Minutes Asleep



ITT: 36 less minutes of sleep : (95% CI 22-50 $p<0.001$)

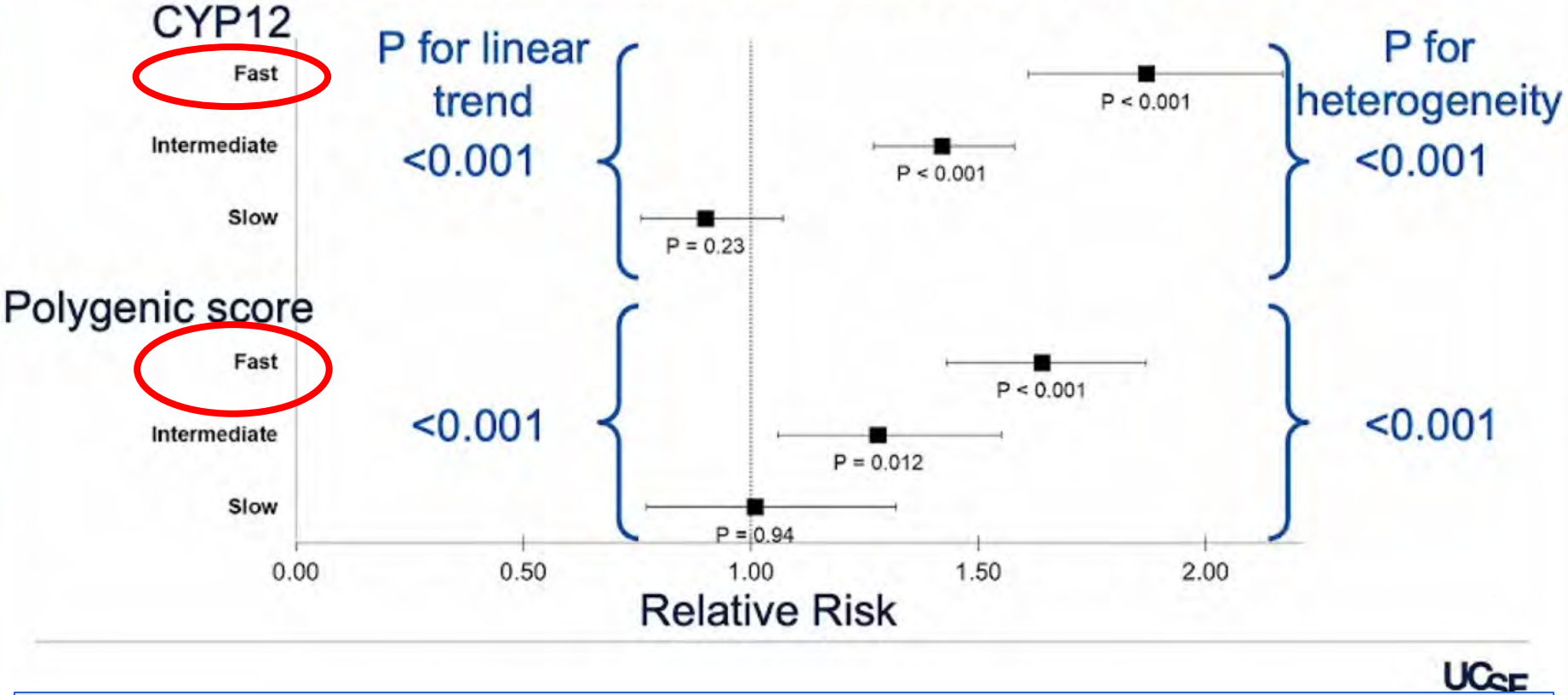
Per protocol: 18 less minutes of sleep: (95% CI 13-23 $p<0.01$)

Results: Daily Average Glucose

- No statistically significant relationships between randomization assignment or per-protocol coffee consumption and daily average glucose levels were observed.

Results: Interaction Analyses by Genotype

Coffee Randomization and PVC counts



2 significant interactions: fast coffee metabolizers had increased risk for PVCs and slow metabolizers experienced more sleep deprivation

Conclusions: Coffee Consumption Resulted in…

- No increase in atrial arrhythmias
  - Less SVT in per-protocol analyses
- More PVCs
  - Faster caffeine metabolizers experienced a heightened response
- A clinically meaningful increase in physical activity
- A clinically meaningful reduction in sleep
  - Slower caffeine metabolizers experienced a more potent effect

7. Cardiac Conduction System Pacing

Conduction system pacing has recently undergone a revival as a meaningful alternative for permanent pacing, particularly for patients with a projected high percentage of pacing

By implanting a lead directly at, or near, the electrical conduction system, we can recreate the normal electrical activity, and maintain synchrony during right ventricular pacing.

