AP Valves 2017: Case Reviews

Conduction Abnormalities: How to Avoid & Manage ?

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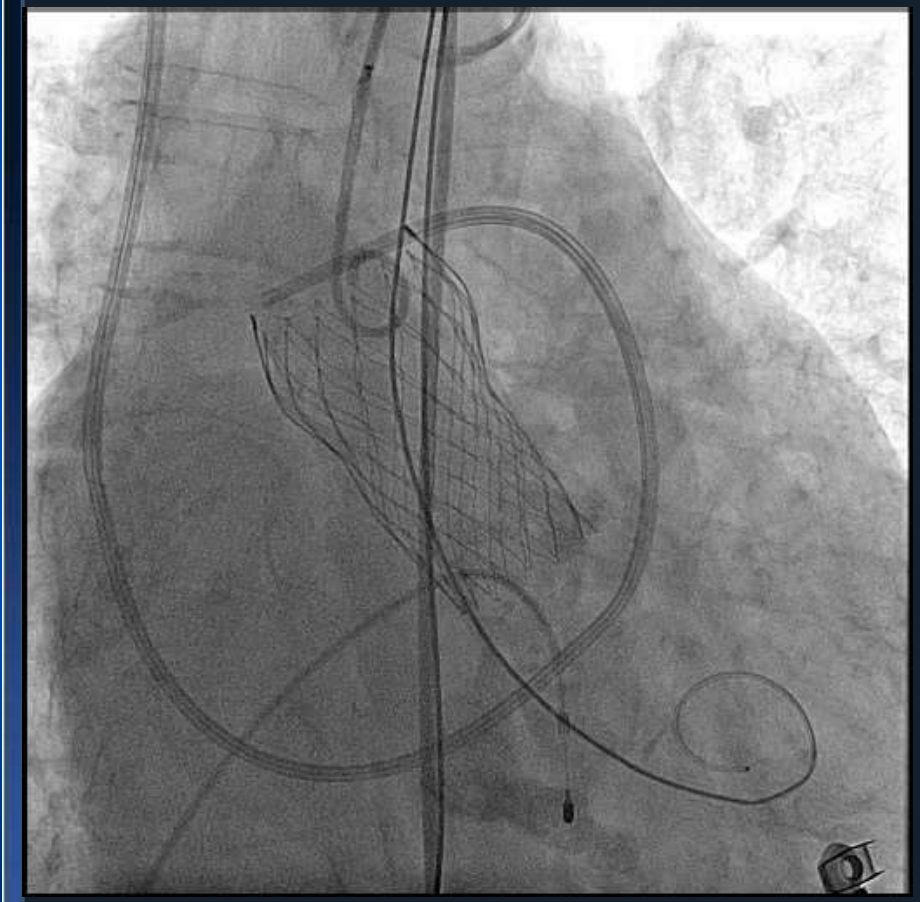
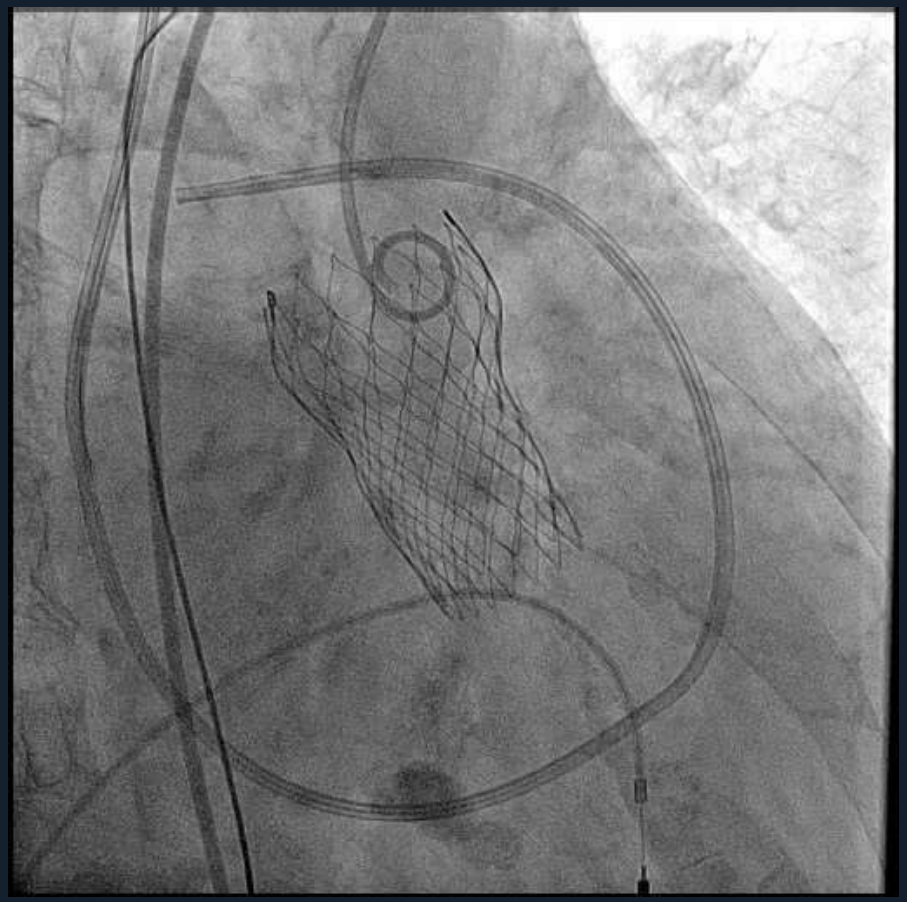
Case

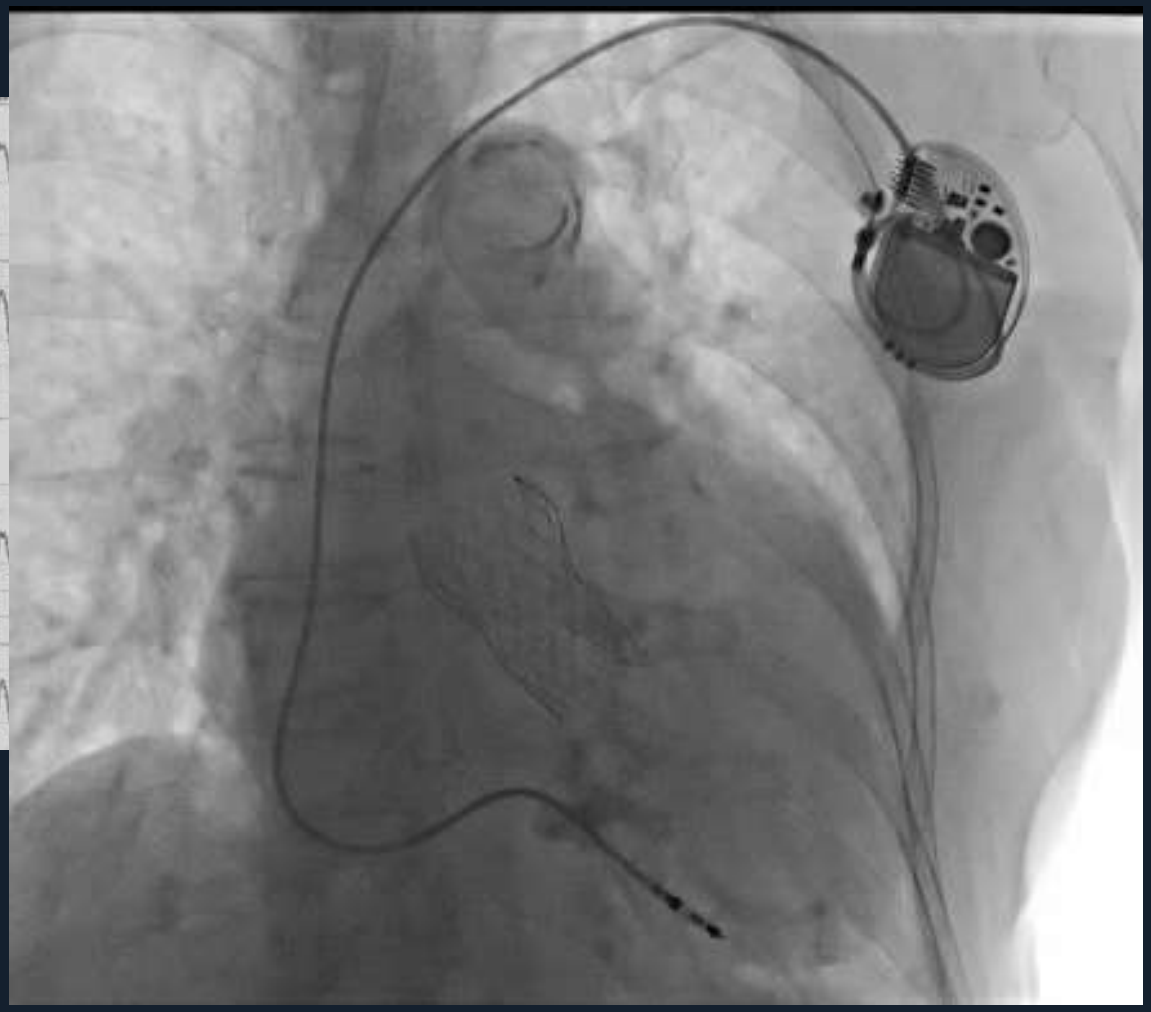
89 yo lady, DM, CKD stage 2, DOE NYHA III





CAVB

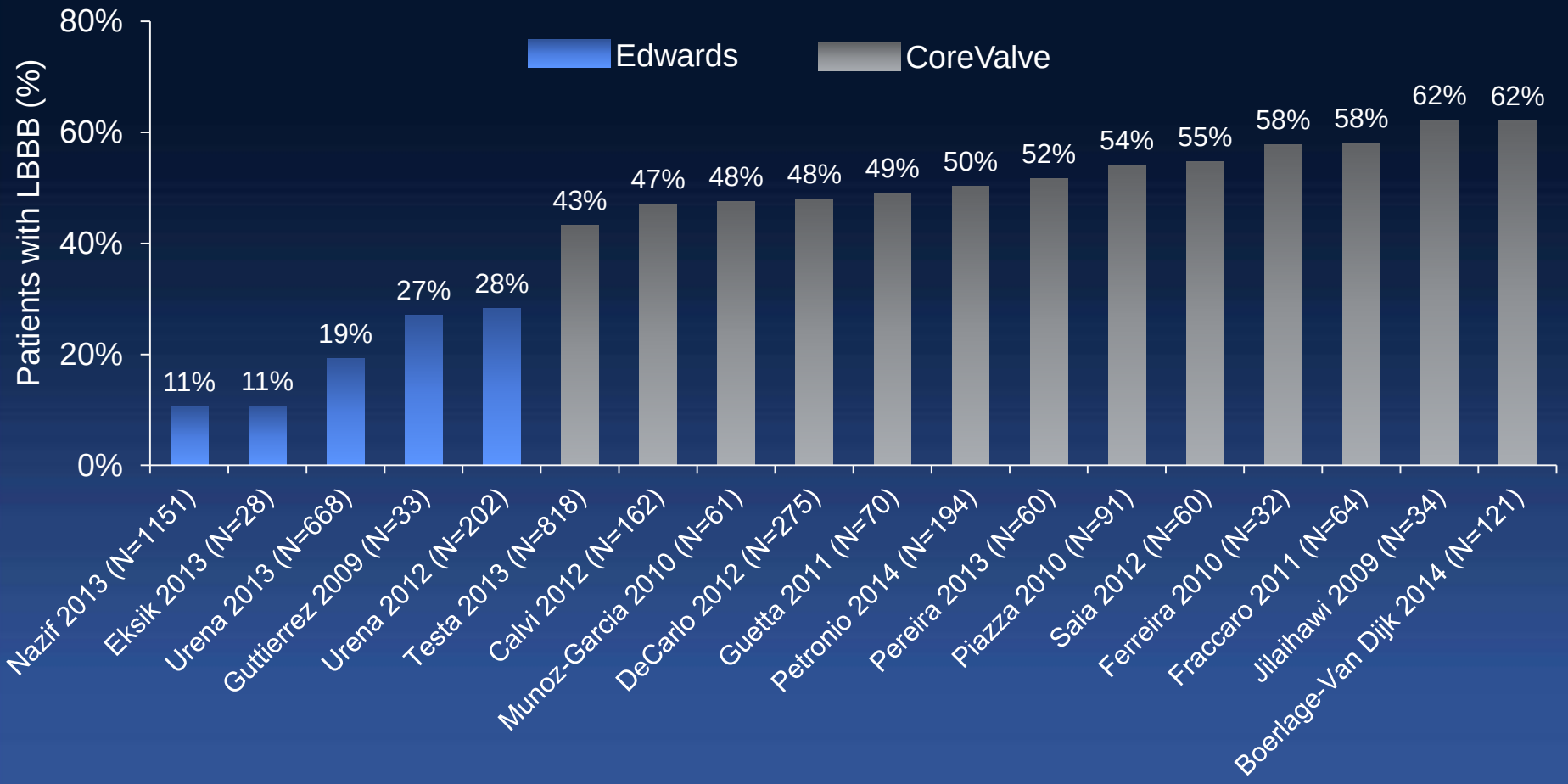
3 days later



Incidences and Impacts on Clinical Outcomes

Incidence of Left Bundle Branch Block: Varies by site, study, valve type

Post-TAVR or hospital discharge



[1]Boerlage-Van Dijk K, et al., *PACE* 2014; 37: 1520-1529; [2]De Carlo M, et al., *Am Heart J* 2012; 163: 492-9; [3]Ferreira N, et al., PACE 2010; 33: 1364-1372; [4]Fraccaro C, et al., *Am J Cardiol* 2011; 107: 747-754; [5]Guetta V, et al., *Am J Cardiol* 2011; 108: 1600-1605; [6]Munoz-Garcia A, et al., *Rev Esp Cardiol* 2010; 63(12): 1444-51; [7]Piazza N, et al., *EuroIntervention* 2010; 6(4): 475-84; [8]Saia F, et al., *Catheter Cardiovasc Interv* 2012; 79(5): 7712-9; [9]Jilaihawi H, et al., *Am Heart J* 2009; 157: 860-6; [10]Calvi V, et al., *J Interv Card Electrophysiol* 2012; 34: 189-95; [11]Pereira E, et al., PACE 2013; 36(5): 559-69; [12]Petronio AS, et al., presented at EuroPCR 2014; [13]Testa L, et al., *Circulation* 2013; 127: 1300-1307; [14]Eksik A, et al., *J Invasive Cardiol* 2013; 25(6): 305-309; [15]Nazif T, et al., *Eur Heart J* 2013; epub ahead of print; [16]Urena M, et al., *J Am Coll Cardiol Intv* 2014; 7(2): 128-36; [17]Urena M, et al., *J Am Coll Cardiol* 2012; 60(18): 1743-52; [18]Gutierrez M, et al., *Am Heart J* 2009; 158: 302-8.

