Paravalve Leak
: Mechanism and Prevention

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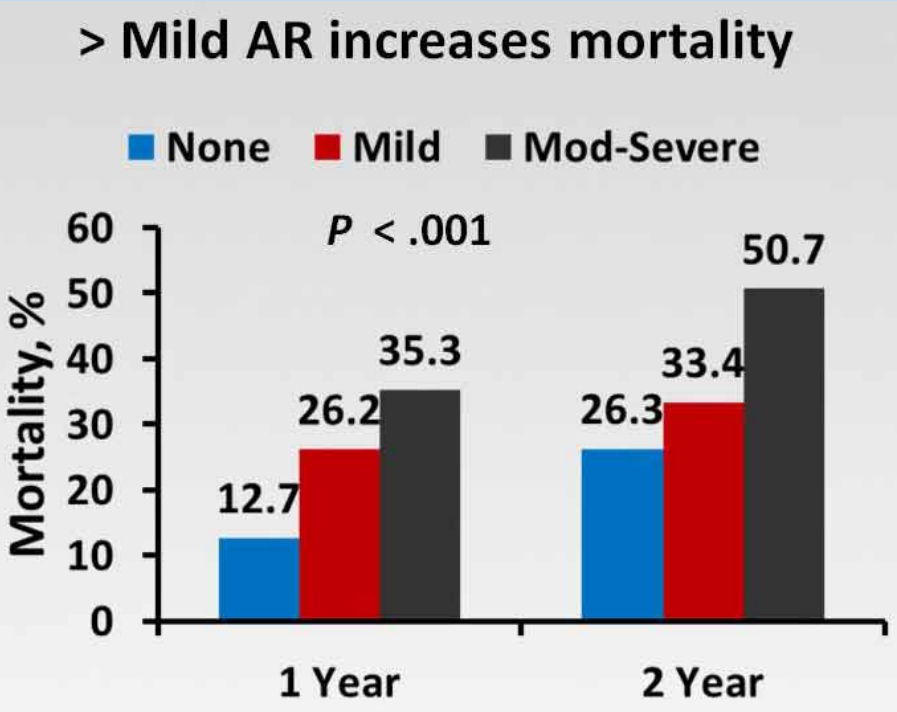
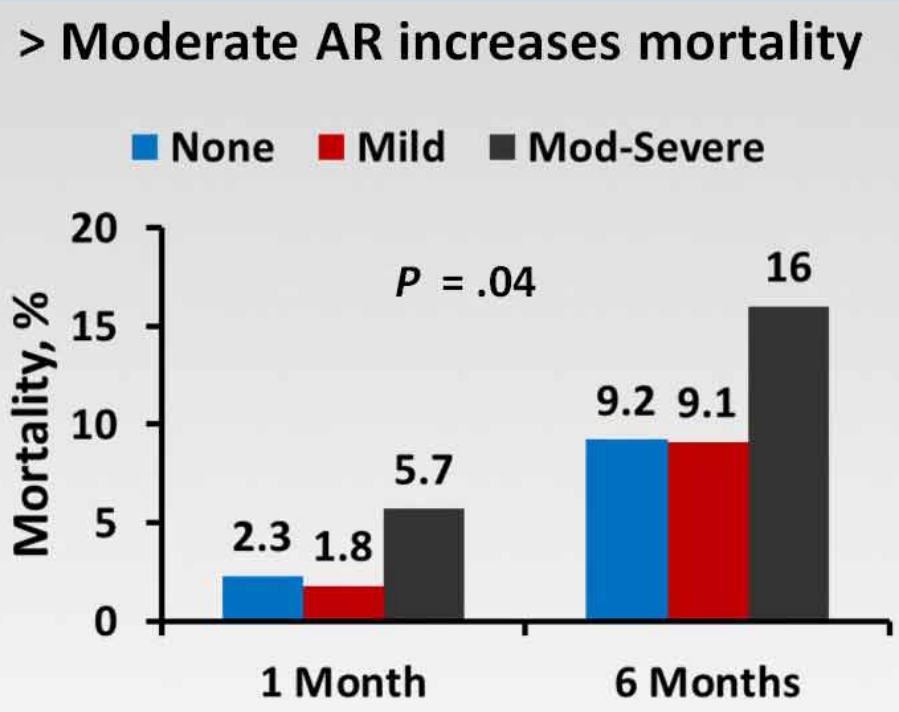
PVL, the new Achilles' heel?

Even mild or moderate PVL can increase mortality





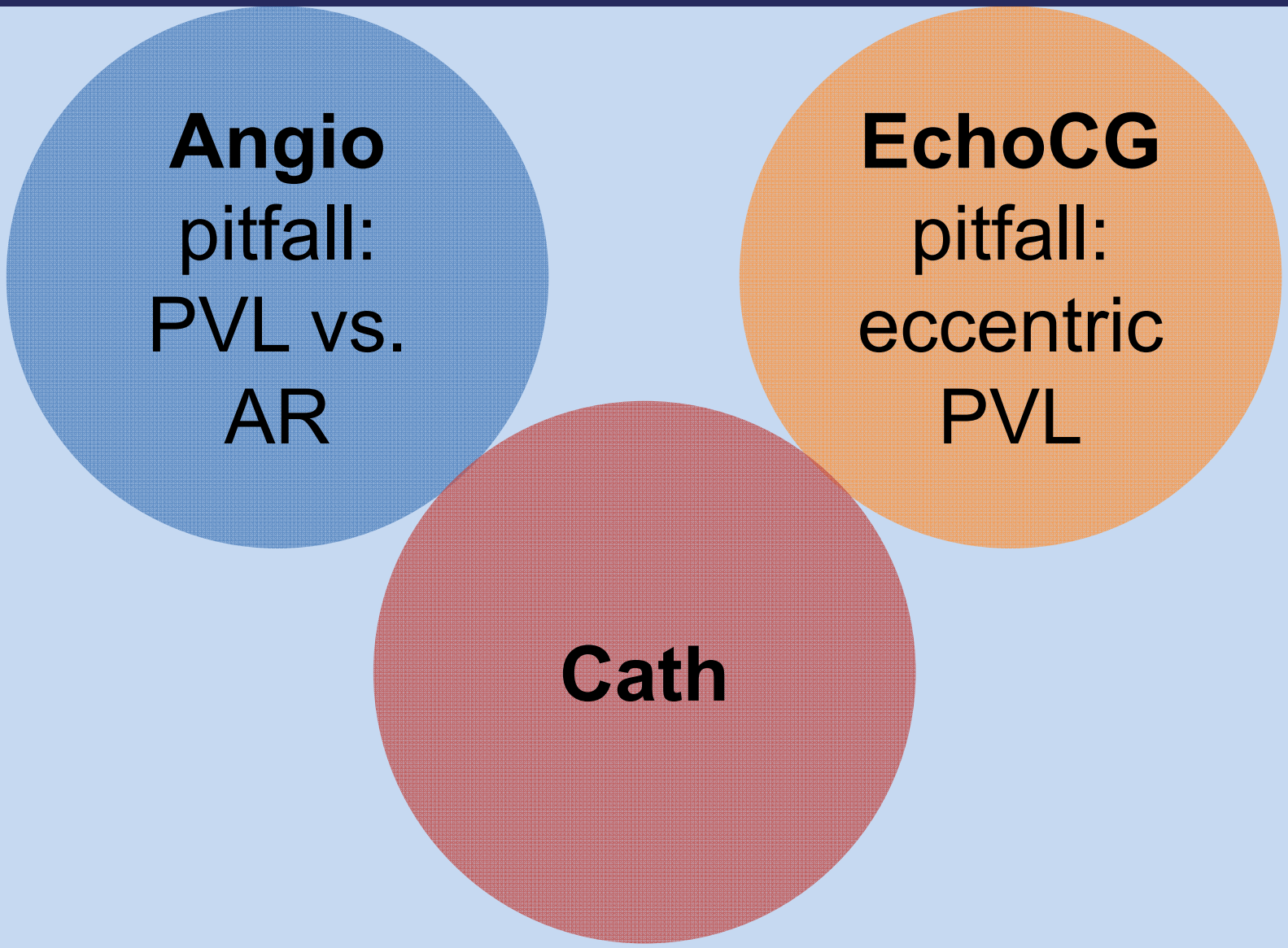
PARTNER Cohort A *Sapien valve*
None/Trace (n = 135);
Mild (n = 165);
Moderate-Severe (n=34)

ADVANCE Registry *CoreValve*
None (n = 166);
Mild (n = 551);
Moderate-Severe (n=132)