Pacing the conduction system allows for physiologic activation of the LV which may result in better hemodynamic response, less negative LV remodeling, and possibly improved clinical outcomes, particular in patients with AV block

Canadian Journal of Cardiology 33 (2017) 1736.e1–1736.e3 www.onlinecjc.ca

Case Report

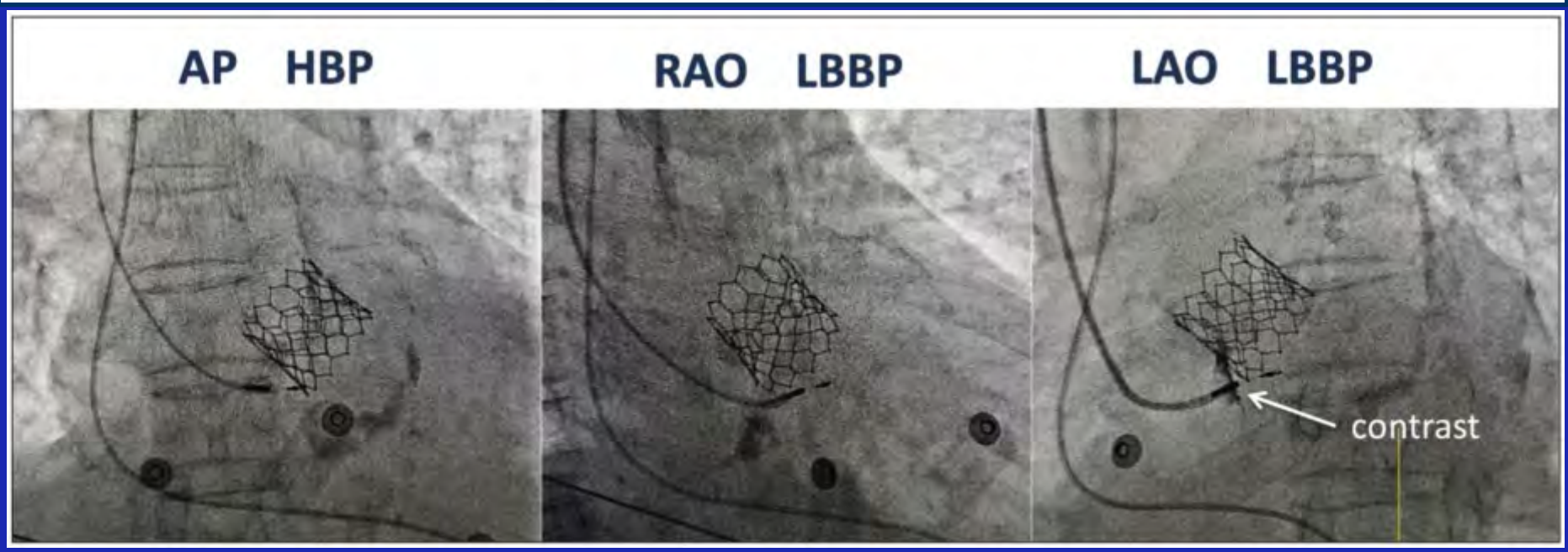
A Novel Pacing Strategy With Low and Stable Output: Pacing the Left Bundle Branch Immediately Beyond the Conduction Block

Weijian Huang, MD, FHRS,[a] Lan Su, MD,[a] Shengjie Wu, MD,[a] Lei Xu, MD,[a] Fangyi Xiao, MD,[a] Xiaohong Zhou, MD,[b] and Kenneth A. Ellenbogen, MD, FHRS[c]