Impact of New LBBB on Mortality

Inconclusive data may result from how pacemakers are treated in the analysis

Study	Valve Type, N	% LBBB Discharge	% LBBB 1 Year	Impact on 1-Yr All-Cause Mortality	Patients in Analysis	Post-TAVI PPM which were excluded
De Carlo[1]	MCV N=275	26.9%	NR	No (p=0.37)	All new LBBB before discharge	PPM prior to discharge
Pereira[2]	MCV N=65	37.5%*	NR	No (0=0.111)	New post procedural LBBB	PPM prior to discharge
Houthuizen[3]	MCV N=387 EDW N=292	34.3%	NR	Yes (p=0.006)	New LBBB within 7 days	All post-TAVI PPM
Houthuizen[4]	MCV N=223 EDW N=253	28.7%	22.7%	Yes (p=NR)	New LBBB that persisted at 1 year	All post-TAVI PPM
Urena[5]	EDW N=202	13.2%	5.0%	No (p=0.610)	New LBBB at discharge	PPM prior to discharge
Franzoni[6]	MCV N=87 EDW N=151	17.2%	NR	No (p=0.42)	New LBBB at discharge	NR
Testa[7]	MCV N=818	27.4%	NR	No (p=0.3)	New LBBB at discharge	PPM within 48 hrs of TAVI
Nazif[8]	EDW N=1151	10.5%	8.5%	No (p=0.73)	New LBBB at discharge	PPM prior to discharge
Urena[9]	EDW N=668	11.8%	NR	No (p=0.174)	New LBBB at discharge	NR
Wenaweser[10]	MCV N=1015	NR	23.1%	No (p=0.393)	New LBBB at 30 days	All post-TAVI PPM

[1]De Carlo M, et al., *Am Heart J* 2012; 163: 492-9; [2]Pereira E, et al., *PACE* 2013; 36(5): 559-69; [3]Houthuizen P, et al., *Circulation* 2012; 126: 720-728; [4]Houthuizen P, et al., *EuroIntervention* 2014; 9(10): 1142-1150; [5]Urena M, et al., *J Am Coll Cardiol* 2012; 60(18): 1743-52; [6]Franzoni I, et al., *Am J Cardiol* 2013; 112(4): 554-559; [7]Testa L, et al., *Circulation* 2013; 127: 1300-1307; [8]Nazif T, et al., *Eur Heart J* 2013; epub ahead of print; [9]Urena M, et al., *J Am Coll Cardiol Intv* 2014; 7(2): 128-36; [10]Wenaweser P, et al., presented at EuroPCR 2013

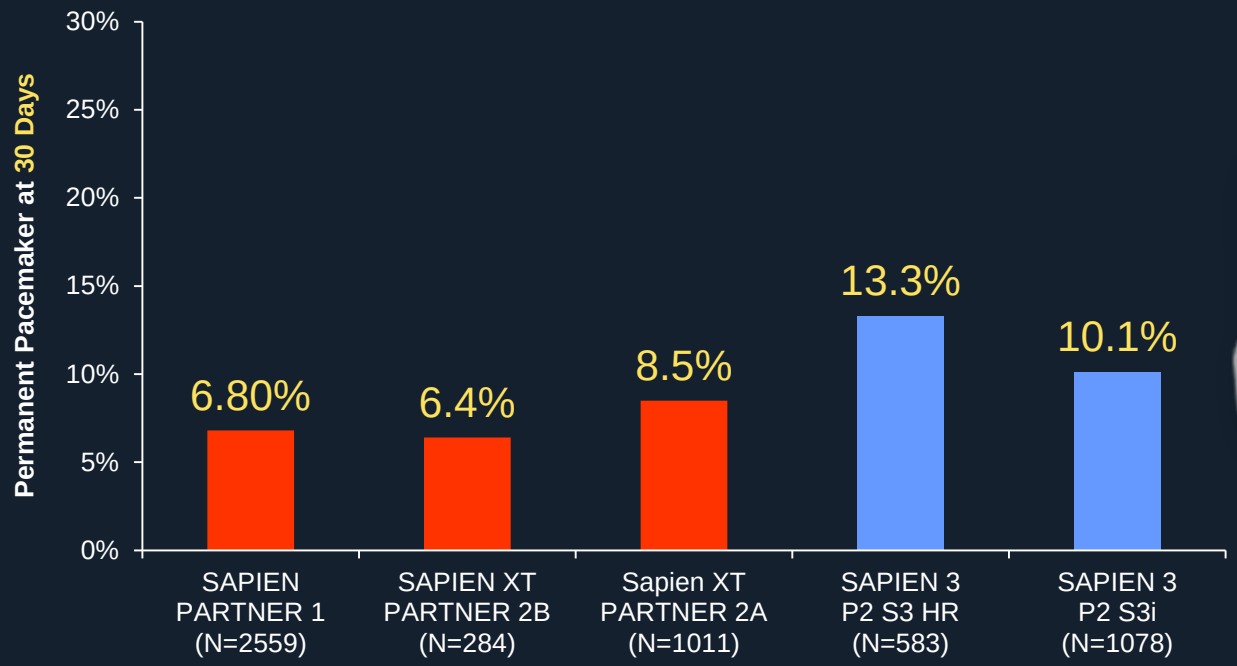
Incidence of Pacemaker post TAVR

	Studies	Patients	Pacemaker	Sapien	CoreValve
Khatri et al	44	12,116	13.1%	6.4%	25.4%
Siontis et al	41	11,210	17%	6%	28%

- Meta-analyses have analyzed the rates of new PPM with the early generation devices
  - Medtronic CoreValve ~ 25-32%
  - Edwards Sapien (XT) ~ 6%

Khatri. Ann Intern Med 2013, Siontis. JACC 2014, Mohananey. Cir Cardiovasc Intv 2017

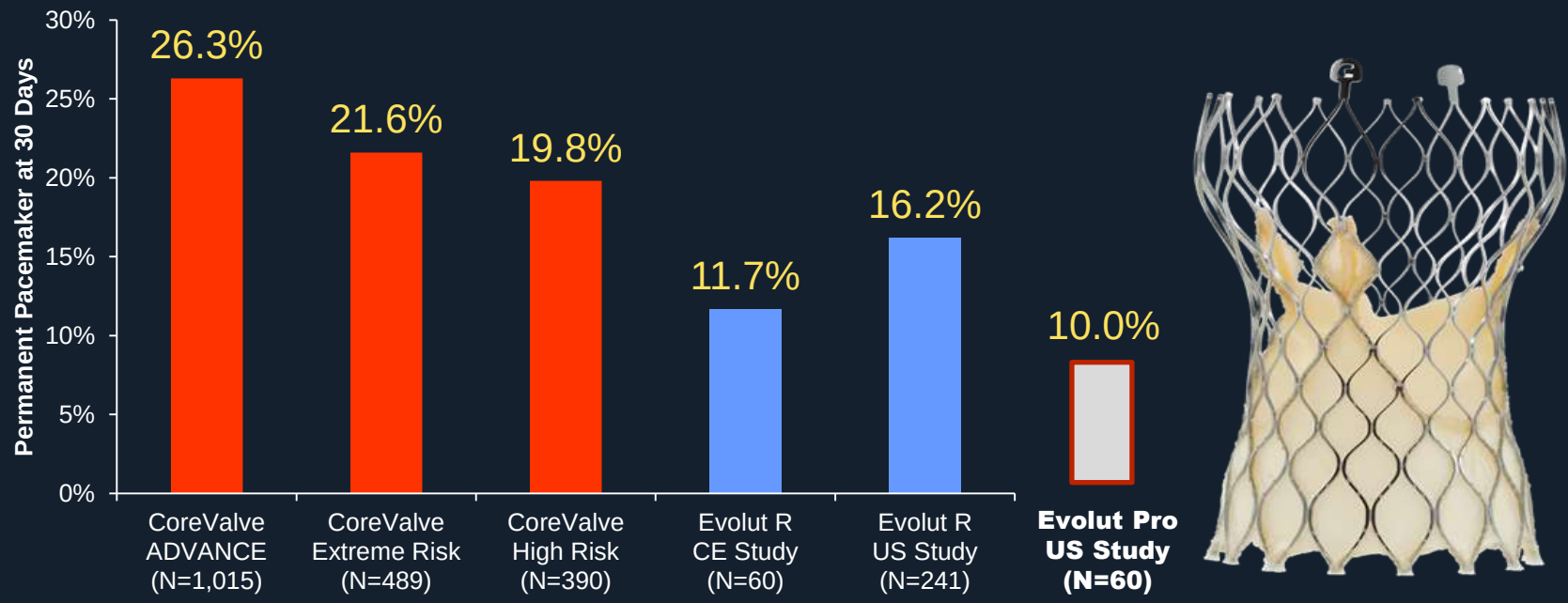
Newer Generation Devices: Edwards SAPIEN 3



Nazif TM. *J Am Coll Cardiol Intv* 2015;8:60-9.; Webb JG. *J Am Coll Cardiol Intv 2015;8:1797-806.*; Leon MB. *N Engl J Med* 2016;374:1609-20.; Kodali S. Eur Heart J. 2016;37:2252-62

Adapted from Nazif T. TVT 2017

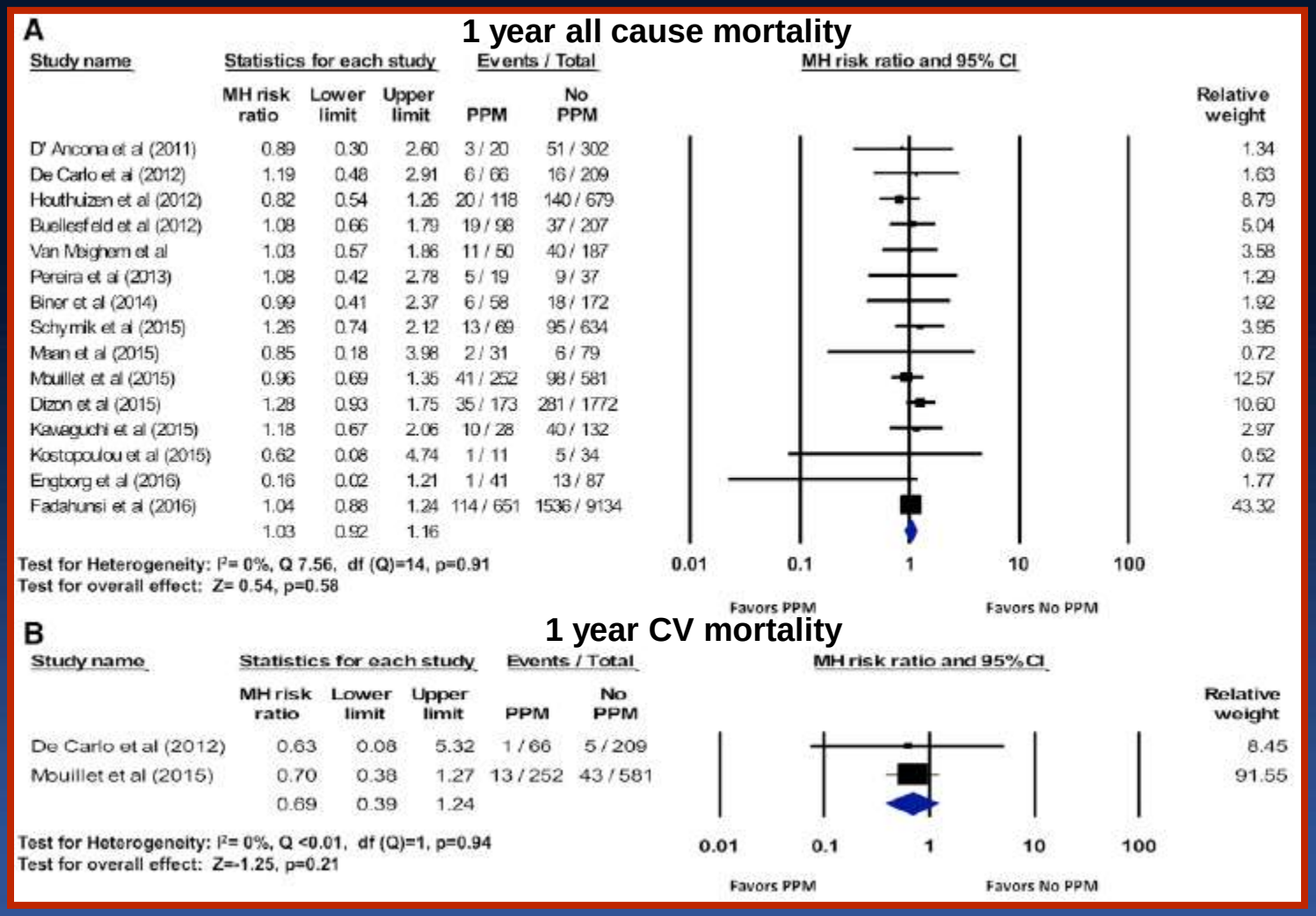
Newer Generation Devices: Medtronic Evolut-R



Linke A. *Eur Heart J* 2014;35:2672-84; Popma J. *J Am Coll Cardiol* 2014;63:1972-81; Adams D. *N Engl J Med* 2014;370:1790-8; Manoharan G. *J Am Coll Cardiol Intv* 2015;8:1359-67; Williams MR presented at ACC 2016, Forrest J presented at ACC 2017

Adapted from Nazif T. TVT 2017

Clinical Impact of PPM After TAVR

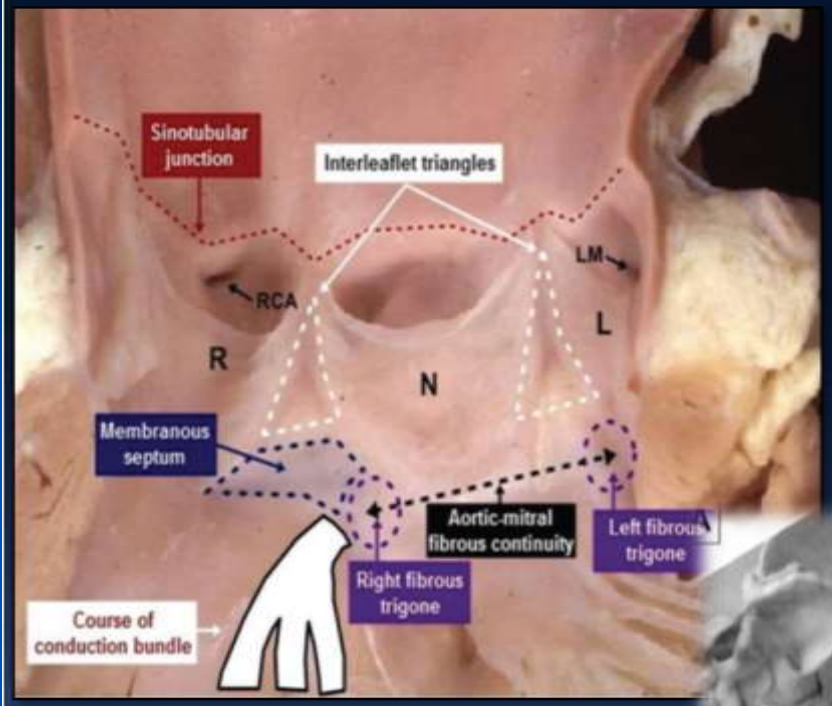


PPM implantation is not assosciate with increased risk of death, CV death, stroke, MI both at short- and long-term follow-up.

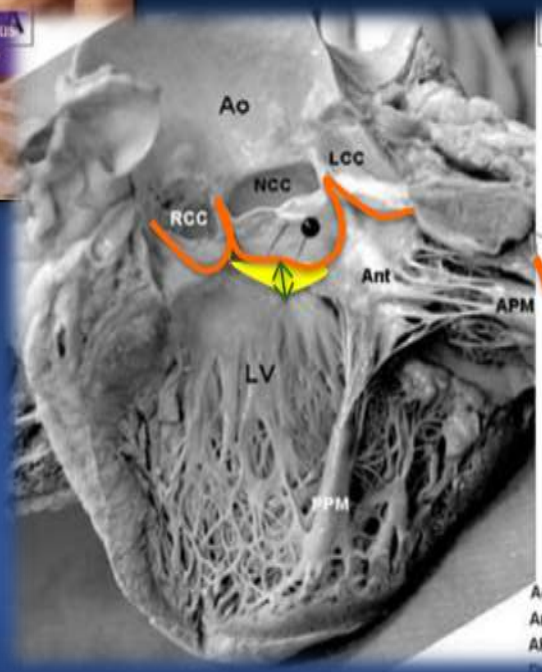
Mohananey D. Cir Cardiovasc Interv 2017

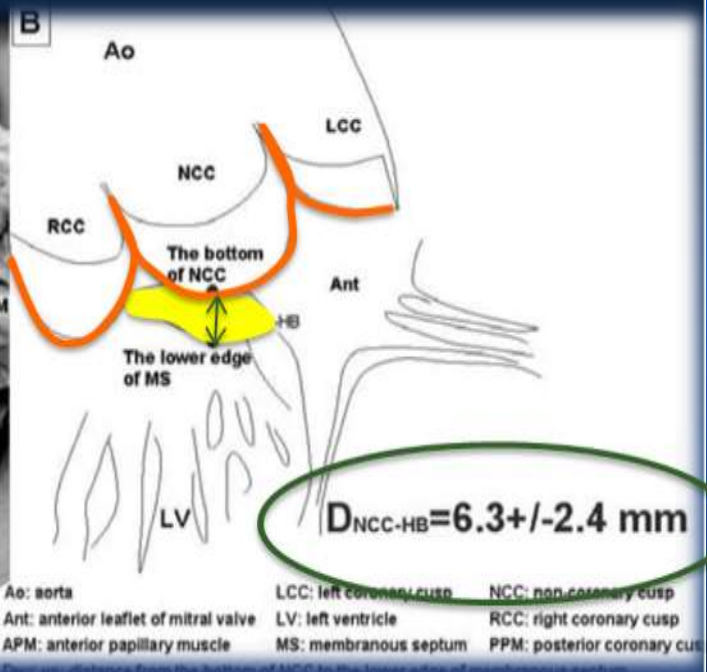
Mechanism and Time Course of Recovery

Anatomical Considerations



- Close proximity of the aortic valve to the cardiac conduction system[1]
- Distance between non-coronary cusp and His-bundle: on average, 6.3 mm
- Distance varies among individuals, but is usually <10 mm