Kodali SK. et al. N Engl J Med 2012;366:1686-95

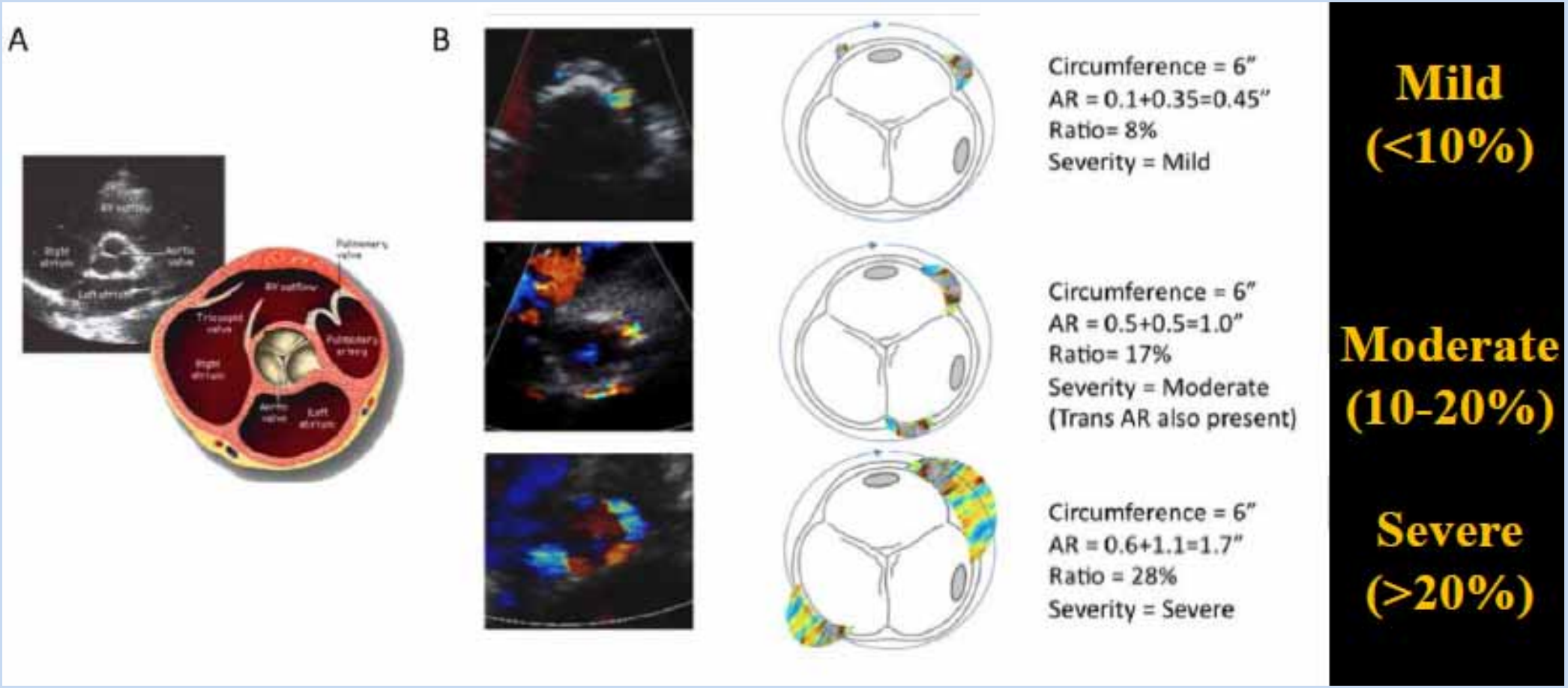
Linke A. et al. TCT 2012

Importance of multimodality approach



Each one can potentially underestimate PVL in a particular situation

Example: grading by circumferential extent



Note that the different cutoff of severe PVL (20%) according to VARC-1 definition

Bloomfield GS. et al. J Am Coll Cardiol Img. 2012;441-55

Severity of PVL (**VARC 2**): 2-D echo is a standard

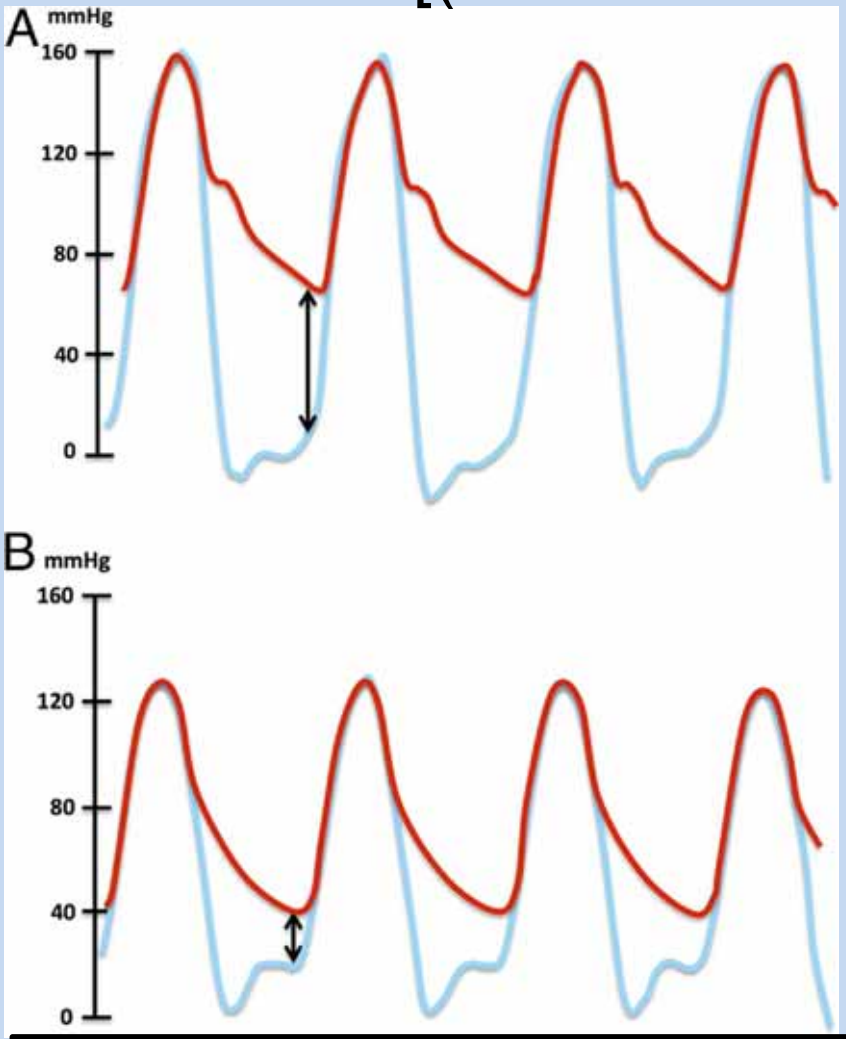
	Prosthetic aortic valve regurgitation		
	Mild	Moderate	Severe
Semi-quantitative parameters			
Diastolic flow reversal in the descending aorta (PW)	Absent or briefly early diastolic	Intermediate	Prominent, holodiastolic
Circumferential extent of prosthetic valve paravalvular regurgitation*	<10%	10-29%	≥30%
Quantitative parameters			
Regurgitant volume, ml/beat	<30ml	30-59ml	≥60ml
Regurgitant fraction	<30%	30-49%	≥50%
ERO area	0.10cm^2	0.10-0.29cm^2	≥0.30cm^2