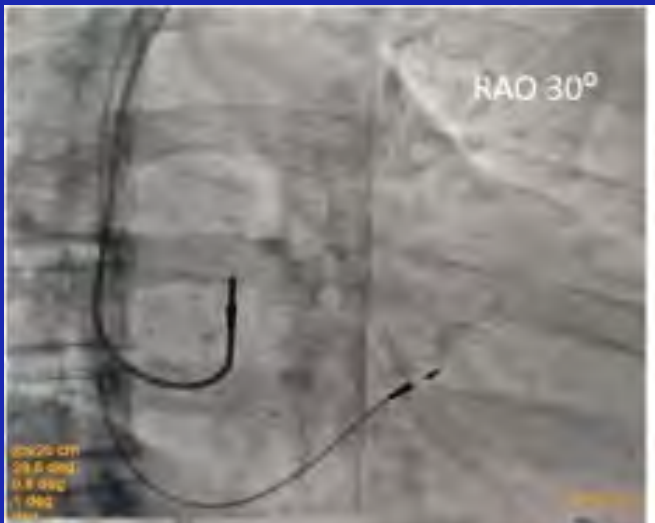
[a] *Department of Cardiology, First Affiliated Hospital of Wenzhou Medical University, Key Lab of Cardiovascular Disease of Wenzhou, Wenzhou, China*

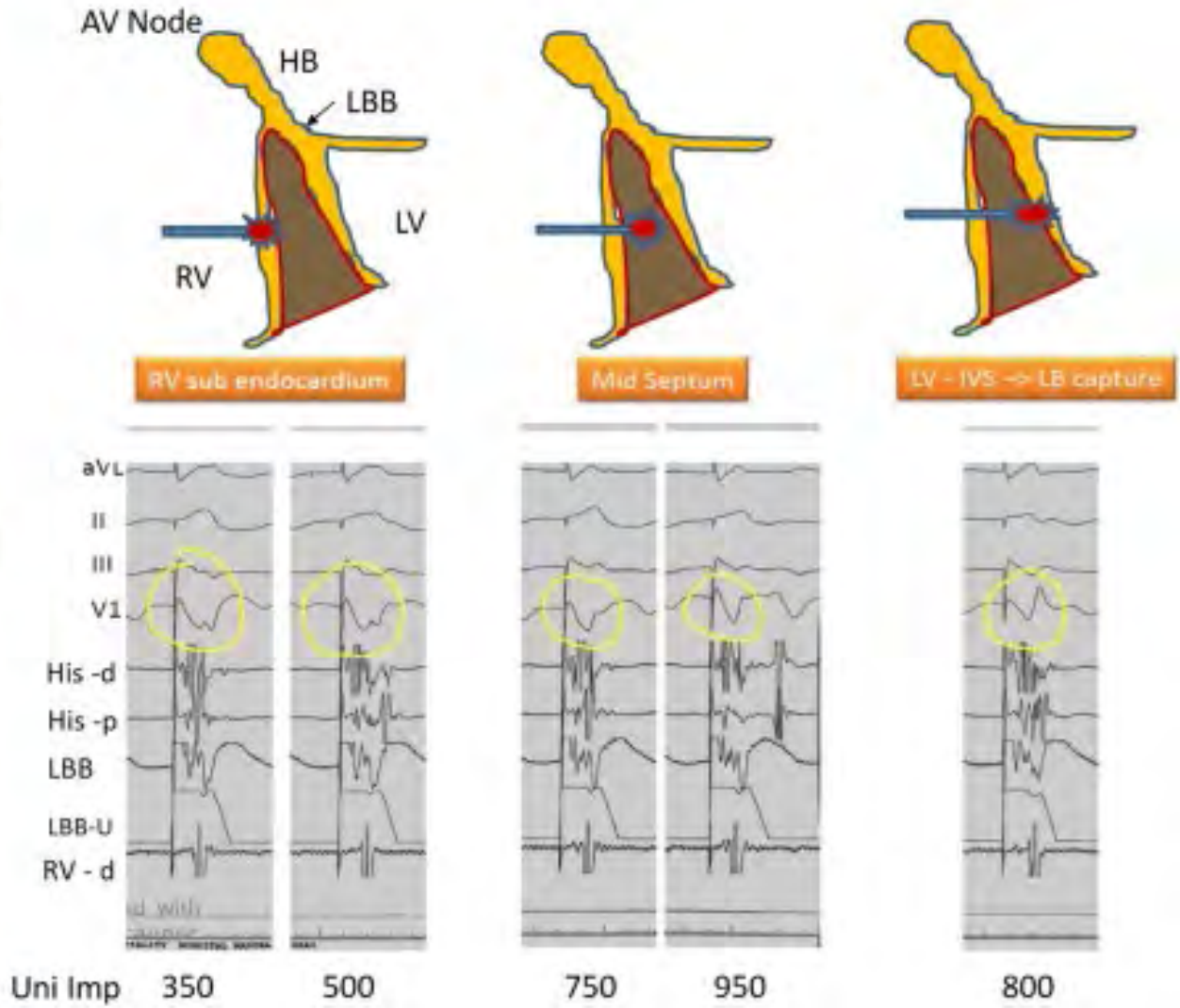
[b] *CRHF Division, Medtronic PLC, Mounds View, Minnesota, USA*