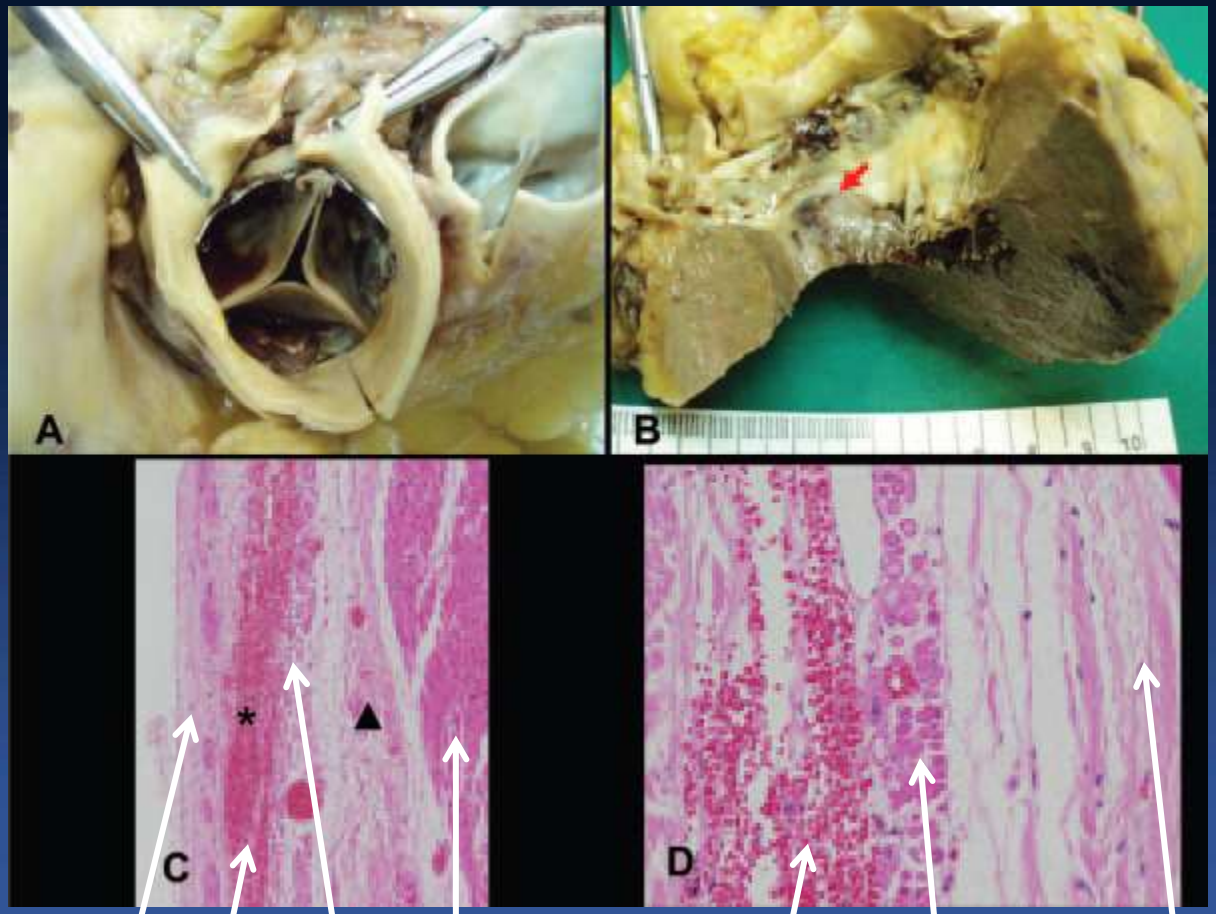
[1] Igawa O. *Circ J* 2009; 73 Suppl I: 257.

Anatomical Considerations

Prosthetic valves may contact the conduction system, causing injury (inflammation, or in this case, hemorhage)[1]

Appropriately implanted **Edwards Sapien** valve:

Following removal of prosthetic valve, hemorrhagic lesions observed



Hematoxylin and eosin, x10

Hematoxylin and eosin, x40

[1] Moreno R., et al., *Circ ulation* 2009; 120: e29-30.

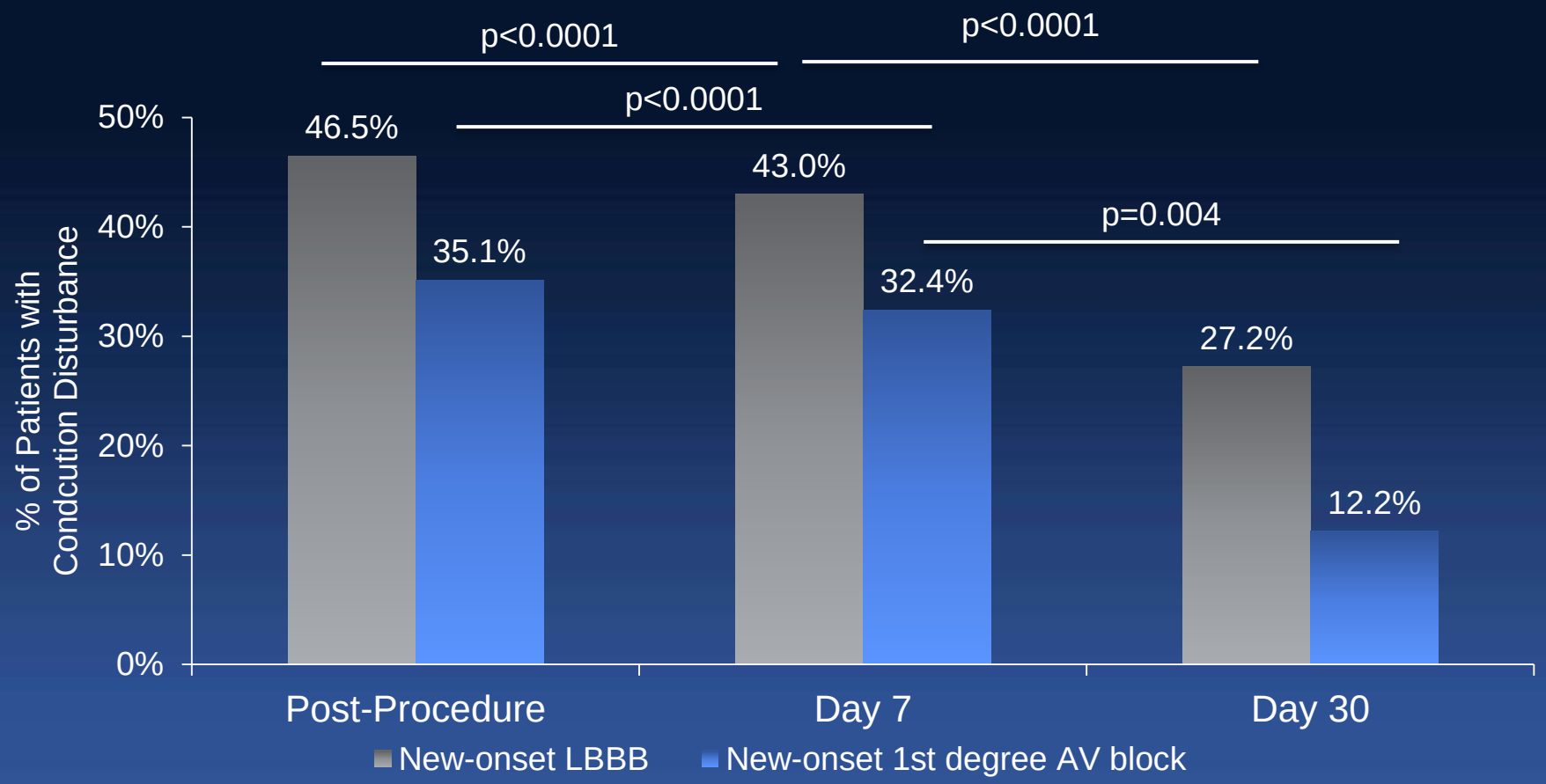
Mechanism of Conduction Disturbances

- *Conduction abnormalities may resolve due to the transient nature of some TAVR-induced tissue injury*

Mechanical (Direct) Injury	Ischemic (Indirect) Injury
• Wall tension due to radial for ce • Procedural Inflammation • Procedural Edema	• Tissue compression during BAV • Hypotension during rapid pa cing (BAV procedure) • Other hypotensive episodes

Conduction Disturbances Resolve with Time

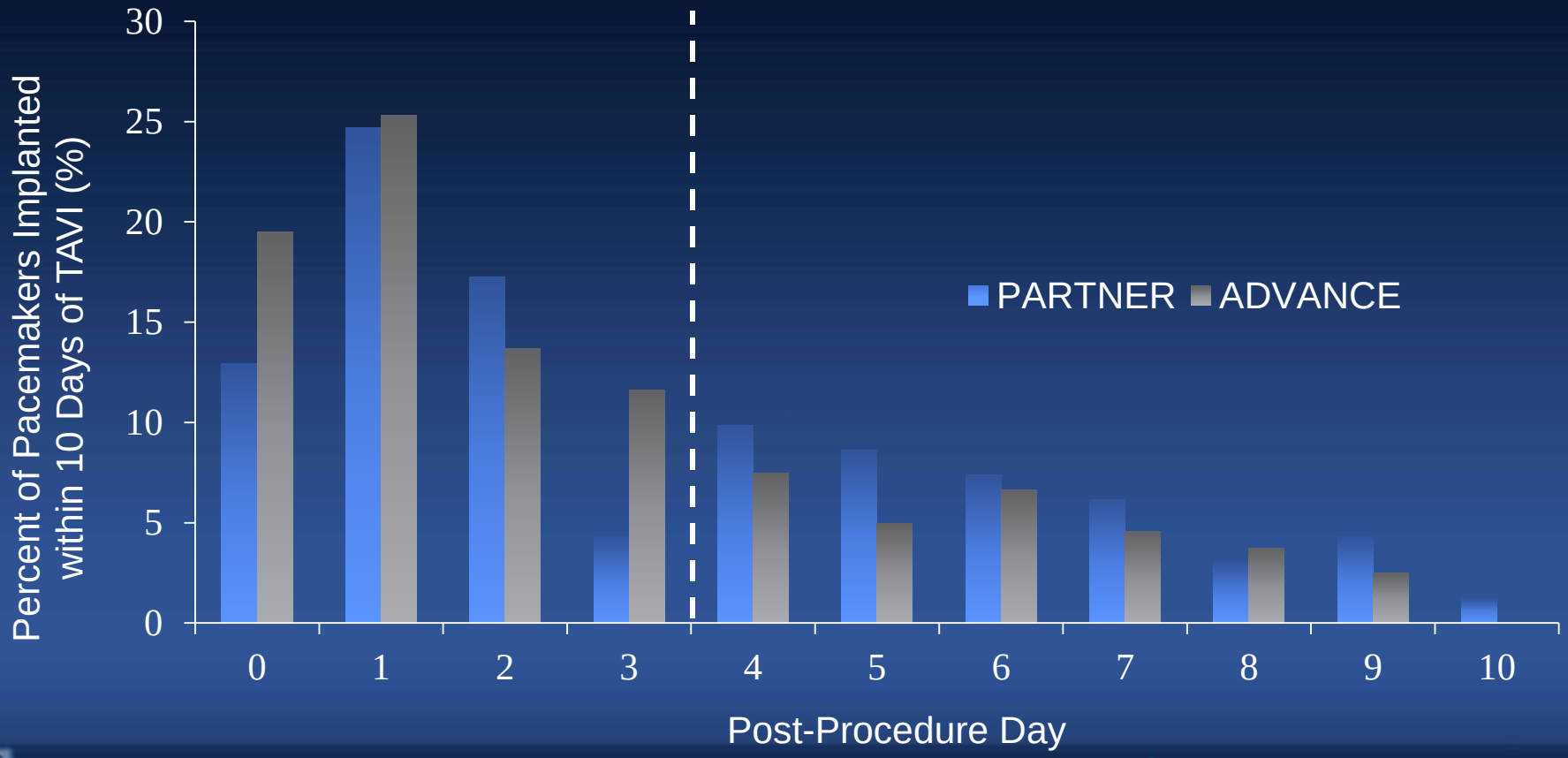
- *Paired analyses in ADVANCE II showed that 42% of new LBBB and 65% of new 1st degree AV block resolved spontaneously by day 30[1]*



Patients with normal baseline AV conduction were considered for new-onset AV block. Patients with normal baseline IV conduction were considered for new-onset LBBB.
New-onset is defined as a new conduction disturbance which initiates within 48 hours of TAVI.
Patients receiving new permanent pacemakers were excluded.
Paired data for each type of conduction disturbance. LBBB n=114, 1st degree n=74
[1]Petronio S, et al., presented at EuroPCR 2014

Timing of Permanent Pacemaker Implants

- Of pacemakers implanted within 10 days of TAVI, the majority had been implanted by day 3 in both PARTNER and ADVANCE.
- Some proportion of conduction disturbances (all types) will spontaneously resolve, though the time course for a given patient is difficult to predict.
- Consider watchful waiting.



[1]Nazif T, et al., *J Am Coll Cardiol Intv* 2015; 8:60-9; [2]Arnold S, et al., *Circ Cardiovasc Interv* 2014; 7:829-36

Predictors : Manageable or not

Predictors of Conduction Disturbances

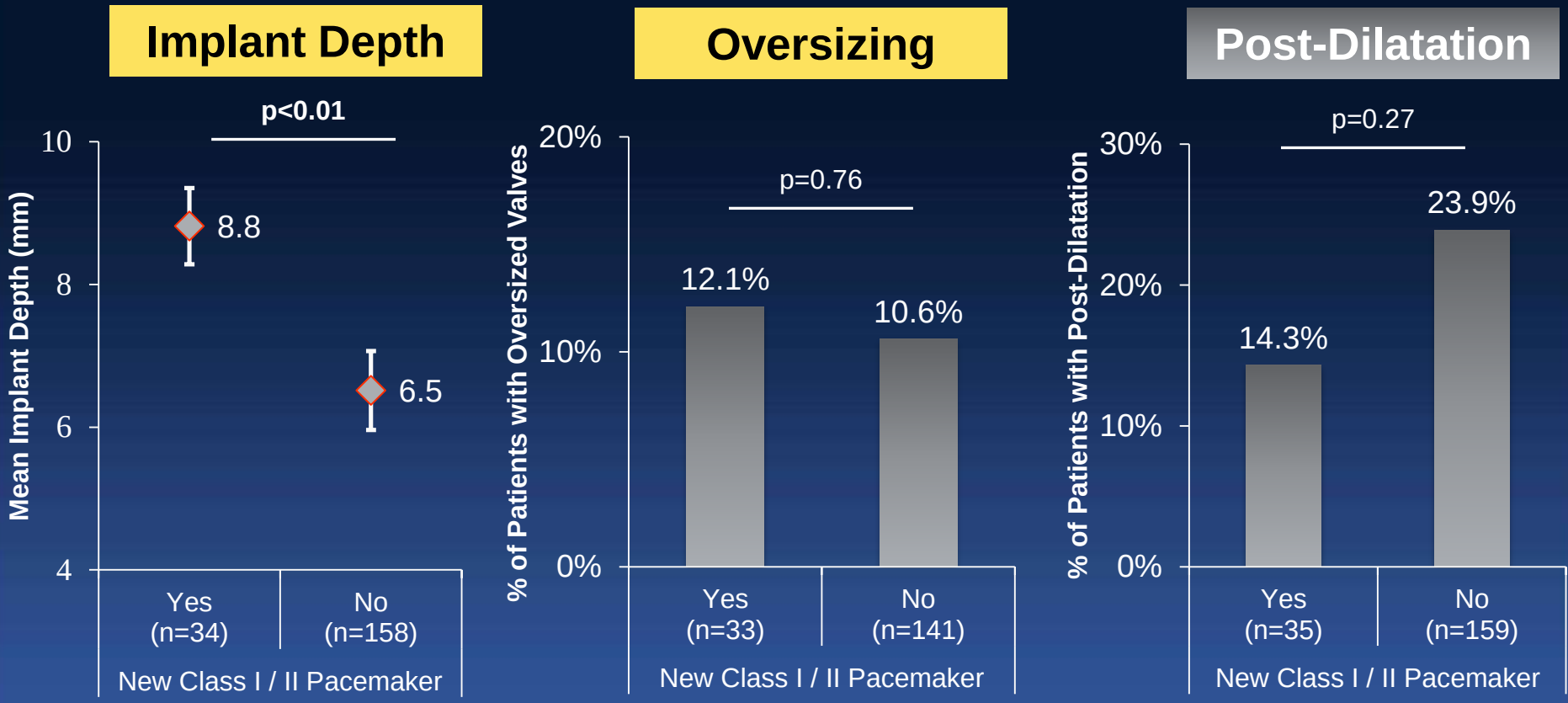
- More than 40 studies have been published on predictors of post-TAVR conduction disturbances (CDs) and permanent pacemaker implant (PPM)
- Studies varied in size, rigor, and the univariable characteristics which were considered, but some central themes emerged:

Clinical	Anatomical	Procedure and Operator-Related
• Male gender[3]	• Variations in location of LBBB exit point[1]	• Radial force of the pro sthesis[3]
• Age > 75 years[9]	• Septum thickness[1,6]	• Implant Depth[2,3,7]
• Previous MI[3]	• Thickness of the non-coronary cusp[1]	• Balloon Aortic Valvulo plasty[8]
• RBBB[2,3,4,5,7]	• Membranous septum l ength[12]	• Application of PPI gui delines[10]
• Other pre-existing conduction disturbances[3,4,8,9]		• Learning Curve[11]

[1]Jilaihawi, et al. Am Heart J 2009; [2]Munoz-Garcıa, et. al. JACC CV 2012; [3]Piazza et. al. EuroIntervention 2010; [4]De Carlo , et. al. Am Heart J 2012; [5]Calvi, et. al. JICE 2011; [6]Saia, et. al. Cath Card I ntv 2012; [7]Fraccarao, et. al. Am J Card 2011; [8]Khawaja, et. al. Circ 2011; [9]Schroeter et. al. EuroPACE 2011; [10]Wenaweser, et. al. presented at EuroPCR 2013; [11]Meredith, et. al. presented at TCT 2012 ;[12] Hamdan, et al. JACC Cardiovasc Interv 2015

Procedural Considerations – Manageable !