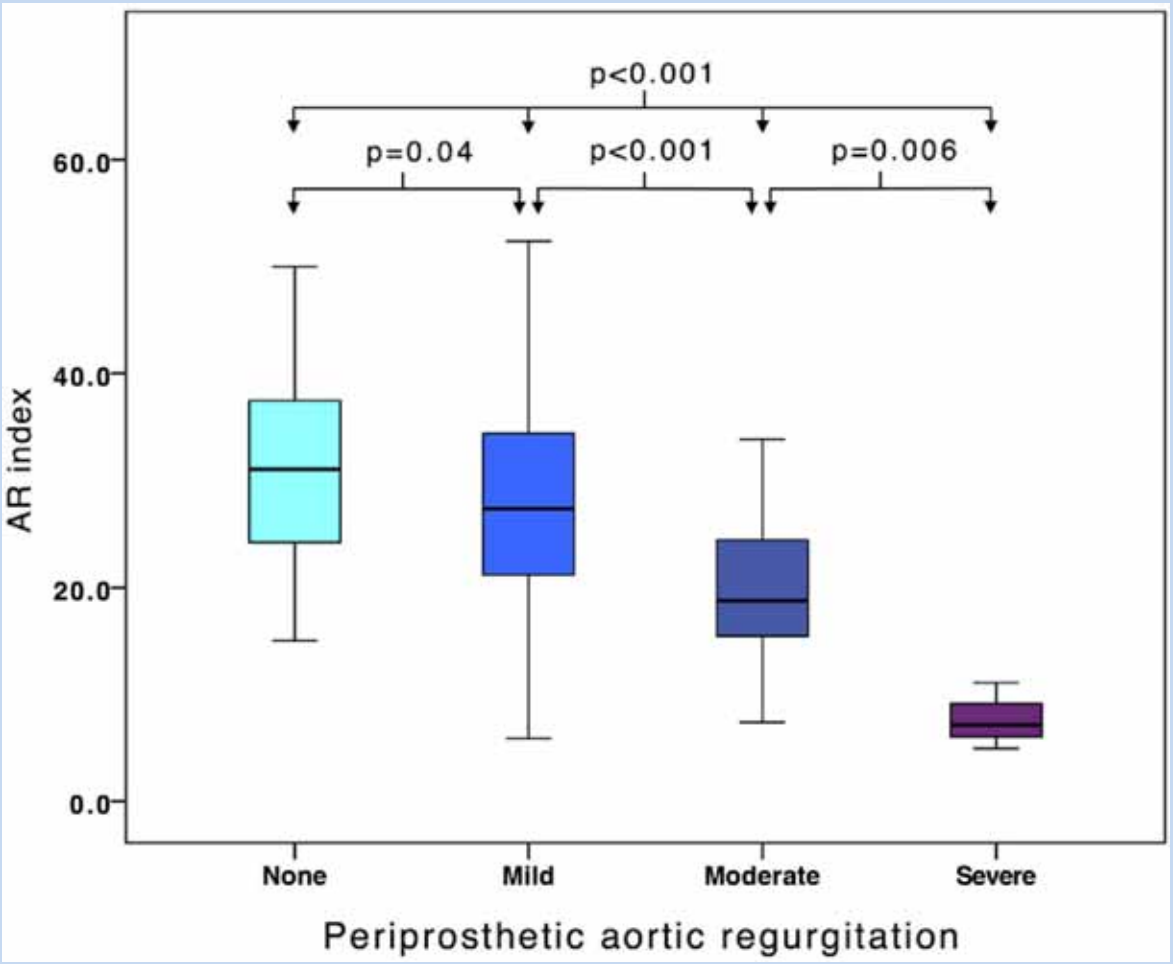
*Not well validated and may overestimate the severity c/w the quantitative Doppler

Kappetein AP. J Am Coll Cardiol. 2012;60:1438-54

Change of hemodynamics: LVEDP

AR index = [(DBP – LVEDP)] / SBP] x100



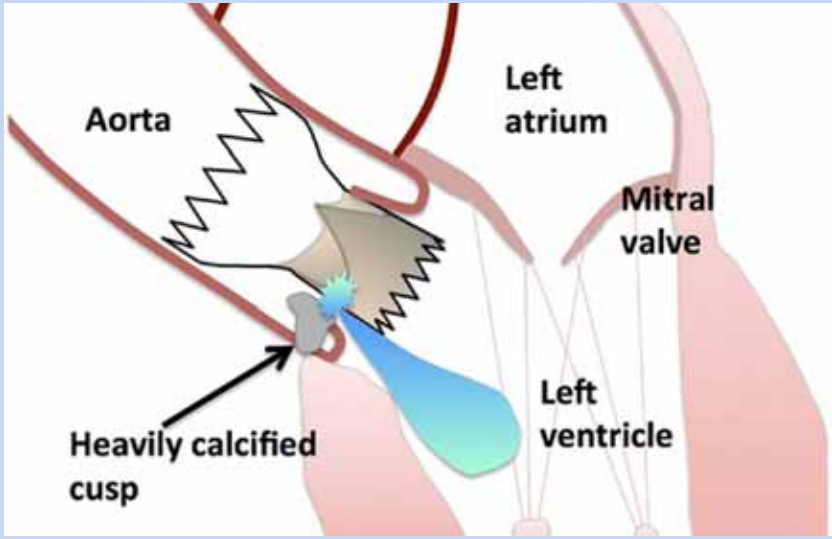


AR index can be complementary to the echocardiographically assessed severity of PAL

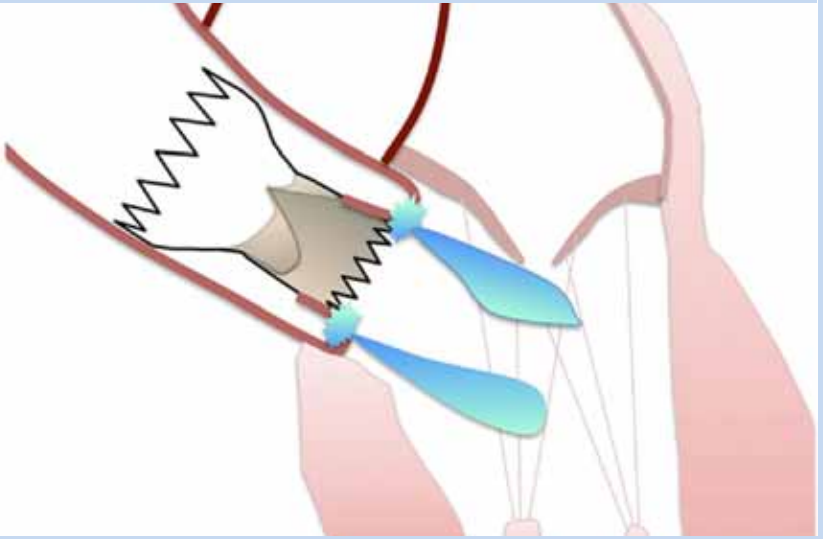
Sinning JM. et al. J Am Coll Cardiol 2012;59:1134–41

Proposed Mechanisms of PVL

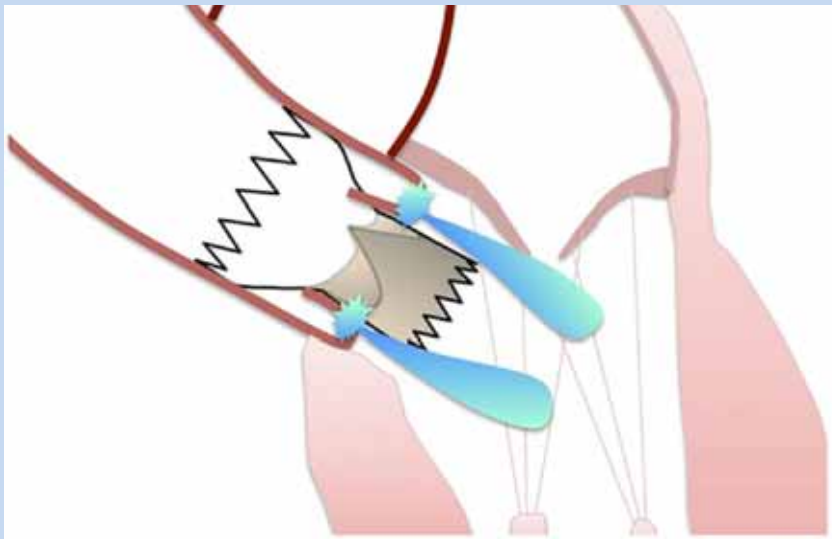
Calcification



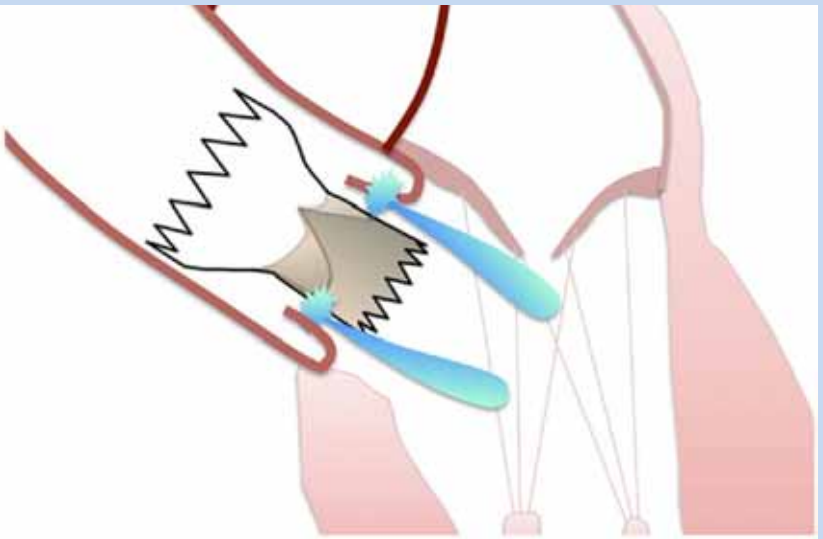
Malposition – too shallow



Malposition – too deep



Size mismatch



Sinning JM. et al. J Am Coll Cardiol 2012;59:1134–41

Strategy to avoid PVL

1. Calcification → pre-procedural planning or patient selection
2. Size mismatch → Accurate sizing
3. Malposition → Optimal positioning
4. Identification or quantification of PVL
5. Correction by additional intervention