[c] *Department of Cardiology, Virginia Commonwealth University Health System, Richmond, Virginia, USA*

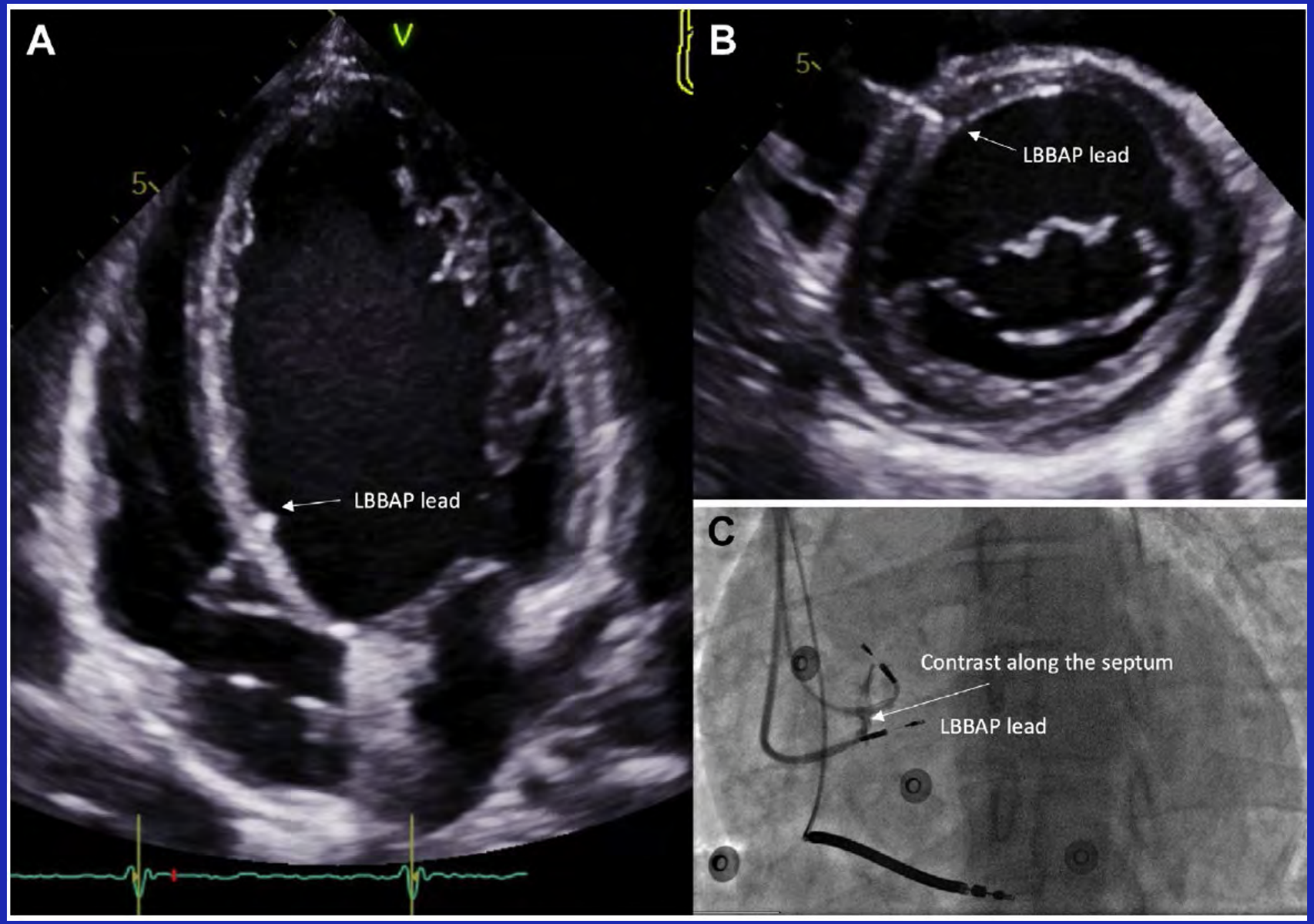


Left Bundle Branch Pacing



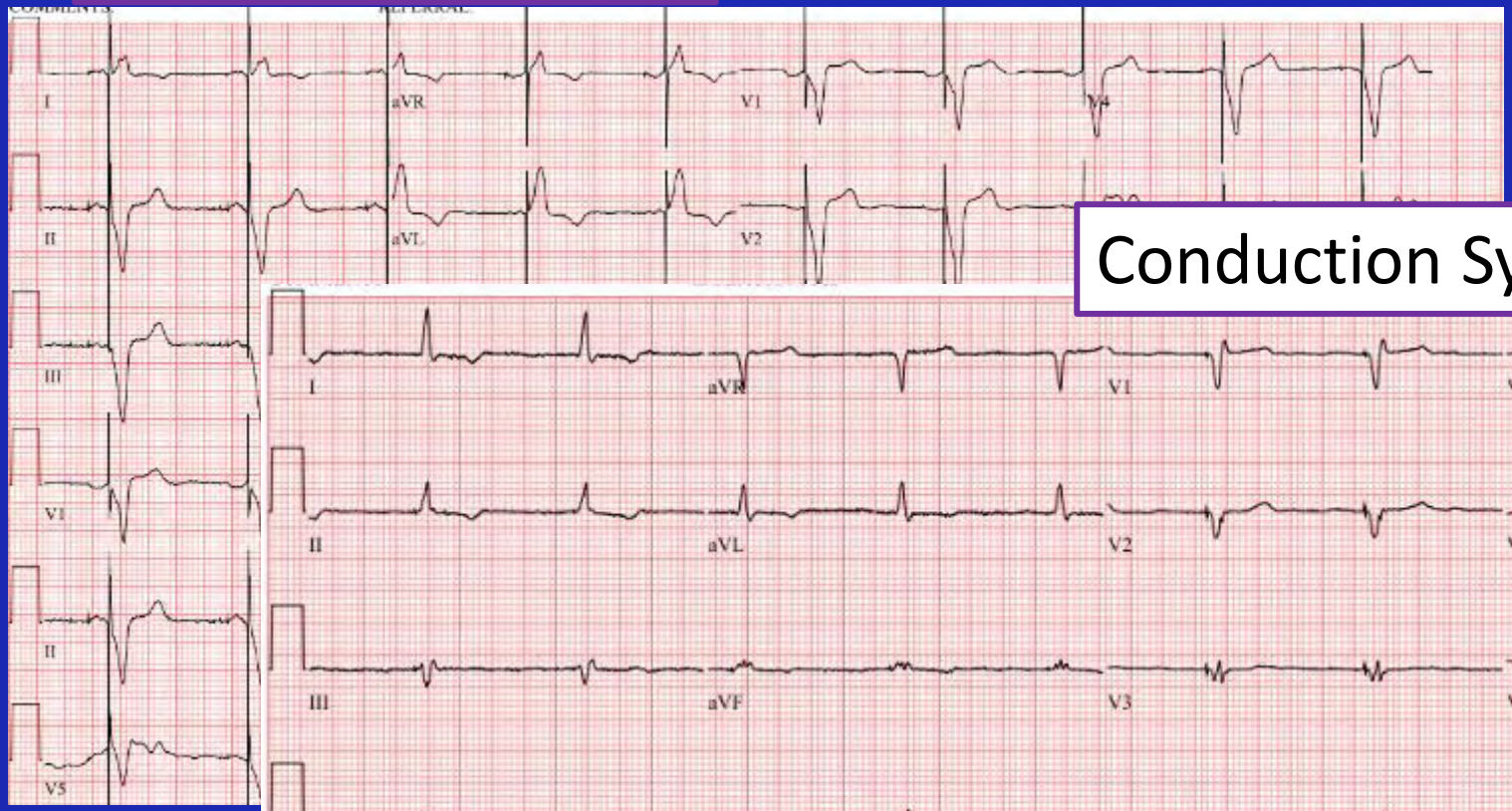


Increase in impedance until we reach the left bundle

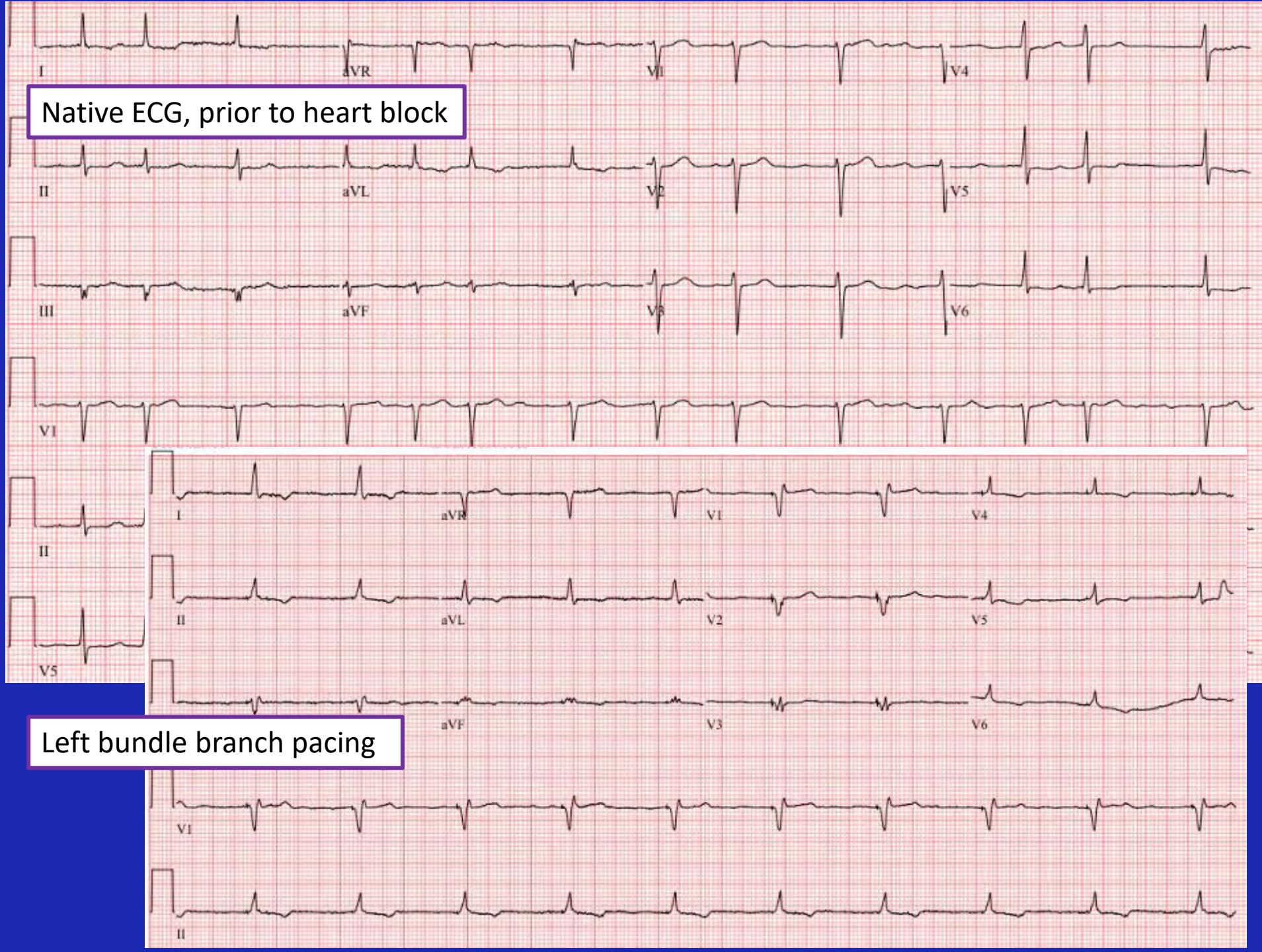

A
LBBAP lead
B
LBBAP lead
C
Contrast along the septum
LBBAP lead

80F Post-op TAVI develops complete heart block, dependent on temporary pacing wire. What should we do now?

Standard RV pacing



Conduction System Pacing


Native ECG, prior to heart block
I
aVR
V4
II
aVL
V5
III
aVF
V6
V1
II
V5
I
aVR
V1
V4
II
aVL
V2
V5
aVF
V3
V6
V1
II
Left bundle branch pacing

Conclusion

1. Concomitant left atrial appendage closure at time of cardiac surgery in addition to OAC reduces the risk of stroke in patients with atrial fibrillation
2. No change to the endocarditis prophylaxis guidelines
3. We should be careful about sending asymptomatic patients with severe aortic stenosis for early surgery
4. Aspirin 81mg vs 325mg: no difference
5. Caffeine does not have any negative impact for atrial arrhythmias
6. A look to the future of pacing