ADVANCE II confirmed that implant depth is the strongest procedural predictor of new PPM[1]

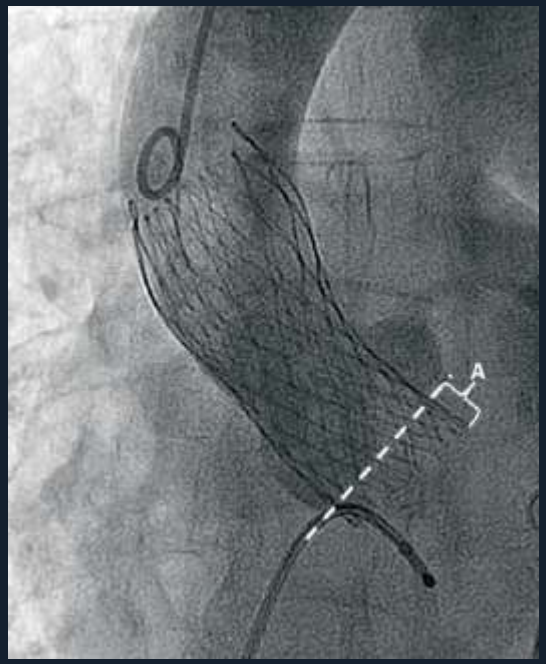


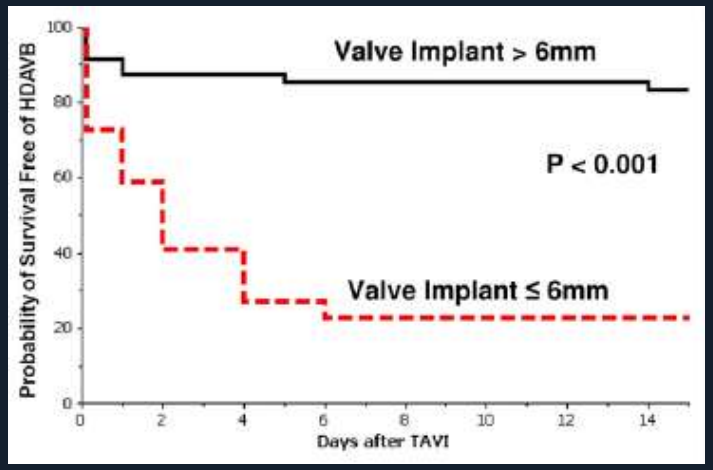
Error bars are standard error
Implant depth defined as the distance from the lower edge of the non-coronary leaflet to the ventricular edge of the frame
*Oversizing occurs when a valve is implanted in an annulus that is smaller than the range defined by the CoreValve sizing guide
% Oversizing = 100 x ([Perimeter of CoreValve– CT Derived Perimeter of the Annulus] / CT Derived Perimeter of the Annulus)

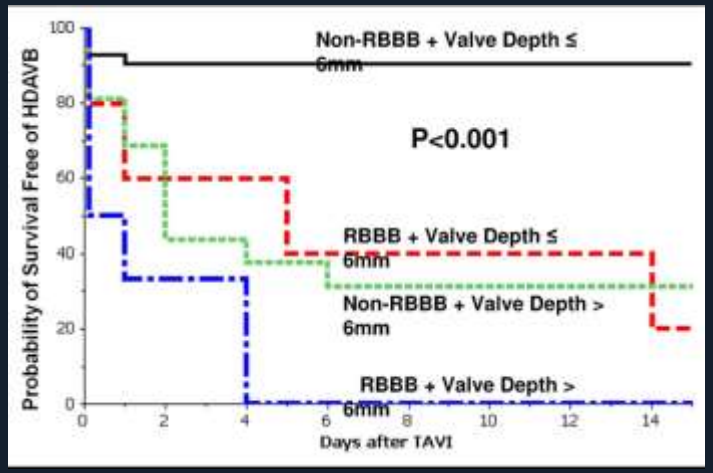
[1]Petronio S, et al., presented at EuroPCR 2014

How to Avoid?
1. High, Shallow Implantation

Depth of Implantation: CoreValve







Gueta et al. AJC 2011

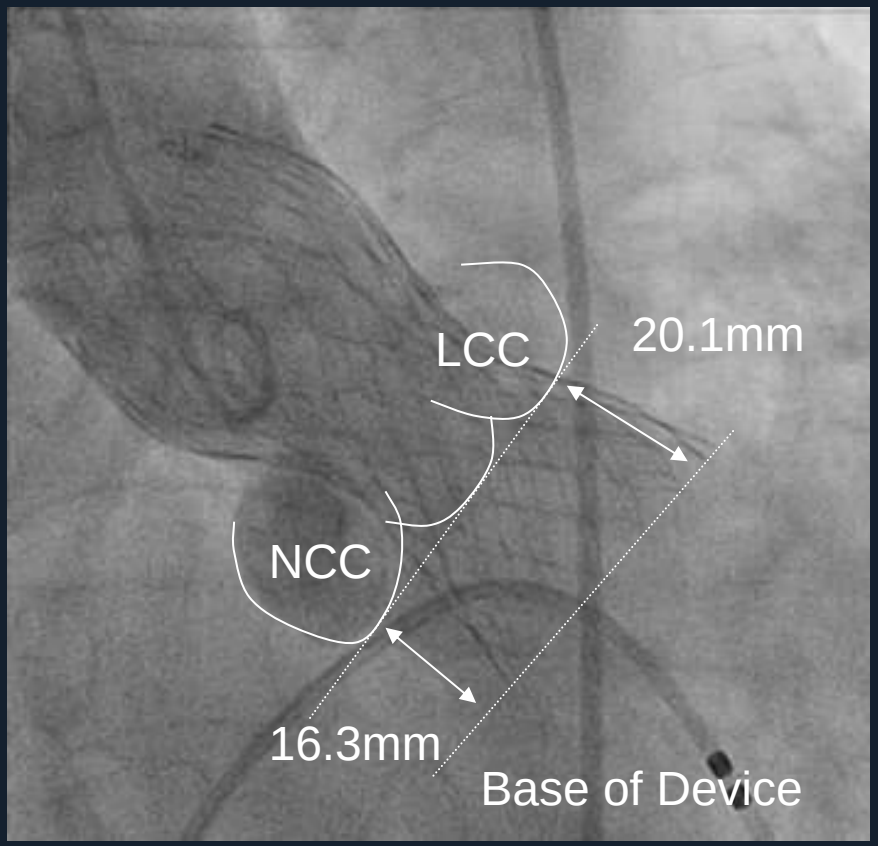
Depth of Implantation: CoreValve

- Kammler et al: MDCT in 53 Patients before and after TAVR with CoreValve

- Depth of Implantation:
  - PPM (9.7 vs 6.3 mm, p=0.001)
  - >6 mm depth sensitivity 89%

Kammler et al. J Cardiol 2016

Device Depth : CoreValve
6 AP centers, N=117 patients

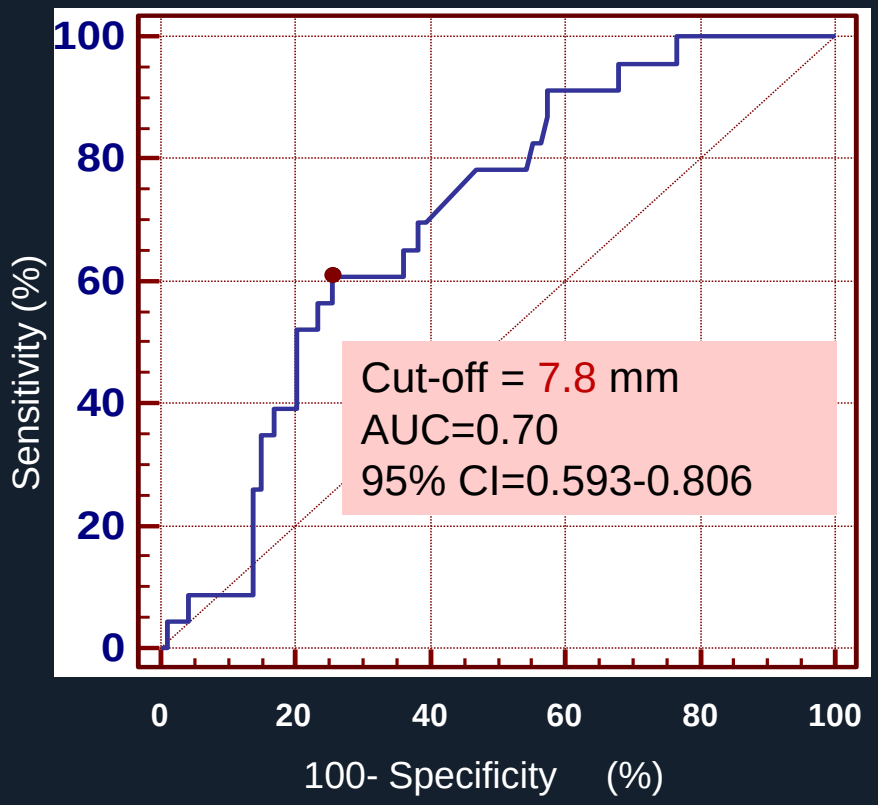


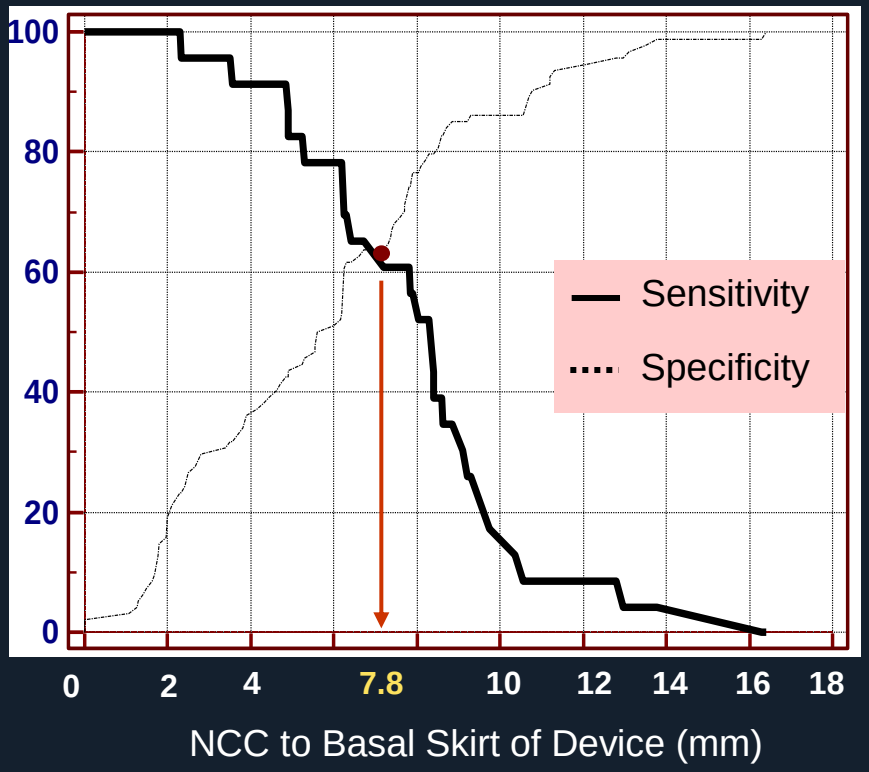
29 mm with PPM

NCC, non-coronary cuspid; LCC, left coronary cusp; PPM, permanent pacemaker

AP Corevalve registry. Kim et al. 2014 ACC. J Inv Cardiol 2015

Device depth vs. PPM

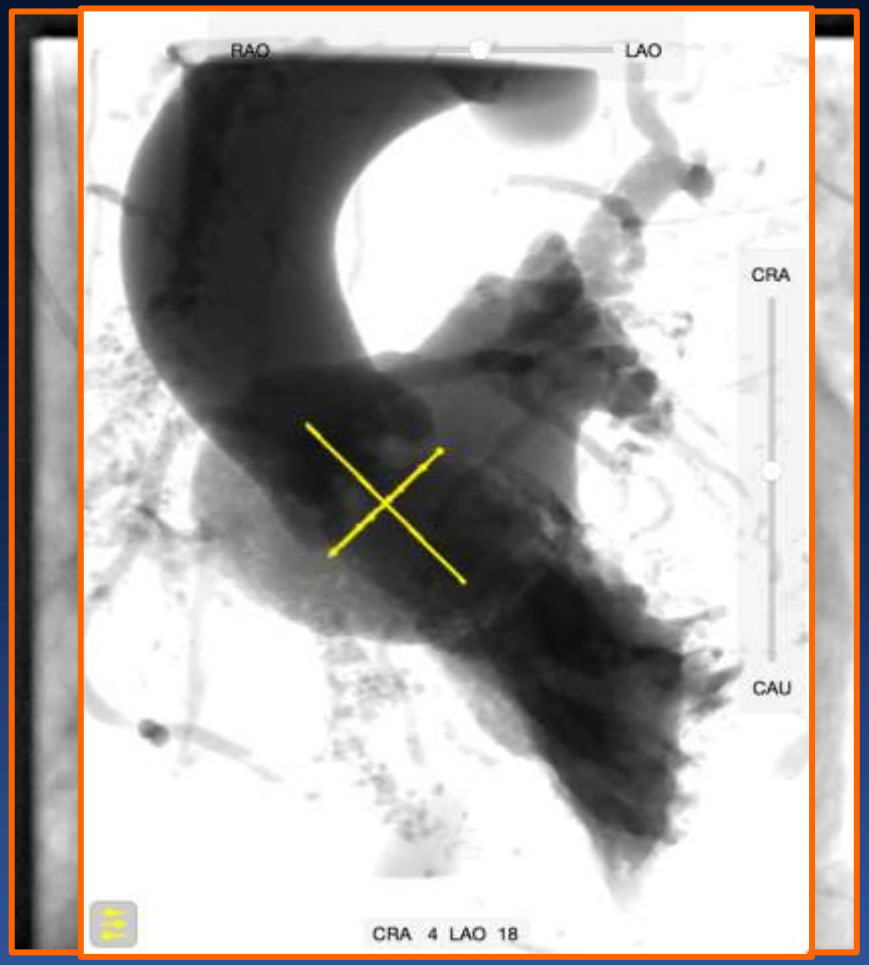




Sensitivity 60.87%, Specificity 74.47%
PPV 35.14%, NPV 87.5%
Accuracy 70.94%

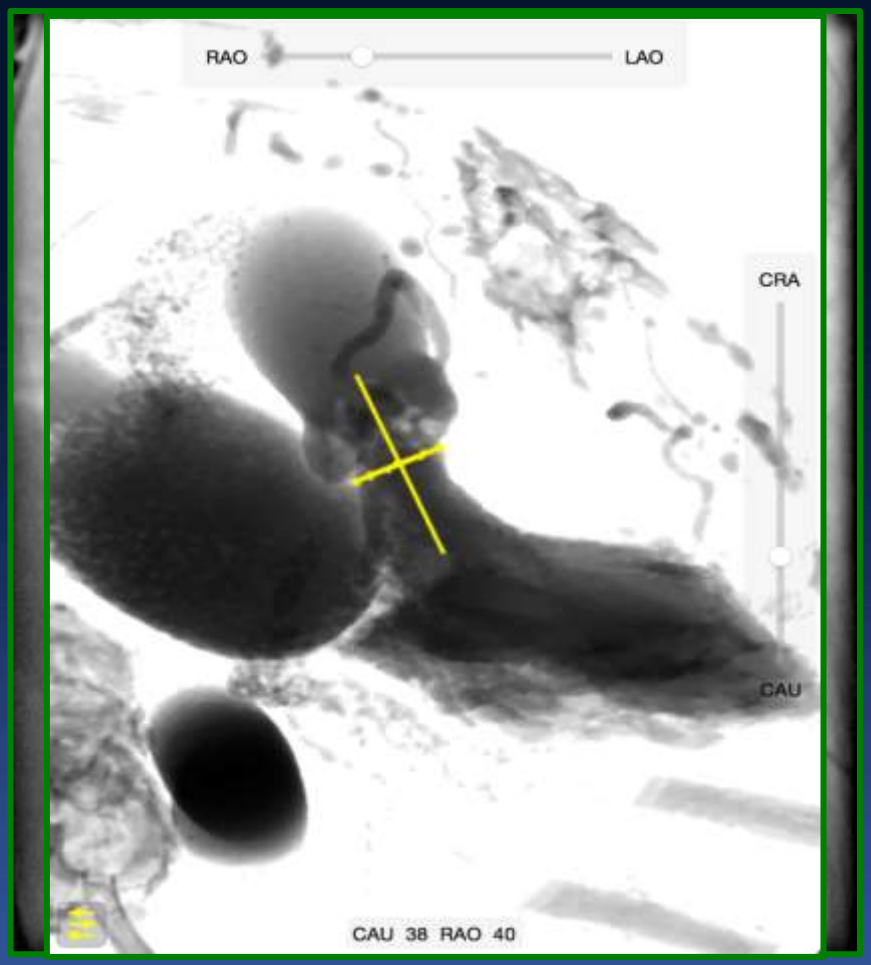
AP Corevalve registry. Kim et al. 2014 ACC. J Inv Cardiol 2015

Why do we perceive a relative difference?