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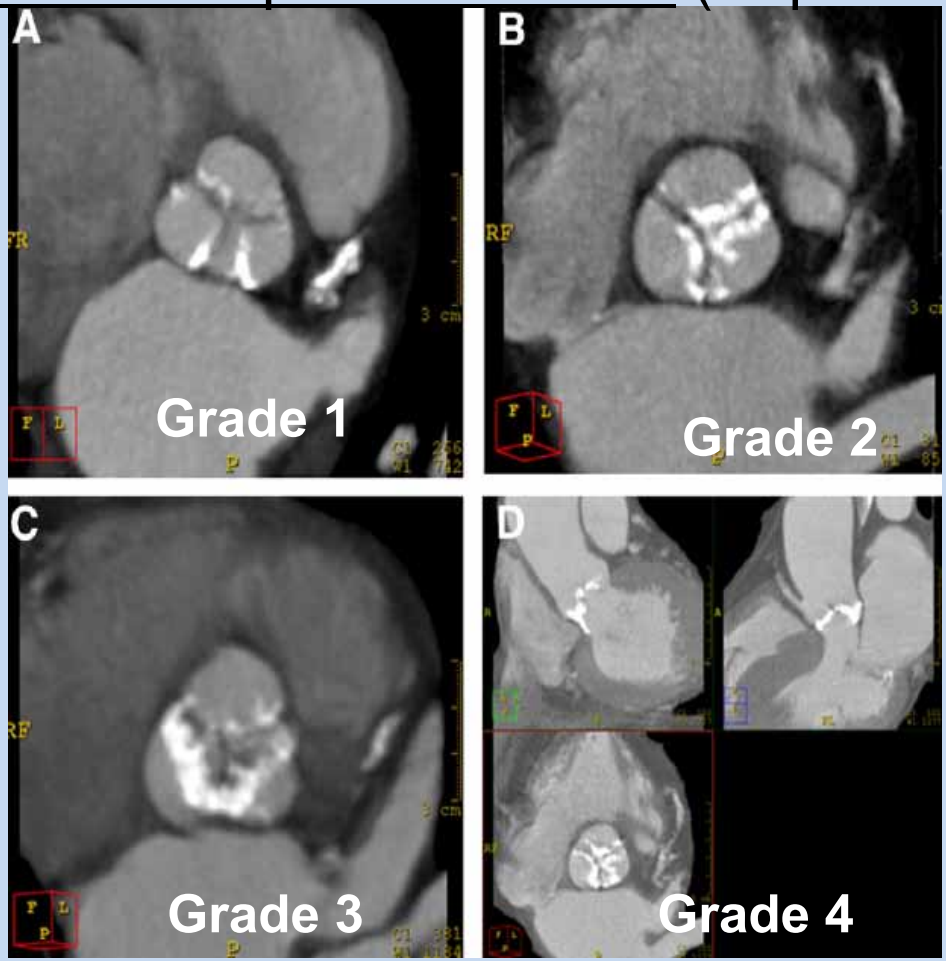
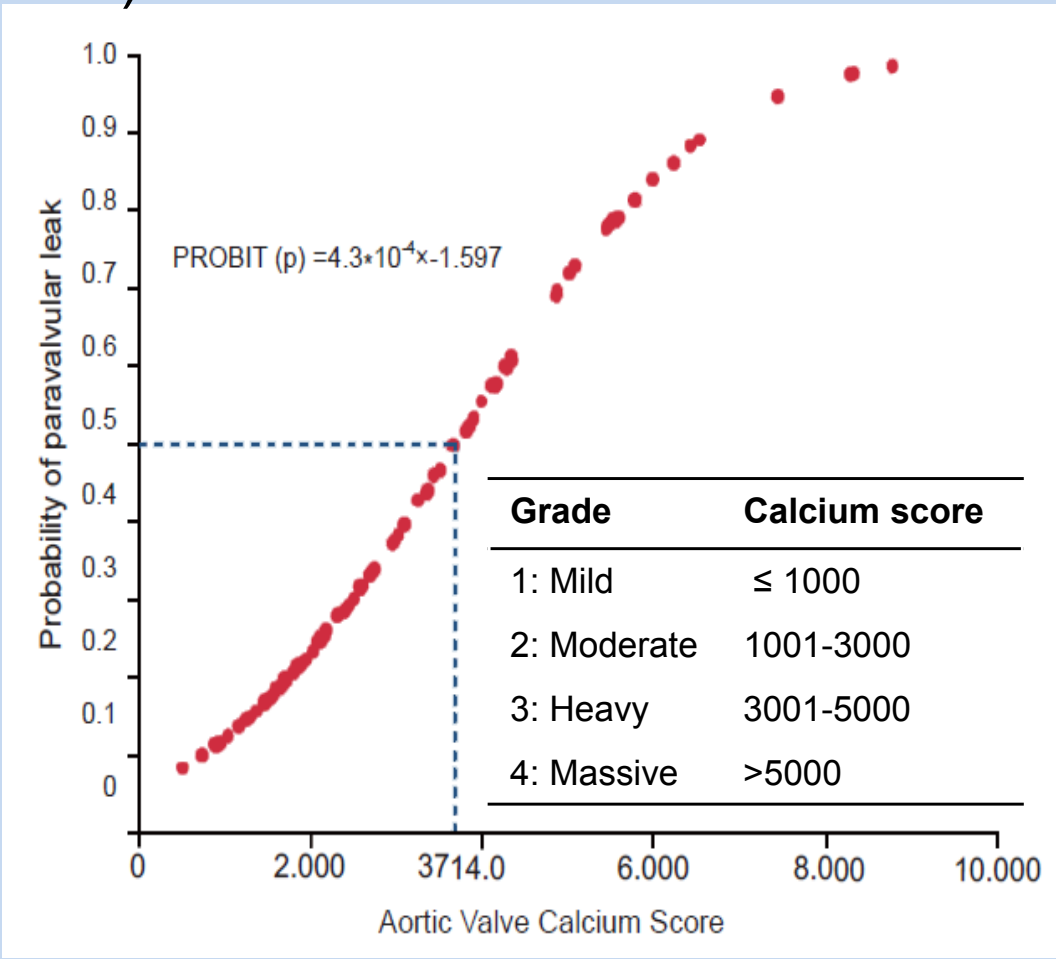
Severity of Calcification

Balloon-expandable valve (Sapien Valve)





Grade	Calcium score
1: Mild	≤ 1000
2: Moderate	1001-3000
3: Heavy	3001-5000
4: Massive	>5000

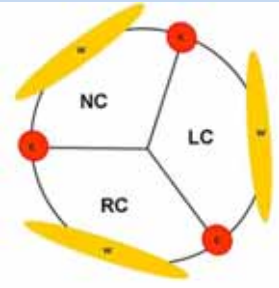
Severe AV calcification is predictive for postoperative relevant PVL

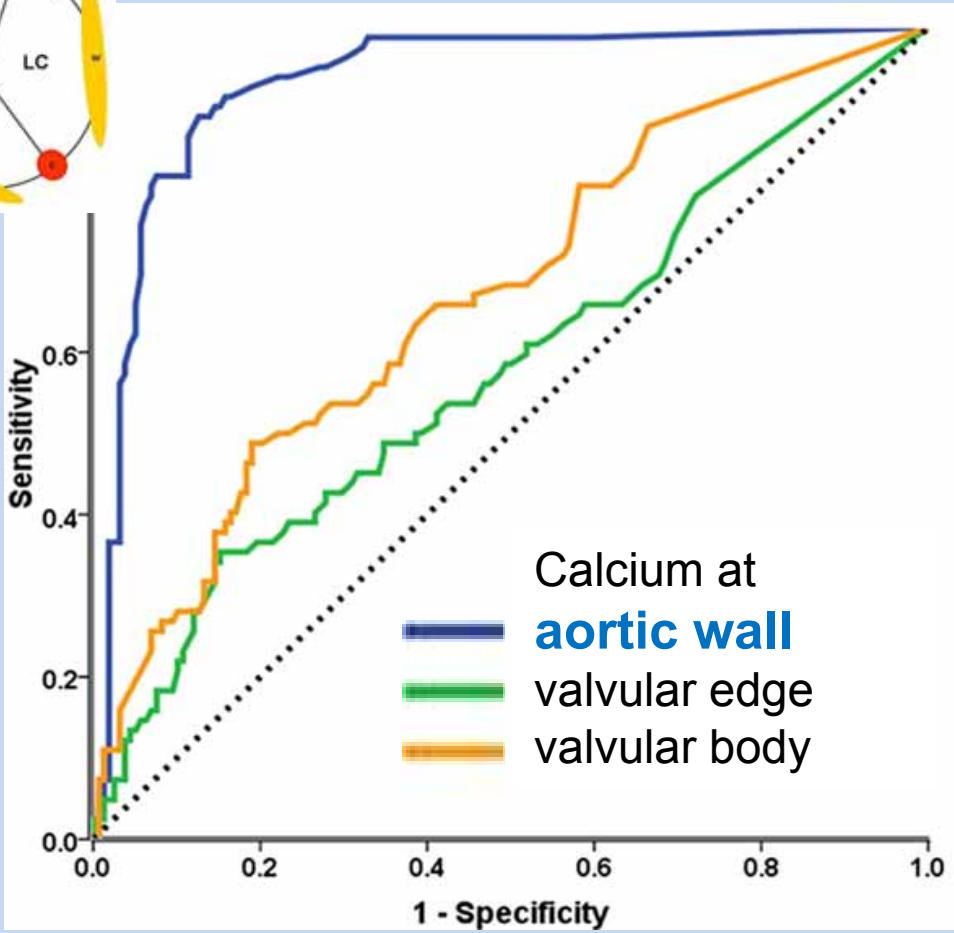
John D. et al. J Am Coll Cardiol Intv 2010;2,233-43