LAO 18 CRA 4
2-chamber view

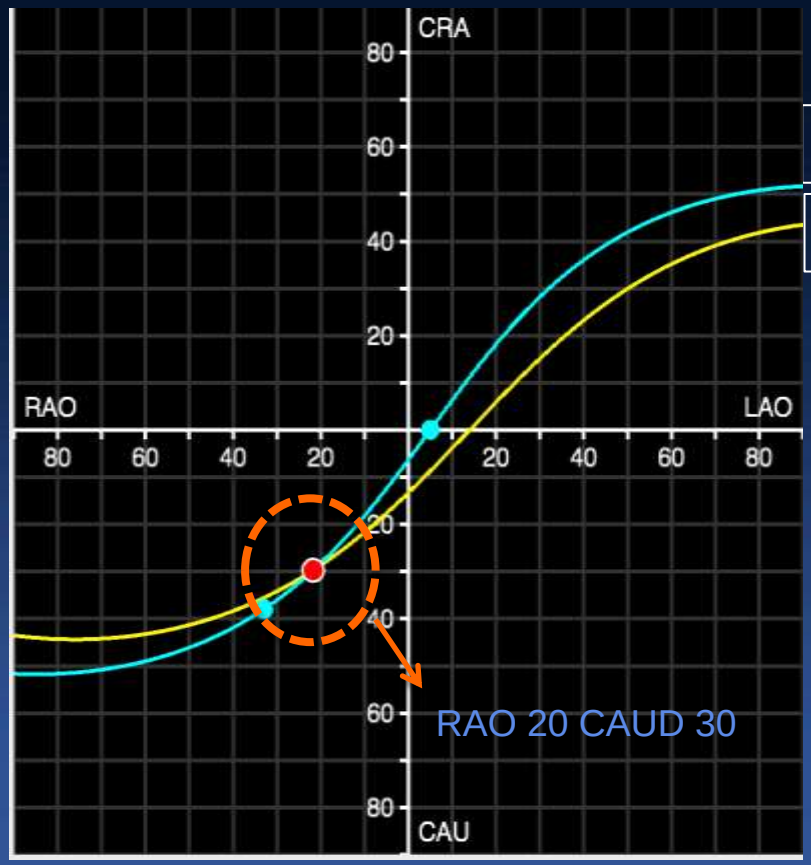
Traditional – LVOT foreshortend



RAO 40 CAU 38
3-chamber view

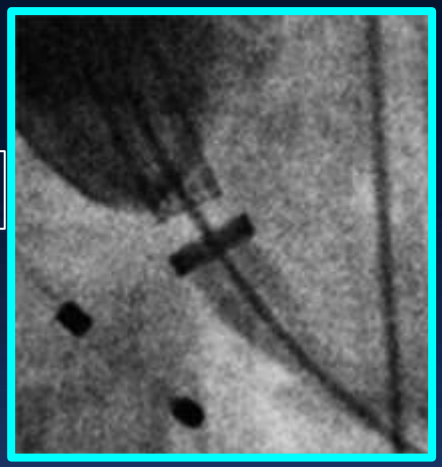
LVOT elongated

Intersection between aortic annulus and delivery catheter S-curves



Delivery catheter

Aortic annulus



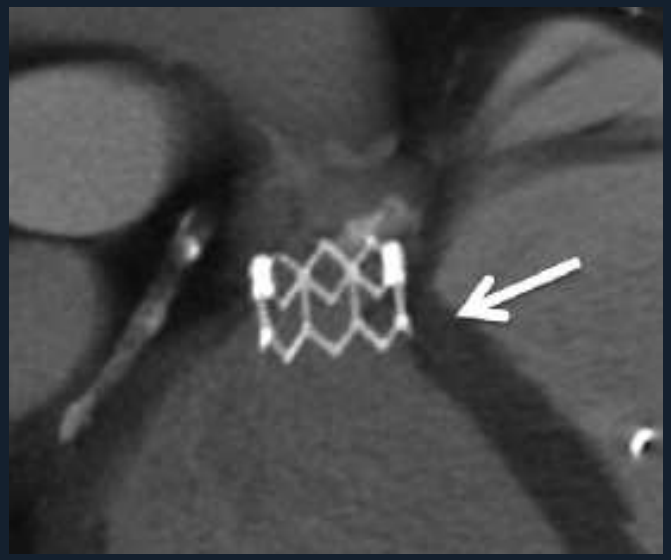
Adapted from N. Piazza EuroPCR 2015

Depth of Implantation SAPIEN

- Binder: MDCT in 89 Patients

  before and after TAVR with ESV

- Depth of Implantation:
  - LBBB/CHB (5.5 vs 3.4mm, p=0.01)
  - PPM (7.1 vs 3.5mm, p=0.001)



Binder et al. JACC Cardiovasc Interv 2013;6:462-8.

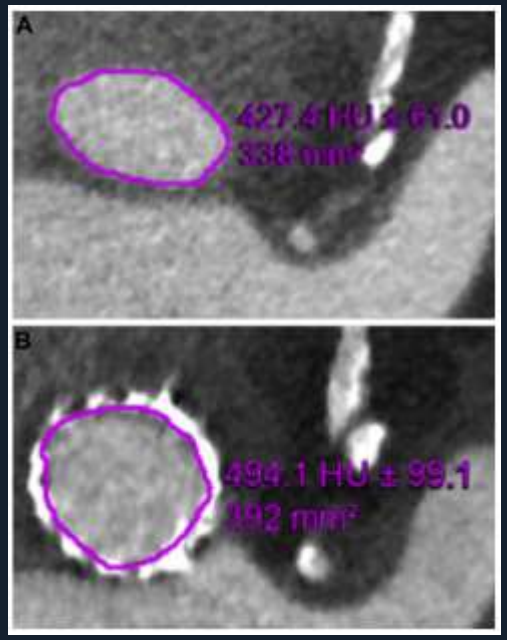
How to Avoid ?

2. Not too much over-size or stretch

THV Over-Sizing

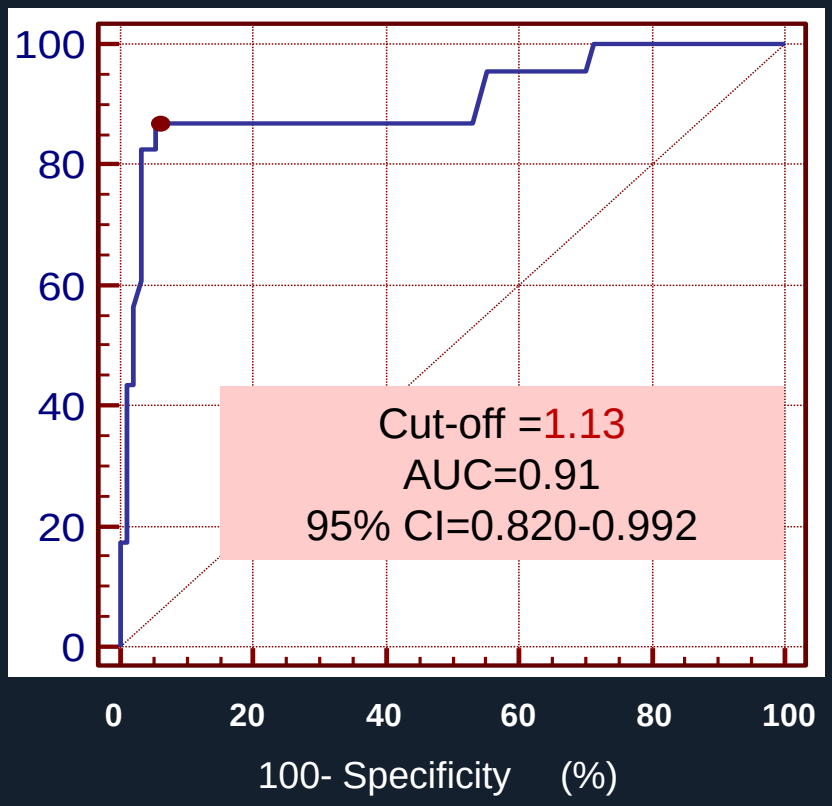
- Katsanos et al: MDCT in 94 Patients before and after TAVR with SAPIEN

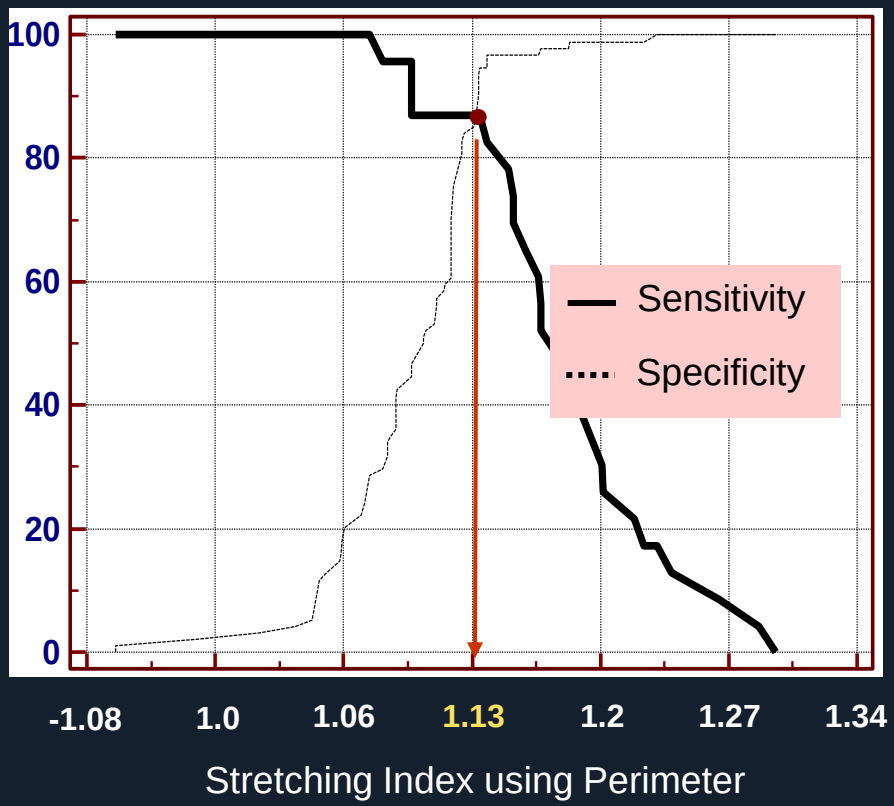
- Independent predictors of PPM included
  - Depth of Implantation: OR 1.4 per mm
  - Annulus Area oversizing > 15%: OR 5.3



Katsanos et al. A J Cardiol 2014

Stretching Index vs. PPM



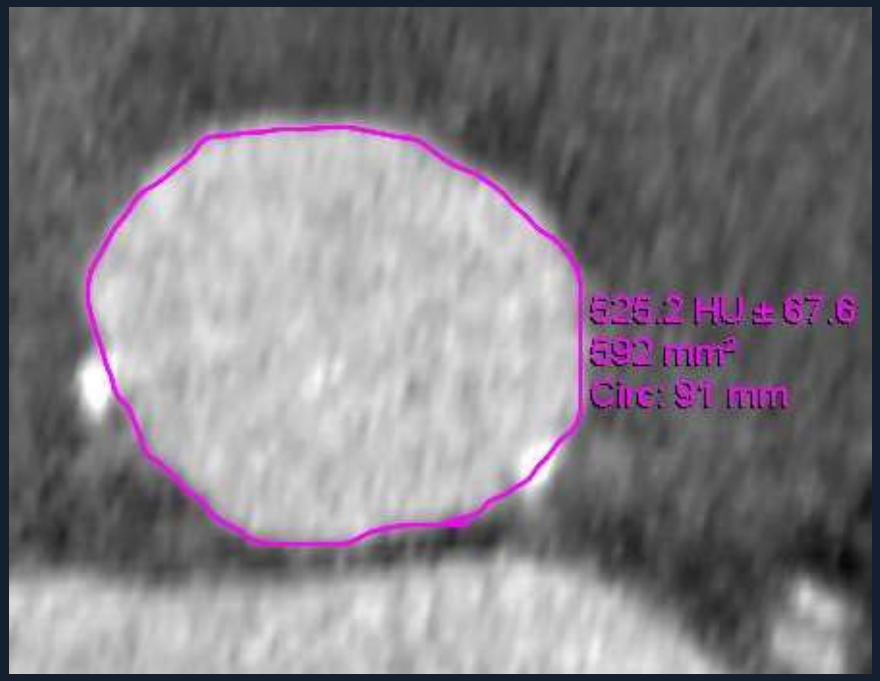


Sensitivity 86.96%, Specificity 94.68%
PPV 80%, NPV 96.74%
Accuracy 93.2%

AP Corevalve registry. Kim et al. 2014 ACC. J Inv Cardiol 2015

Perimeter Stretching Index by CT
Examples – No PPM

31 mm device



Perimeter 91mm; Area 592 mm²

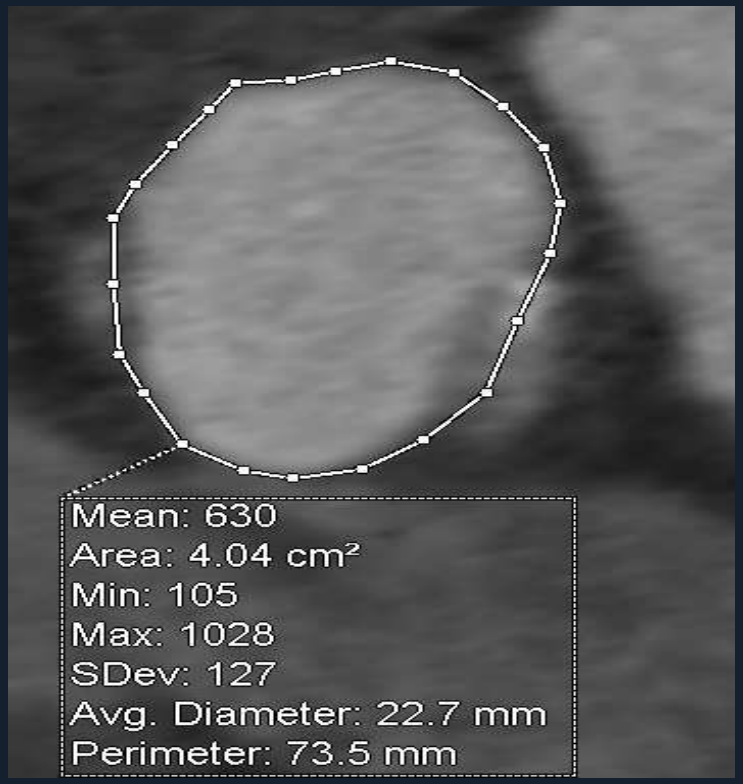
CoreValve, 31 mm
Calculated Perimeter 97.3 mm