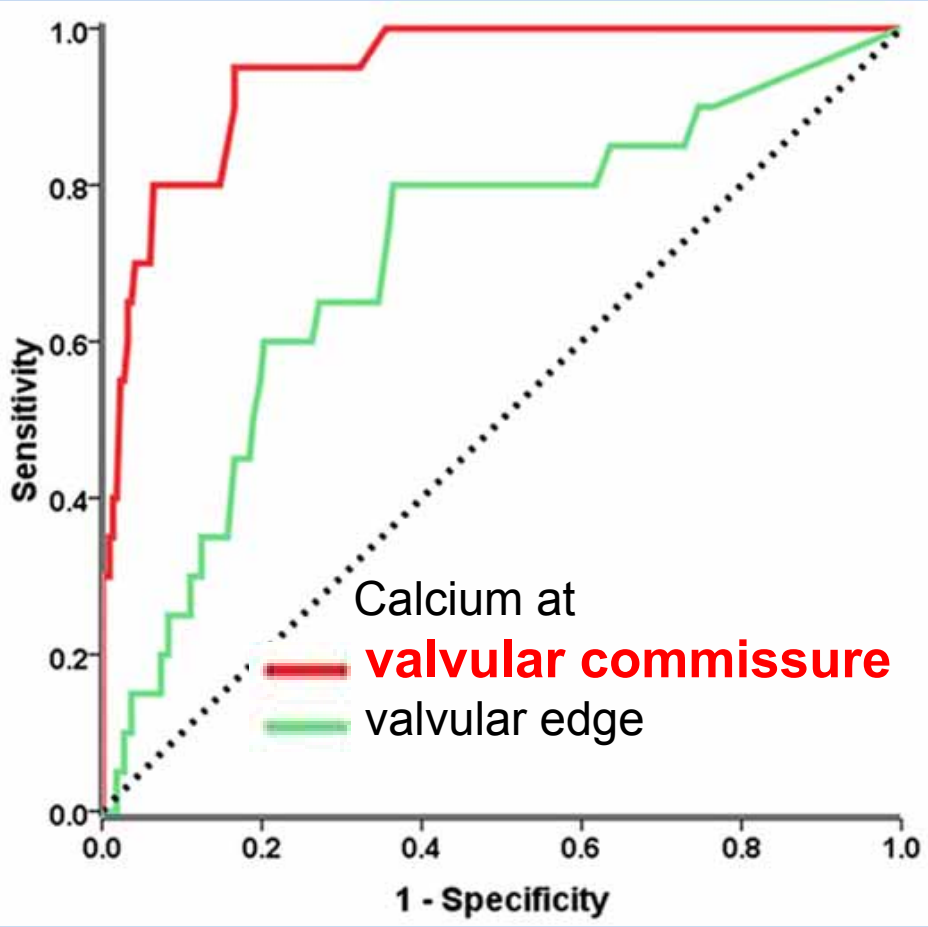
Haensig M. et al. Ann Cardiothorac Surg 2012;1(2):160-164

Location of Calcification

Balloon-expandable valve (Sapien Valve)





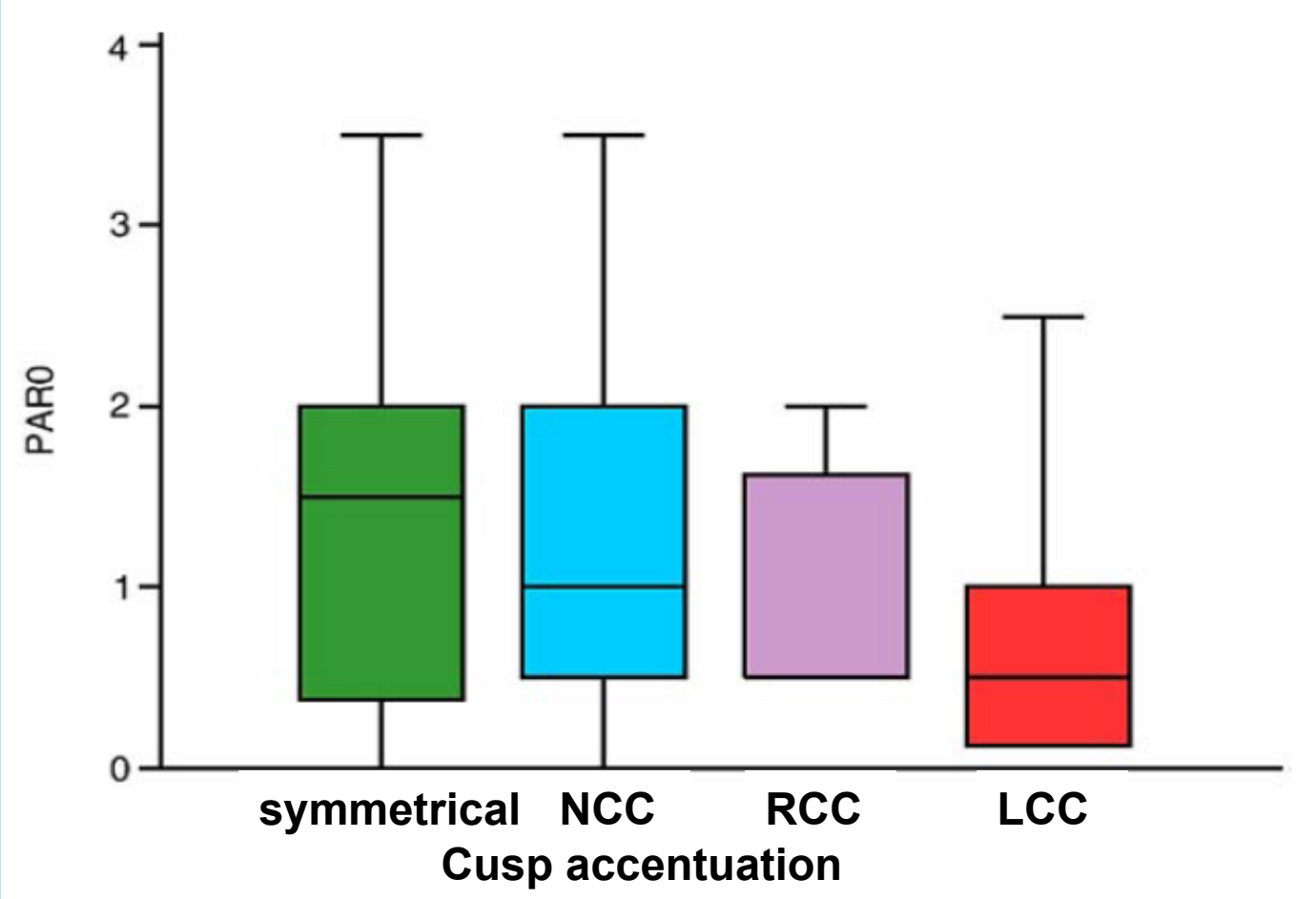


Aortic wall and commissure calcifications confer higher risk of PVL

Ewe SH. et al. Am J Cardiol 2011;108:1470 –147

Symmetricity of Calcification

Self-expandable valve (CoreValve)



*PAR0: AV regurgitation assessed by angiography **acute after** release of the CoreValve