Measured Perimeter 91 mm

= 1.07

Perimeter Stretching Index by CT
Examples – PPM

29 mm device



Perimeter 73.5mm; Area 404 mm²

CoreValve: 29mm
Calculated Perimeter 91.1 mm

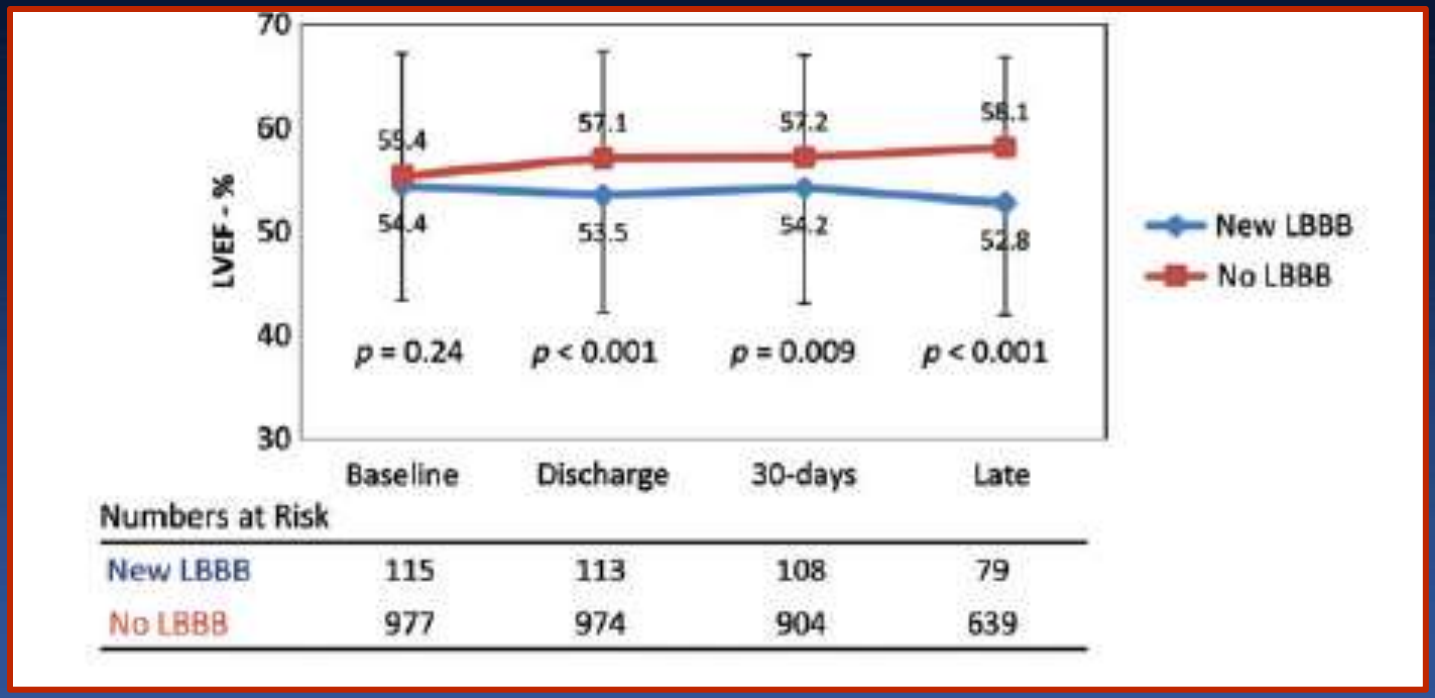
Measured Perimeter 73.5 mm

= 1.24

Beyond Technical Issues

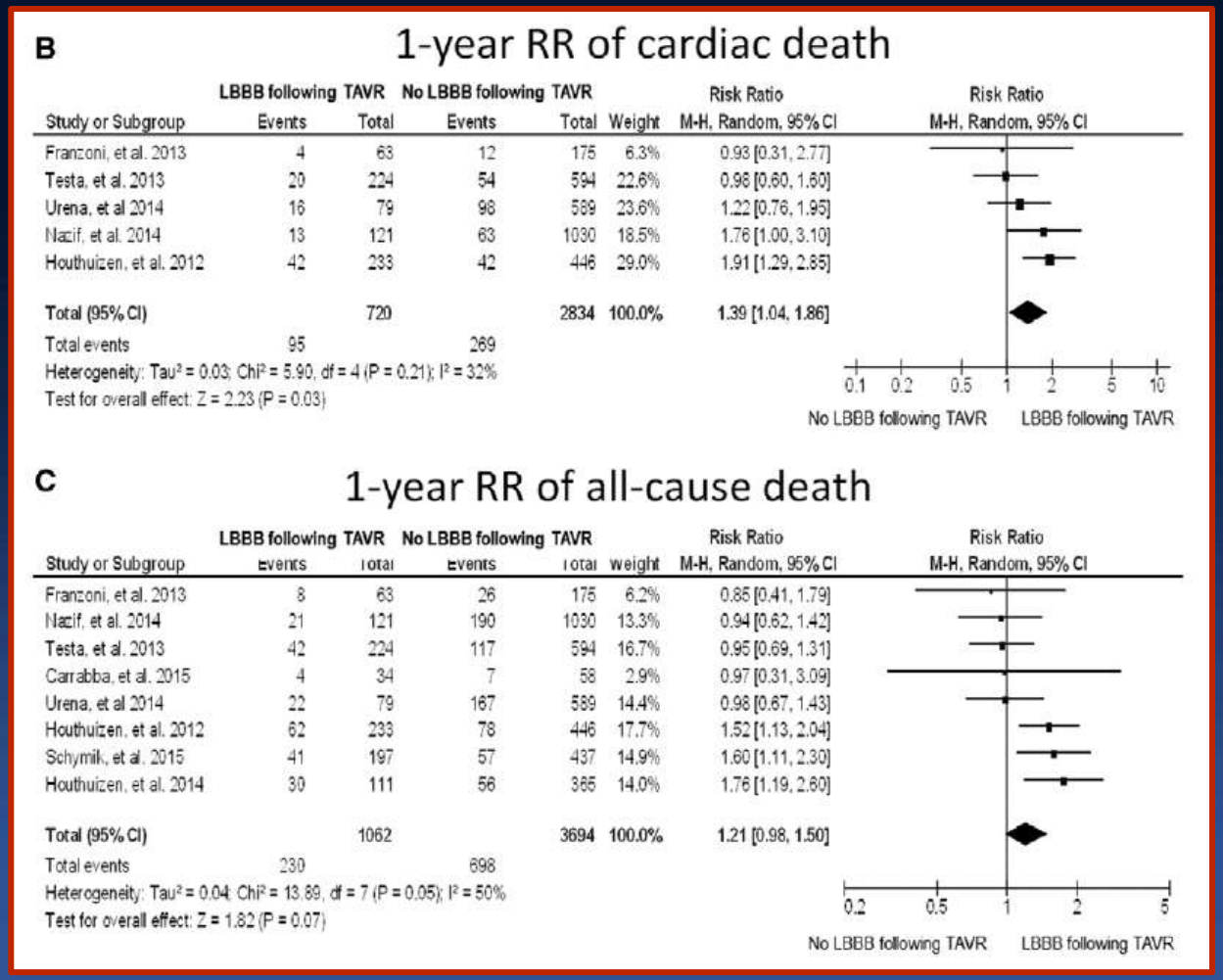
Clinical Impact of Conduction Disturbances: New LBBB and Recovery of LVEF

1151 Patients from PARTNER



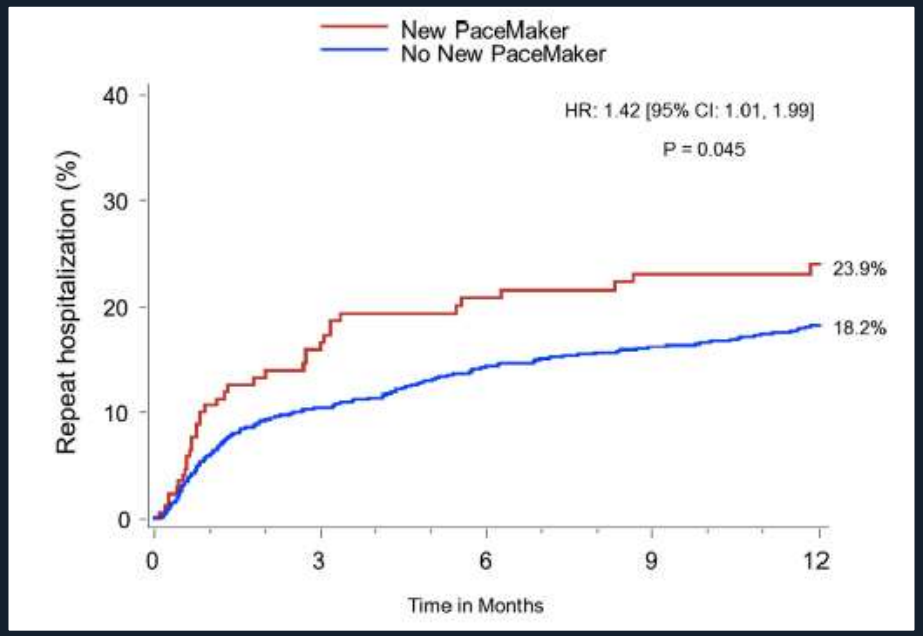
Nazif. European Heart J. 2014;35:1599-607.

Clinical Impact of LBBB after TAVR



Rigueiro, A, et al. Circ Cardiovas Interv 2016;9:e003635

Impact of PPM on Duration of Hospitalization and Re-Hospitalization



- PARTNER : 1973 Sapien
- Post-procedure hospitalization:

  PPM vs No-PPM: 7.3 vs 6.2 days, p<0.001

Nazif et al. JACC Cardiovasc Interv 2015

Additional Costs of PPM after TAVR

Table 5 Factors associated with hospital stay cost (valve excluded): results of the multivariable analysis.

Variable	Model: STS[a]		Model: LES[b]	
	Rate ratio (95% CI)	*P*	Rate ratio (95% CI)	*P*
STS score at inclusion > 10%	1.15 (1.05–1.27)	< 0.01	NA	NA
LES at inclusion > 20%	NA	NA	NR	NR
Warfarin use at inclusion	1.15 (1.04–1.28)	0.01	1.16 (1.05–1.29)	< 0.01
Transapical approach	1.14 (1.03–1.27)	0.02	1.14 (1.02–1.27)	0.02
Use of hybrid room	NR	NR	1.17 (1.02–1.36)	0.03
Complication(s) during procedure	1.19 (1.06–1.33)	< 0.01	1.17 (1.05–1.29)	< 0.01
Pacemaker implantation during hospitalization	1.36 (1.20–1.54)	< 0.001	1.36 (1.21–1.54)	< 0.001
Adjusted R^2	0.14	0.13		

CI: confidence interval; LES: Logistic Euroscore; NA: not applicable; NR: not retained in the final model because not significant; STS: Society of Thoracic Surgeons.

[a] STS score and all other variables except those u

[b] LES and all other variables except those used fo

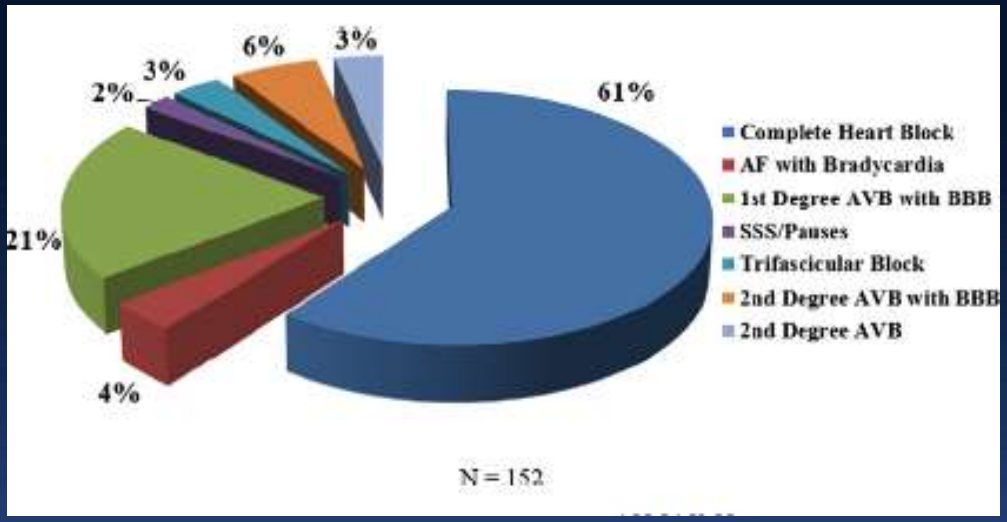
Estimates of the additional cost of complications with respect to different cost units and categories.

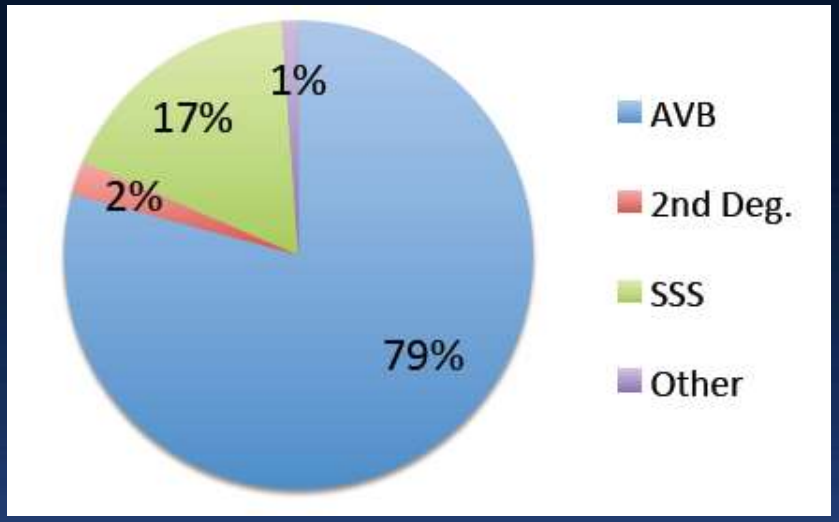
Variables	Number of events	Cost unit (in €)				Cost category (in €)			Total in-hospital costs (in €)
		Normal ward (in €)	ICU (in €)	Cath lab/OR (in €)	Other costs (in €)	Staff costs (in €)	Material costs (in €)	Infrastructure costs (in €)	
Constant (predicted costs in case of no complication)		3707**	3960**	23,815**	2666**	7319**	23,624**	3403**	34,351**
TA instead of TF-TAVI	66	2495**	−393	−104	576	1836+	−968	1422**	2307
Access site bleeding – life threatening	18	−1822+	4277	1142	1804+	1938	3709*	−80	5556
Access site bleeding – major	13	17	590	1589	−234	−59	2674	−545	2066
Access site bleeding – minor	8	491	840	−74	698	1269	265	455	1989
Non-access site bleeding – life threatening	4	929	37,322*	1146	8553*	24,031*	14,238+	9217**	47,494*
Non-access site bleeding – major	7	758	−1392	−197	163	−846	113	197	−533
Non-access site bleeding – minor	12	654	−774	476	11	264	−169	335	432
Vascular complication – major	19	814	455	−611	−55	789	−1493	910	210
Vascular complication – minor	26	780	180	364	286	710	558	295	1563
Stroke (including TIA)	8	1573	−3350	3168	−141	−378	1423	187	1227
Acute kidney injury – stage 1	14	1242	−1688	−185	−602	−519	−438	−238	−1203
Acute kidney injury – stage 2	10	1535	9530+	−545	1181	6034+	3721	2050+	11,811+
Acute kidney injury – stage 3	12	362	17,040**	−1358	4043**	11,931**	4356+	4192**	20,468**
Second valve	4	−994	−1174	13,856**	371	−924	18,302**	−611	16,767**
Atrial flutter/fibrillation	13	132	1078	−1001	245	631	496	276	1397
Pacemaker implantation	56	380	−715	1946*	370	849	−95	690+	1441
Other severe cardiac dysrhythmia	11	1586	5490+	200	3224**	5592*	3001+	2028+	10,611+
Moderate aortic insufficiency	11	−363	510	596	−592	−81	130	−1	46
Adjusted R^2		0.06	0.58	0.28	0.45	0.54	0.45	0.49	0.51
N		163	163	163	163	163	163	163	163

In addition to the complications shown above, 'other complications' as described in Table 1 were also included in the regression analyses.

Chevreul. Arch Cardiovasc Dis 2013, Gutmann. IJC 2015

Indication for PPM After TAVR





N=152, 98% MCV

Steinberg. Am Heart J. 2012;164:664-71

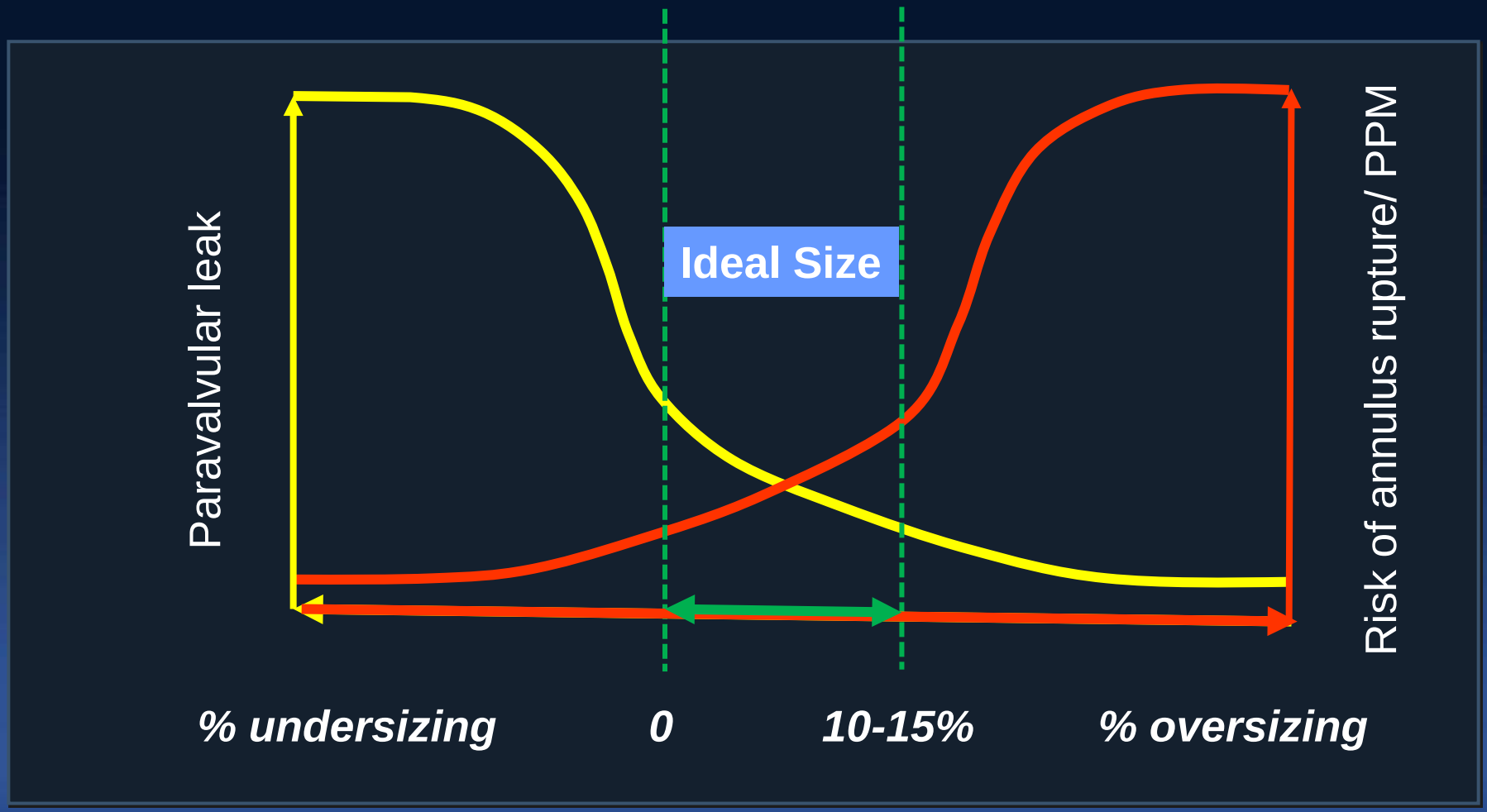
N=173 ESV

Nazif. JACC Intervention 2015

Adapted from Nazif T. TVT 2017

Rupture/ PPM vs. PVL

Annulus Size Assessment is Crucial: Multidisciplinary Image



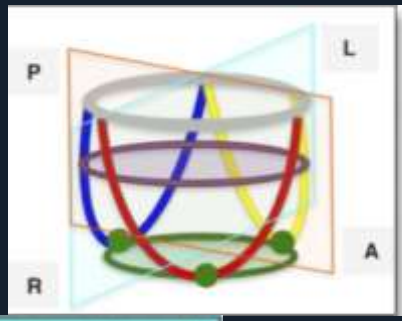
Adapted from Thierry Lefevre; London Valves, 2012

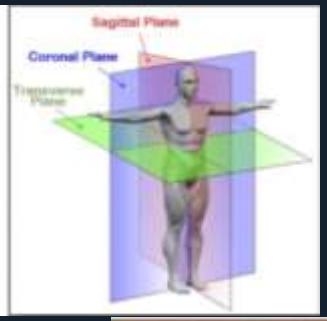
Conclusions

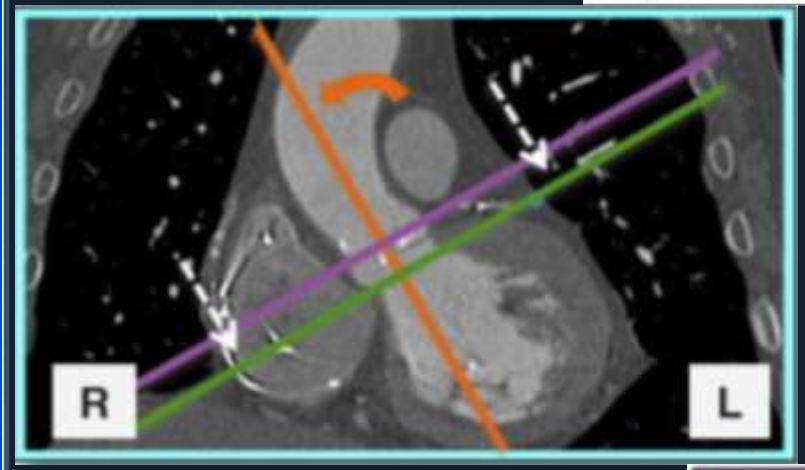
- Conduction disturbances and PPM are frequent complication of TAVR
- Most of them resolve over time as the tissue heals and adapts to the THV valve
- However, the conduction disturbances that remain may not be benign
  - LBBB deterioration to more severe conduction disturbances with time
  - Asynchronous contraction patterns due to LBBB or RV pacing may lead to heart failure
- Risk is determined by a complex between patient substrate (RBBB, calcification, etc) and procedural factors
- Careful attention to positioning THV valves 4-6 mm or less relative to the annulus (self-expanding) and less-oversizing (balloon-expandable) will minimize conduction disturbances
- Watchful waiting prior to PPM implantation may be warranted (conservative strategy by guideline)

Thank you.

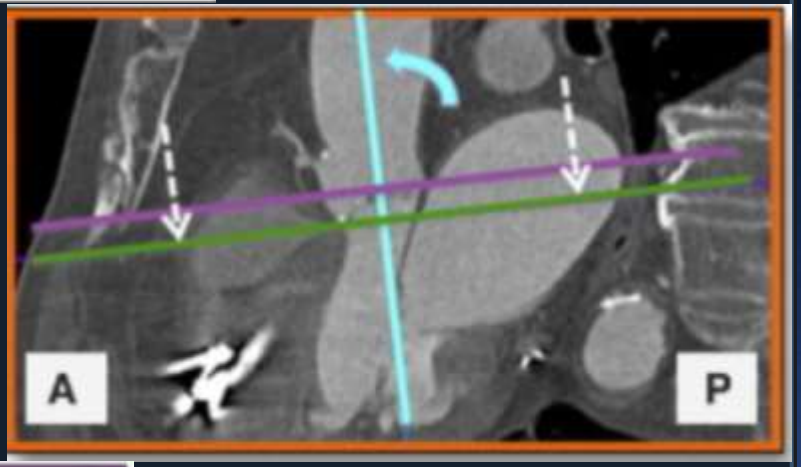
Aortic Annulus on MSCT



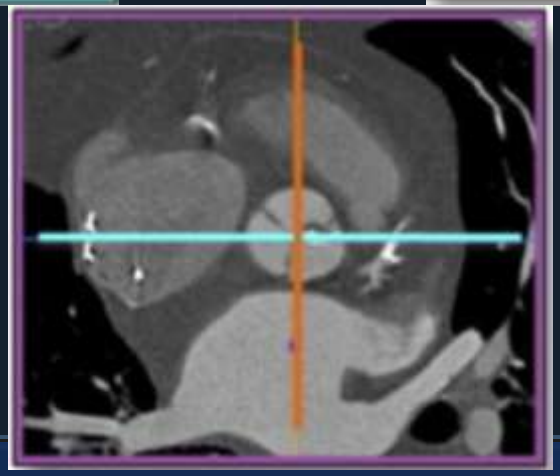




Oblique Coronal Image

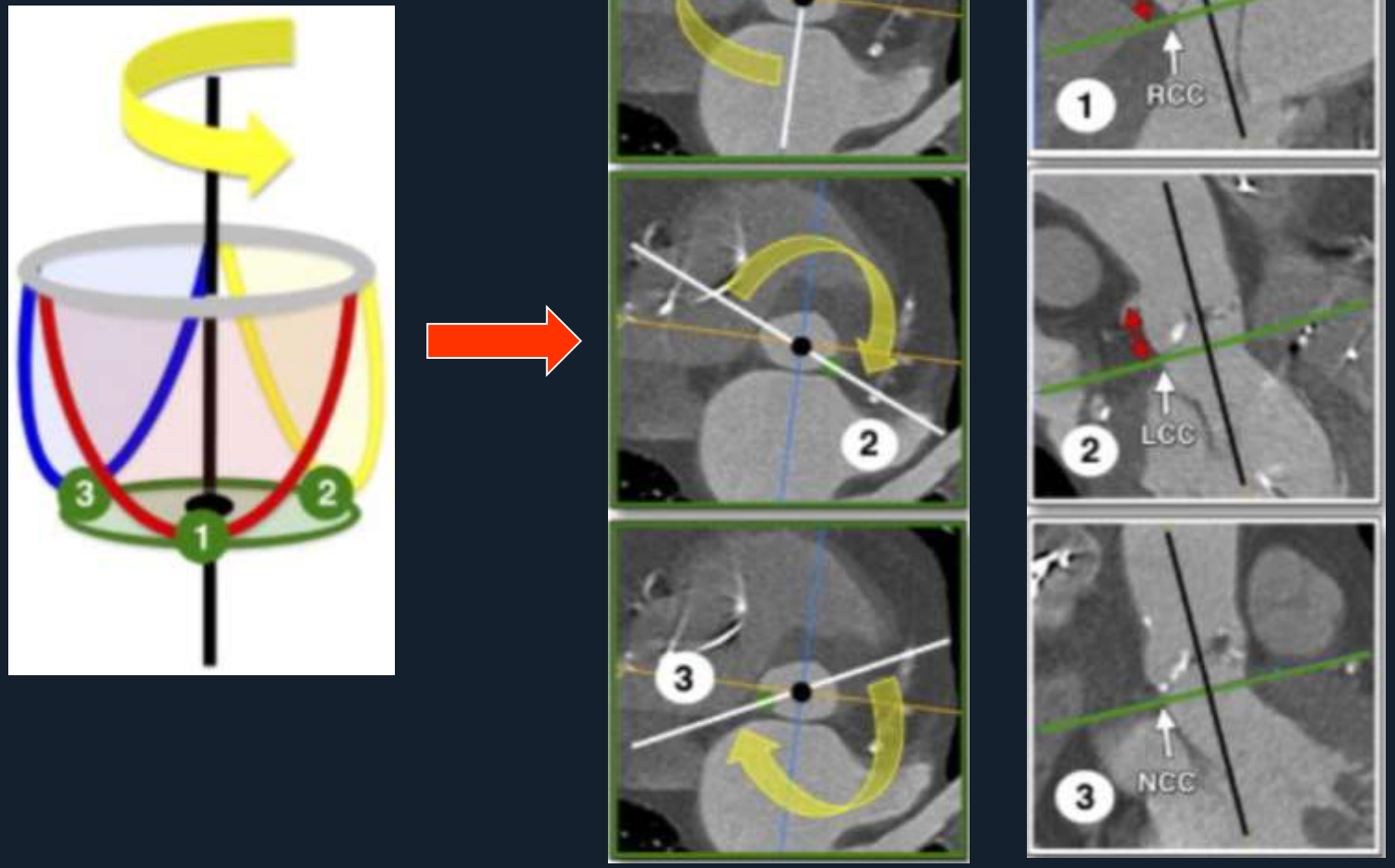


Oblique Sagittal Image



Transverse Image

Aortic Annulus on MSCT

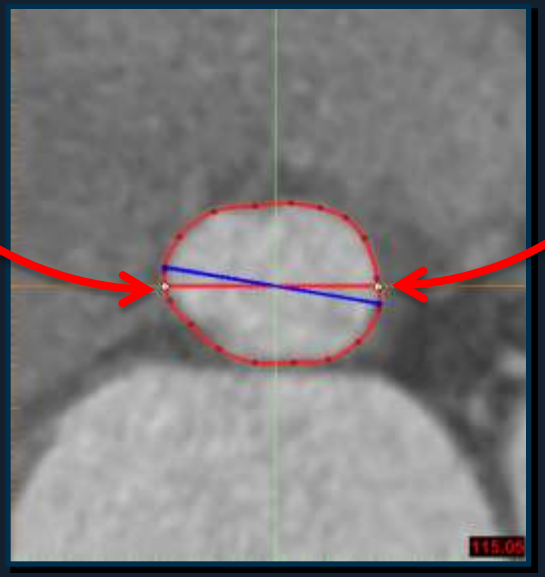


Aortic Annulus on MSCT

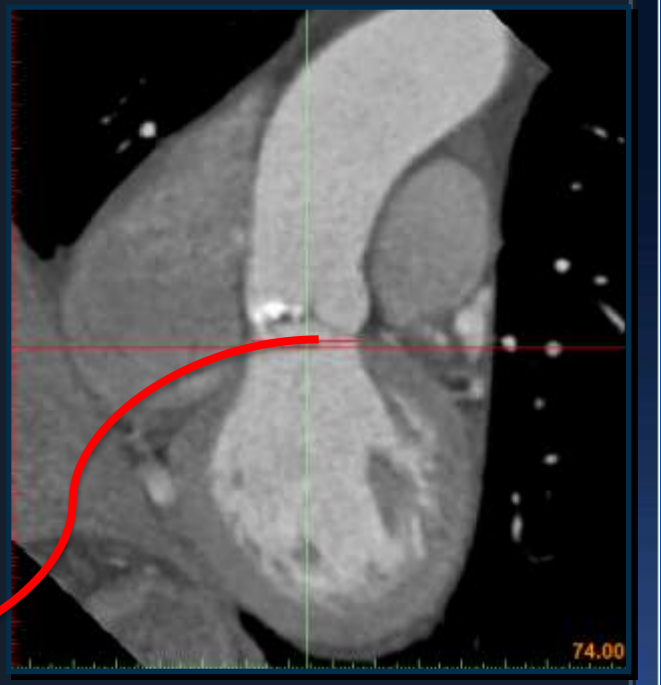
Coronal measurements do not equal those from the annular plane