Visual distribution pattern of calcification is *not* related with PVL grade

John D. et al. J Am Coll Cardiol Intv 2010;2,233-43

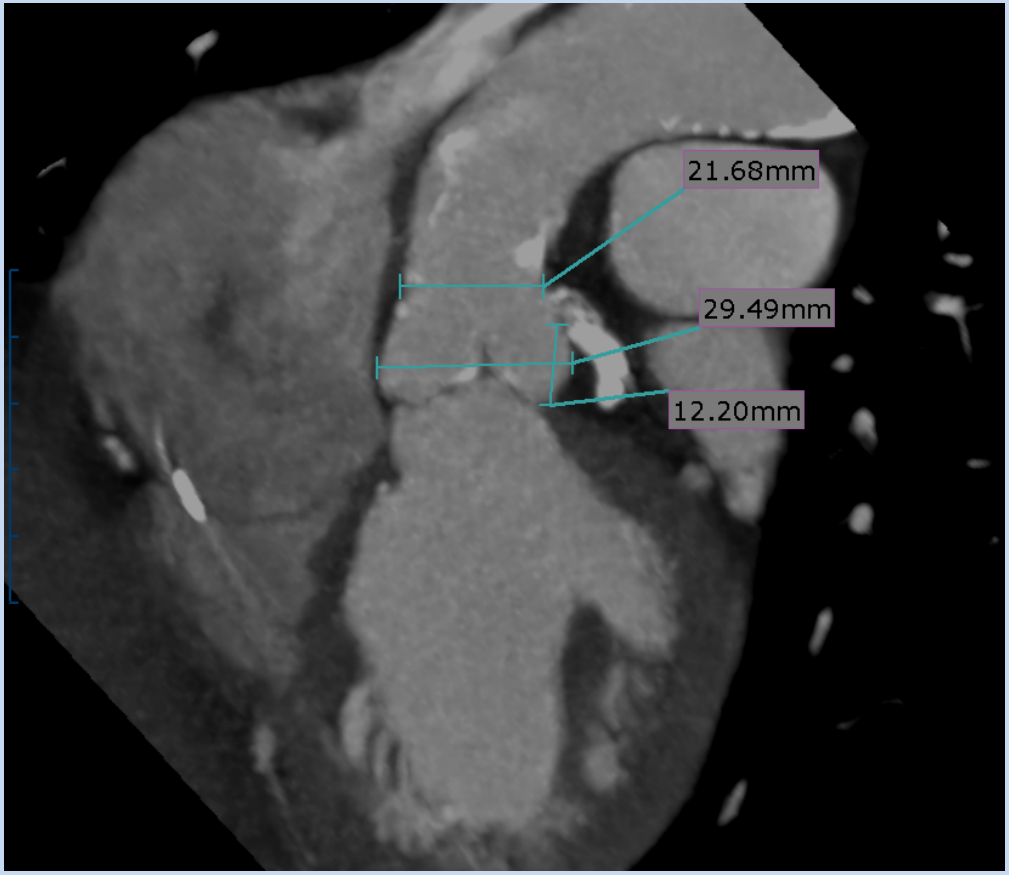
SNUH Experience

Case 1

- Brief history: F/80
  - Chief complaint: aggravation of dyspnea
  - History of OMI, s/p PCI to LM-LCx
  - Complete AV block on pacemaker
- Cardiovascular risk factors
  - diabetes mellitus/hypertension/dyslipidemia (-/+/-)
- Laboratory findings
  - ECG: pacemaker rhythm
  - Echocardiography
    - normal LV size with normal LVEF (59%)
    - AV mean pressure gradient 39 mmHg, AV area 0.47 cm^2
- Logistic EuroSCORE: 7.5%