Coronal Image

MPR



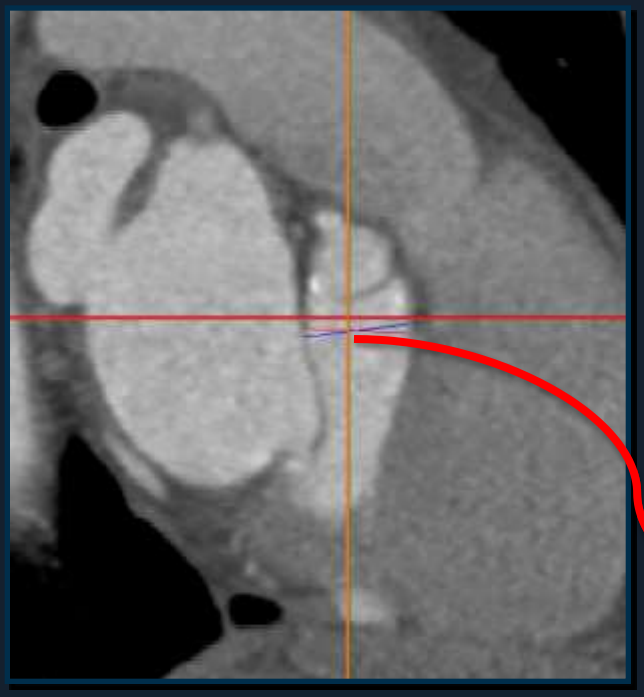
Aortic Annulus



Oblique Coronal Image

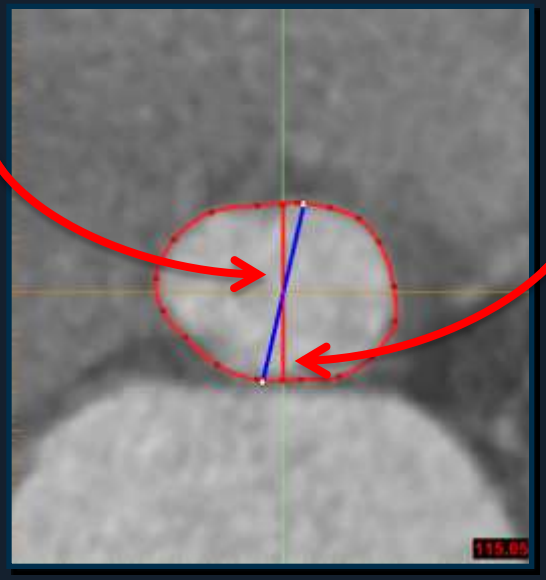
Aortic Annulus on MSCT

Sagittal measurements do not equal those from the annular plane



Sagittal Image

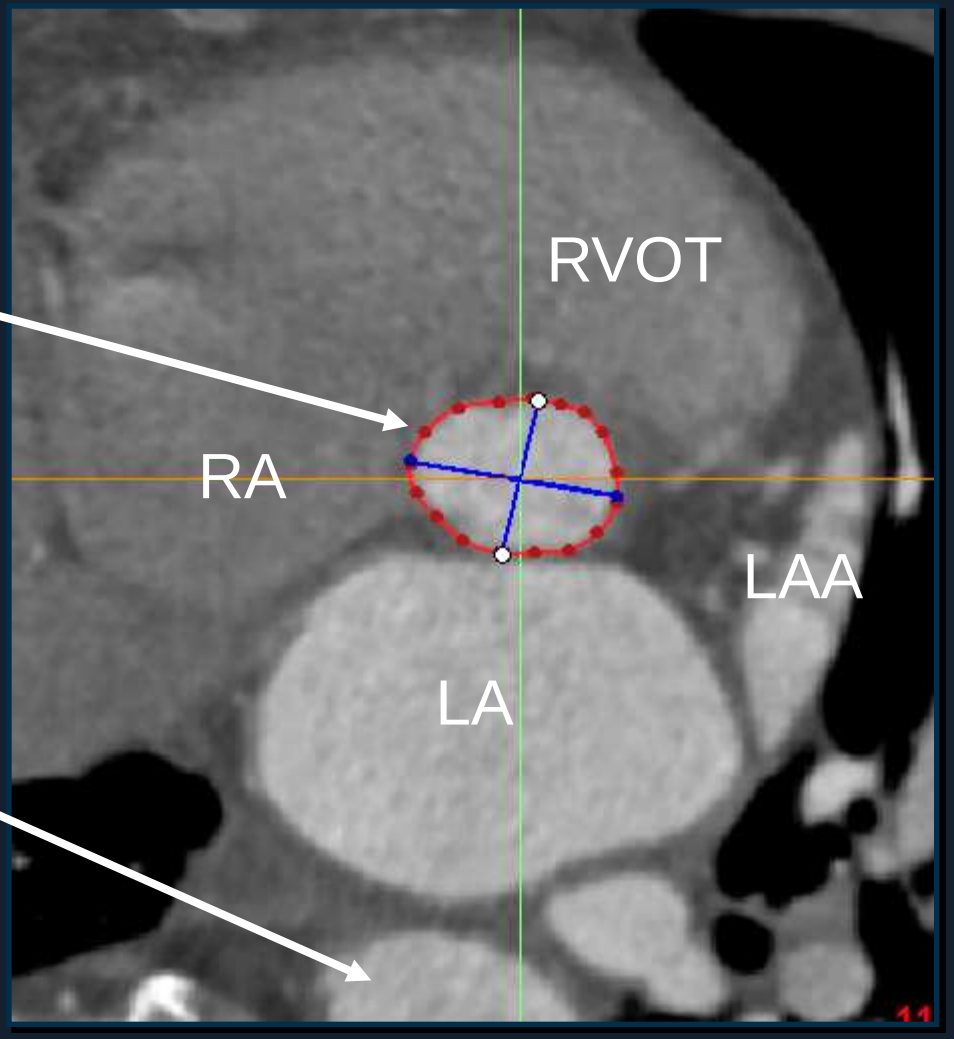
MPR



Aortic Annulus

Oblique Sagittal Image

The Aortic Annulus on MSCT



New CT Parameters

Area-derived virtual Diameter
√(4*Area/π)

Area

Minimum Diameter

Ellipticity Ratio
Maximum Diameter/
Minimum Diameter

Maximum Diameter

Perimeter

Perimeter-derived virtual Diameter
Perimeter/π

CT Sizing for Edwards Valve

J Am Coll Cardiol Img. 2013;6(2):249-262.

CT Sizing for Edwards S3

3D Area - derived Diameter (mm)		20.0	20.2	20.5	20.7	21.0	21.1	21.4	21.7	22.0	22.3	22.6	22.8	23.0	23.1	23.4	23.7	23.9	24.0	24.2	24.7
3D Annular Area (mm^2)		314	320	330	338	346	350	360	370	380	390	400	410	415	420	430	440	450	452	460	480
% Annular Area Over (+) or Under (-) Nominal by 3D CT	23mm	29.3	26.9	23.0	20.1	17.3	16.0	12.8	9.7	6.8	4.0	1.5	-1.0	-2.2	-3.3	-5.6	-7.7	-9.8			
	26mm											29.8	26.6	25.1	23.6	20.7	18.0	15.3	14.8	12.8	8.1
	29mm																				

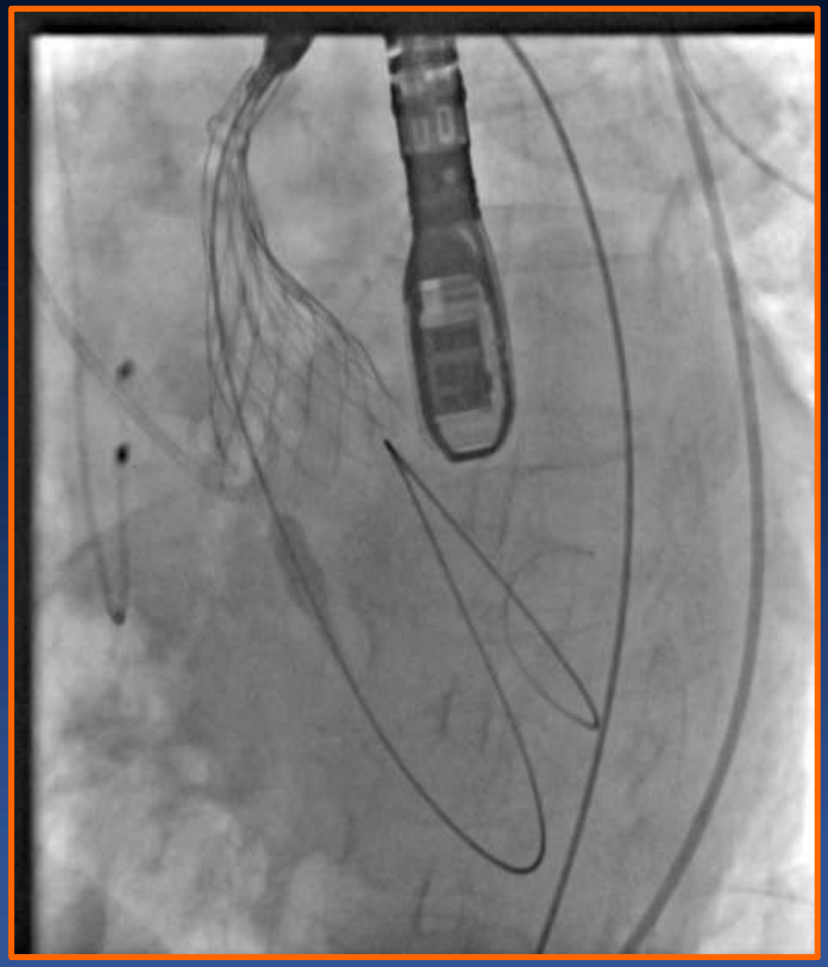
25.0	25.2	25.5	25.7	26.0	26.2	26.4	26.5	26.7	26.9	27.2	27.4	27.6	27.9	28.0	28.1	28.3	28.5	28.8	29.0	29.2	29.4	29.5	29.6	29.9	30.1	30.3
490	500	510	520	530	540	546	550	560	570	580	590	600	610	615	620	630	640	650	660	670	680	683	690	700	710	720
5.9	3.8	1.8	-0.2	-2.1	-3.9	-4.9	-5.6	-7.3	-8.9																	
	29.8	27.3	24.8	22.5	20.2	18.9	18.0	15.9	13.9	11.9	10.0	8.2	6.4	5.5	4.7	3.0	1.4	-0.2	-1.7	-3.1	-4.6	-5.0	-5.9	-7.3	-8.6	-9.9

CT Sizing for CoreValve

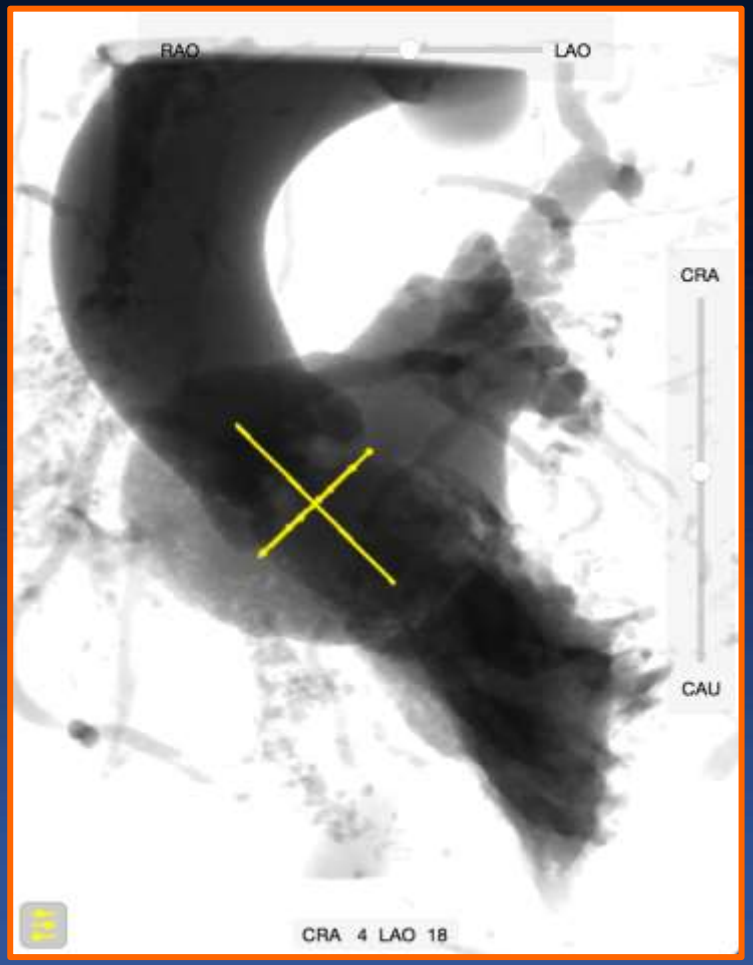
Valve Size	Aortic Annulus Measurements			Sinus of Valsalva Diameter	Native Leaflet to Sinotubular Junction Length	Ascending Aorta Diameter*
	Diameter	Perimeter	Area Range			
23	18-20 mm	56.5-62.8 mm	254.5-314.2 mm	≥ 25 mm	≥ 15 mm	≤ 34 mm
26	20-23 mm	62.8-72.3 mm	314.2-415.5 mm	≥ 27 mm	≥ 15 mm	≤ 40 mm
29	23-26 mm	72.3-81.7 mm	415.5-530.9 mm	≥ 29 mm	≥ 15 mm	≤ 43 mm
31	26-29 mm	81.7-91.1 mm	530.9-660.5 mm	≥ 29 mm	≥ 15 mm	≤ 43 mm

*Ascending Aorta measurements are taken at 30 mm from the aortic annulus for the 23 mm device and at 40 mm from the aortic annulus for the 26, 29, and 31 mm devices.

Valve position too high?

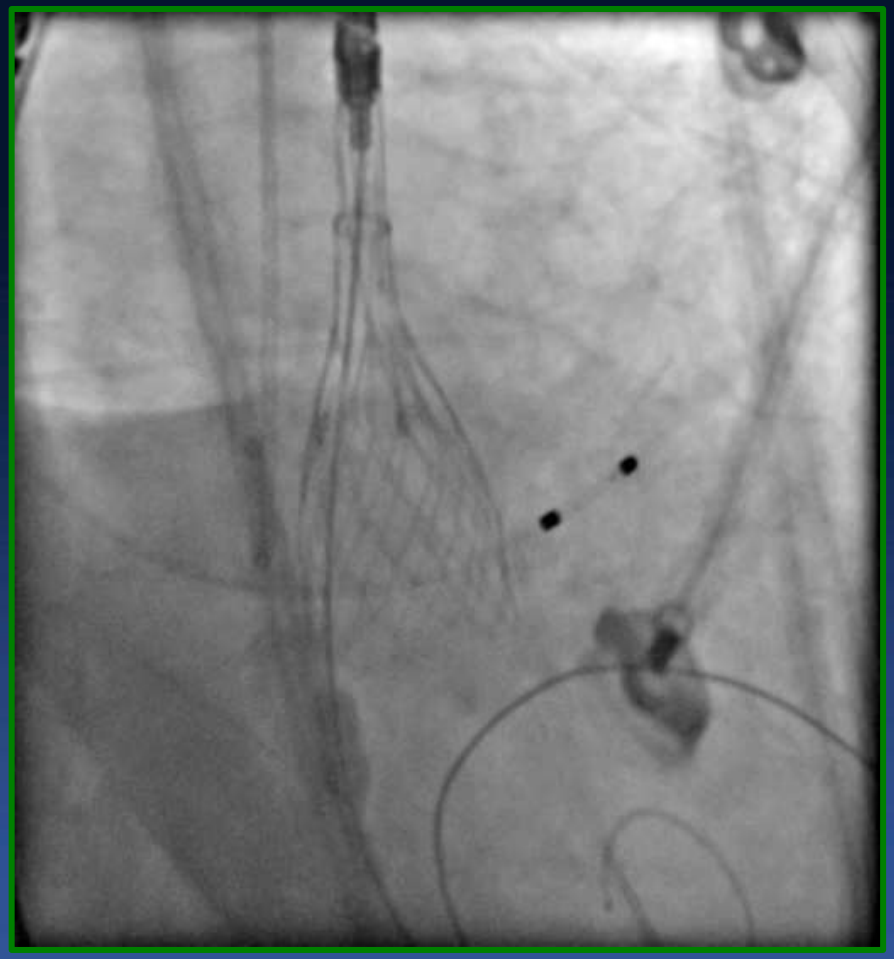


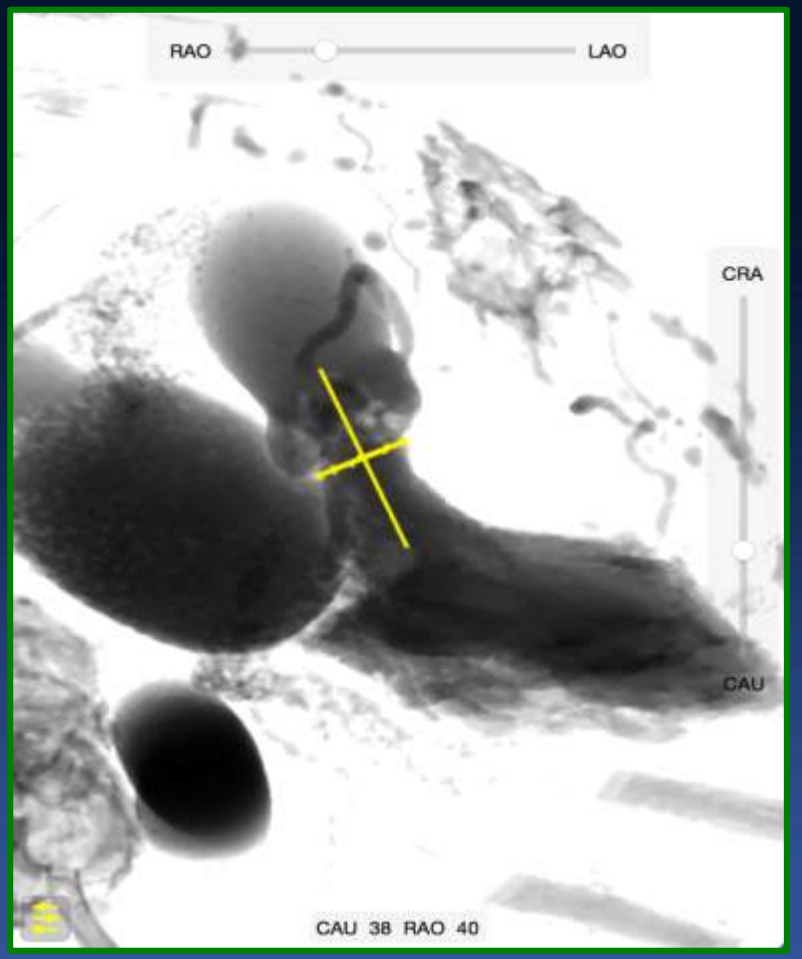
LAO 18 CRA 4



Concomitant TEE

Valve position correct?





RAO 40 CAU 38