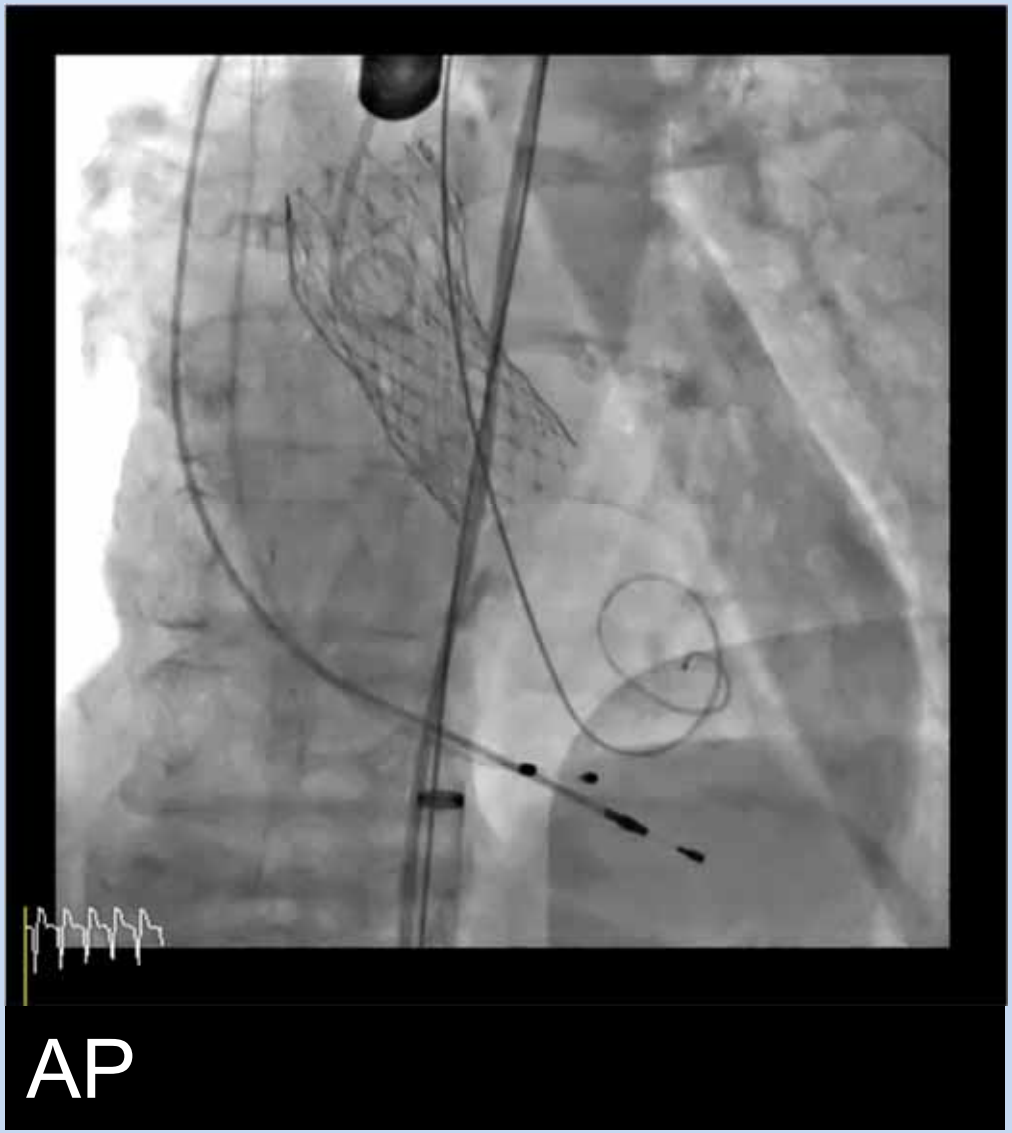
Case 1

Calcification on MDCT

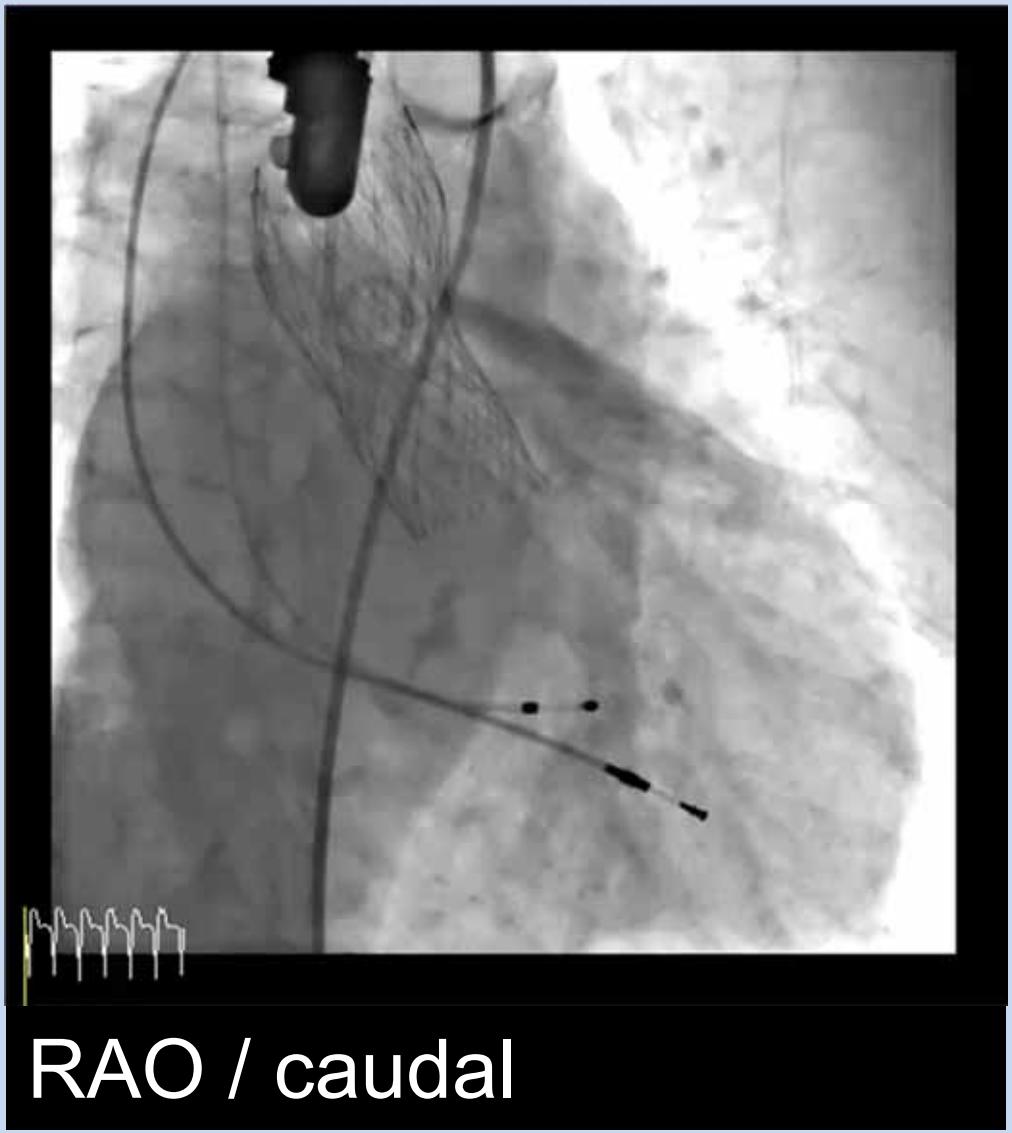


Case 1

PVL on angiography (CoreValve 26 mm)



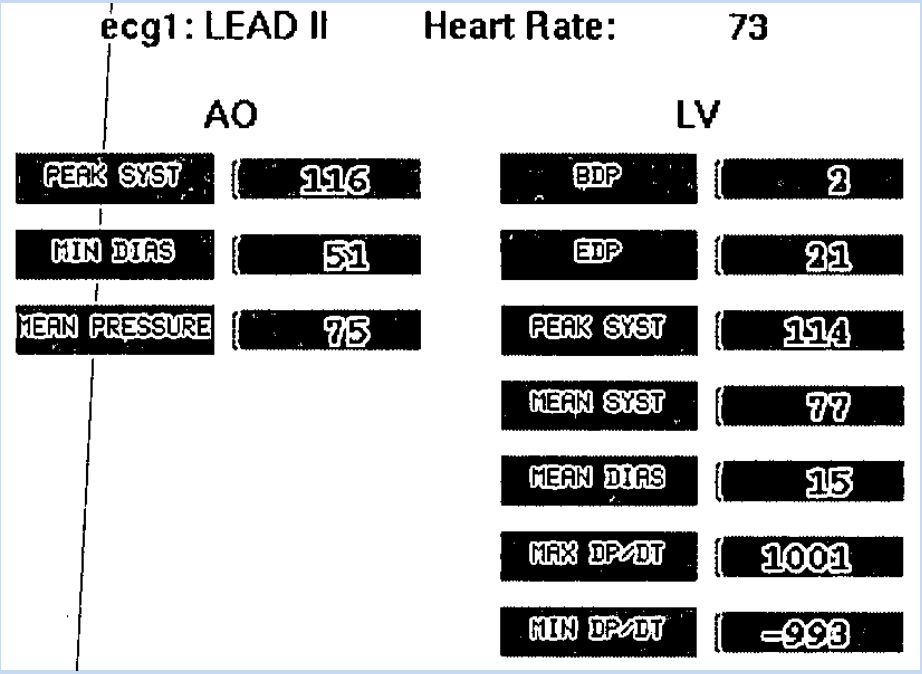
AP

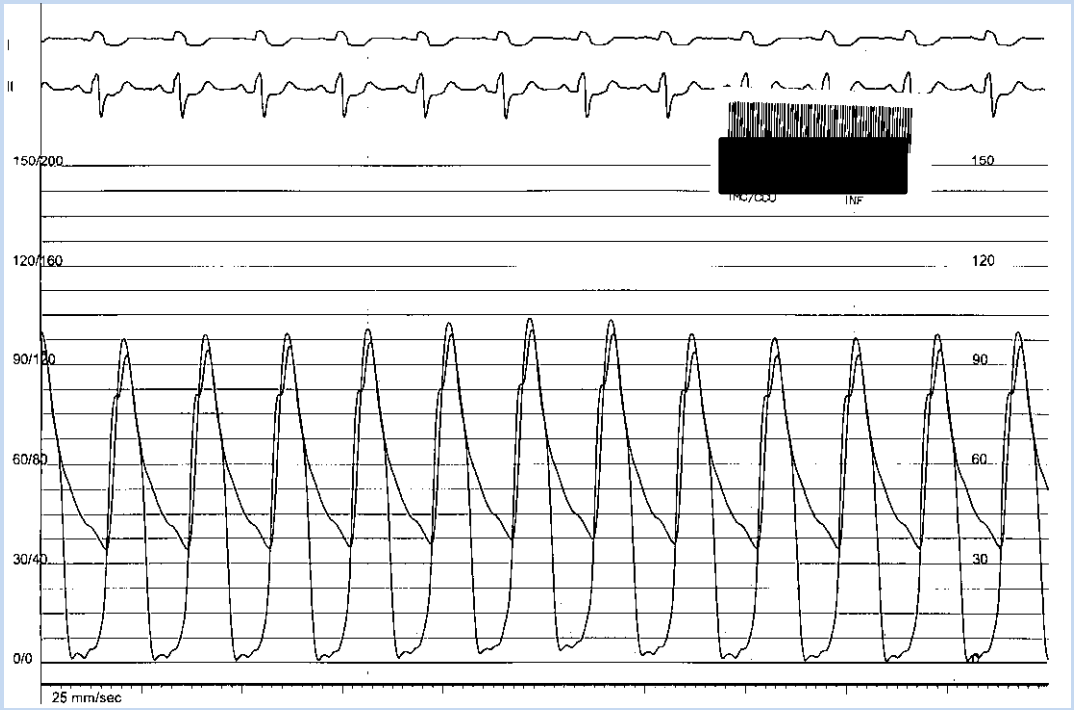


RAO / caudal

Case 1

AR index by catheterization

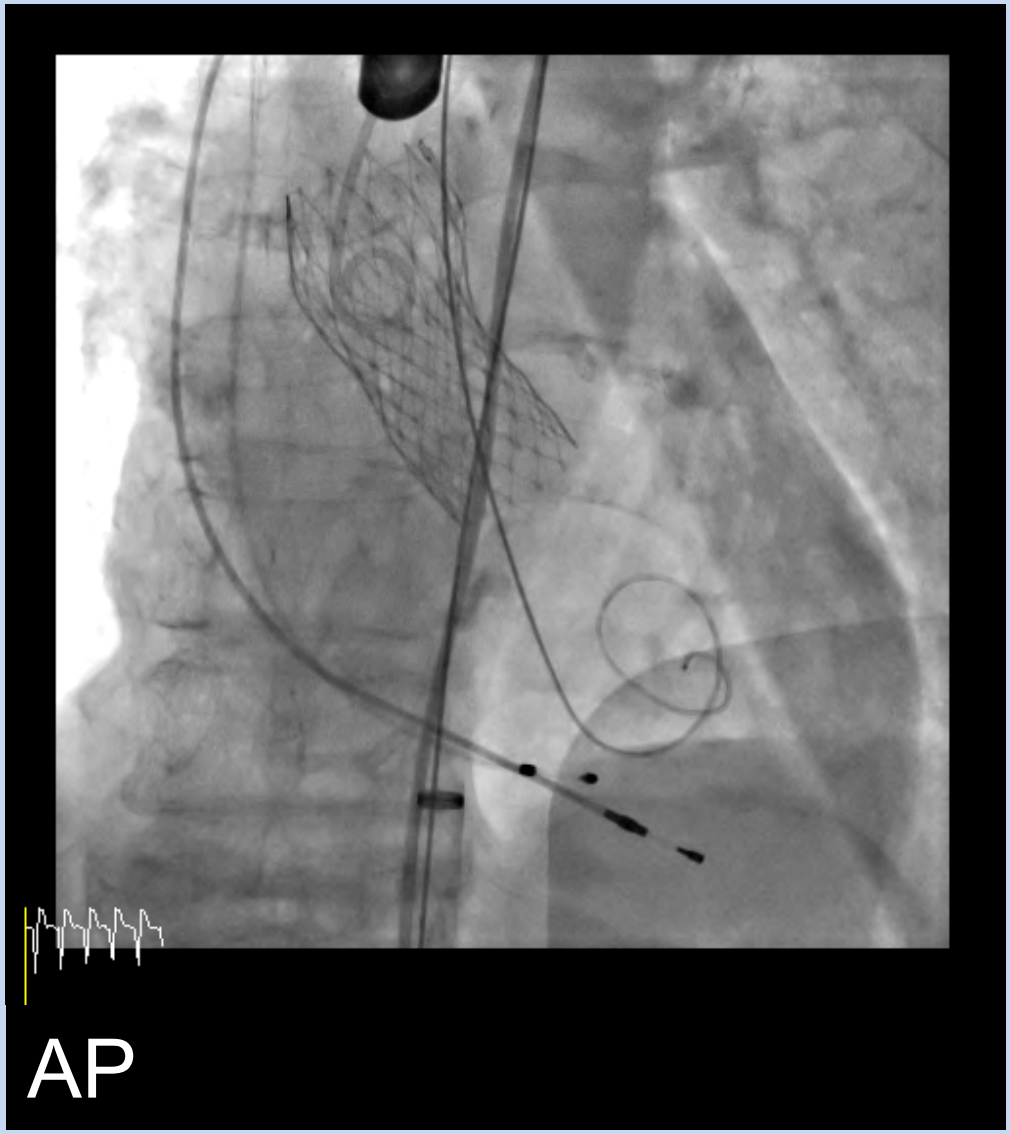


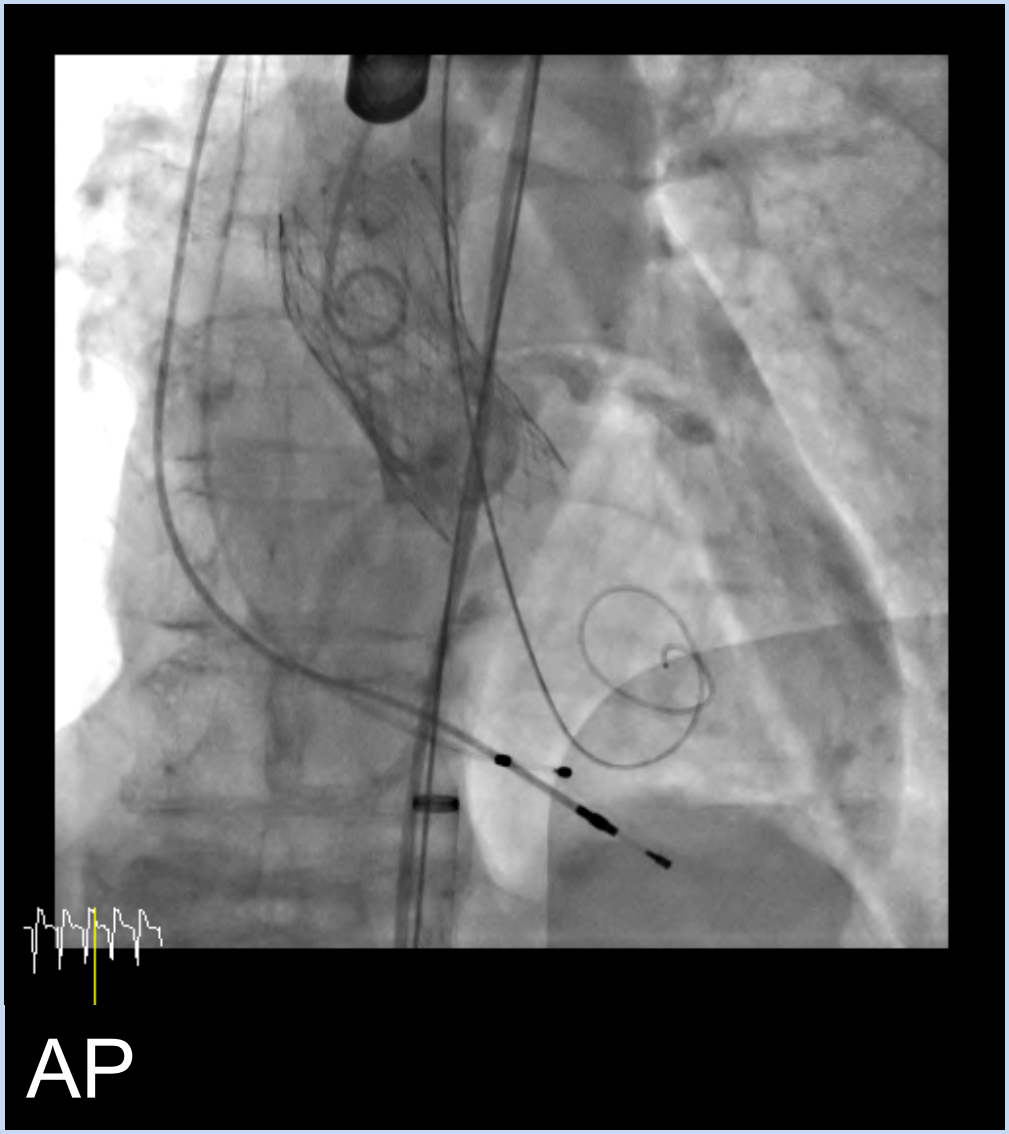


AR index = (51 – 21) / 116 x 100 = 26

Case 1

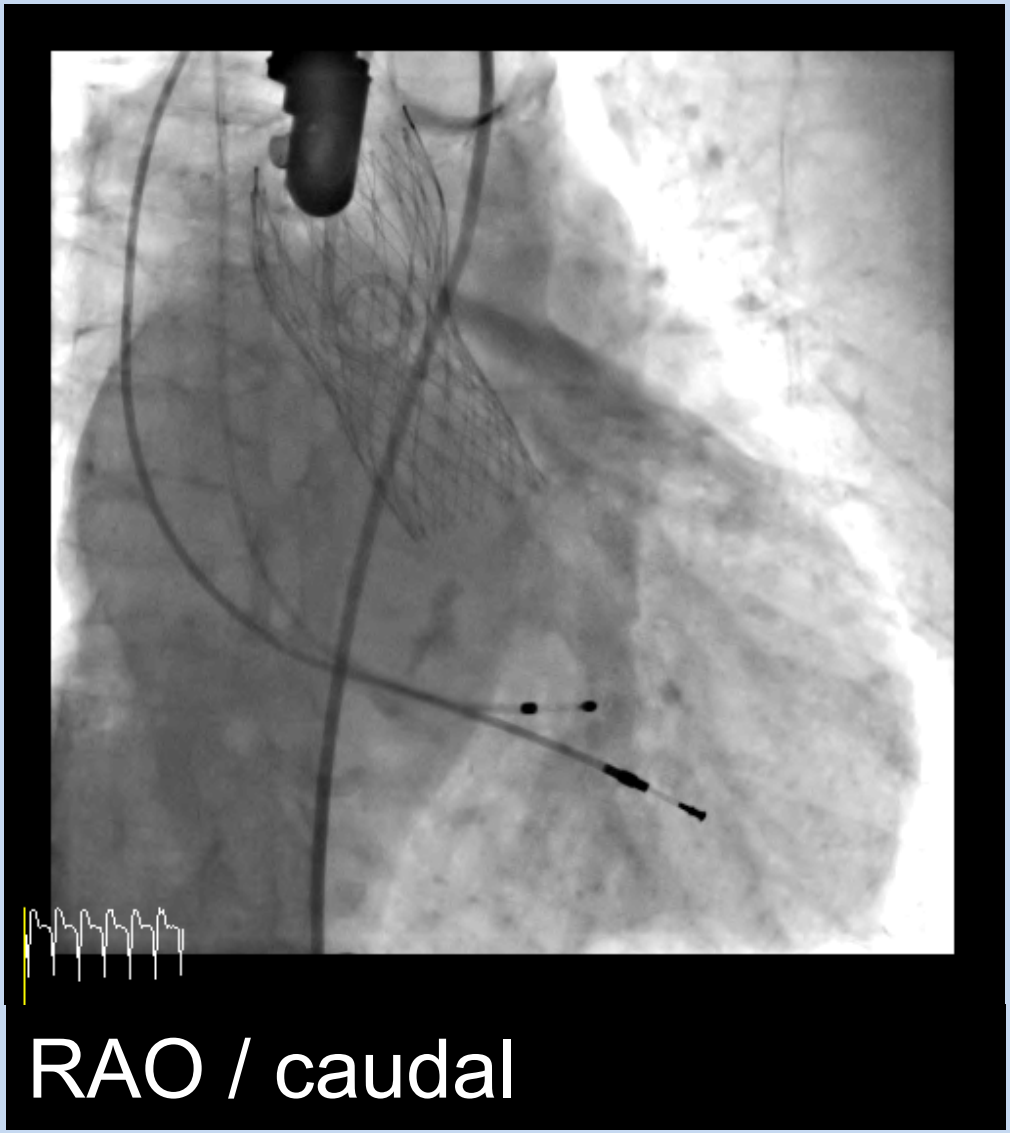
Valve position on angiography



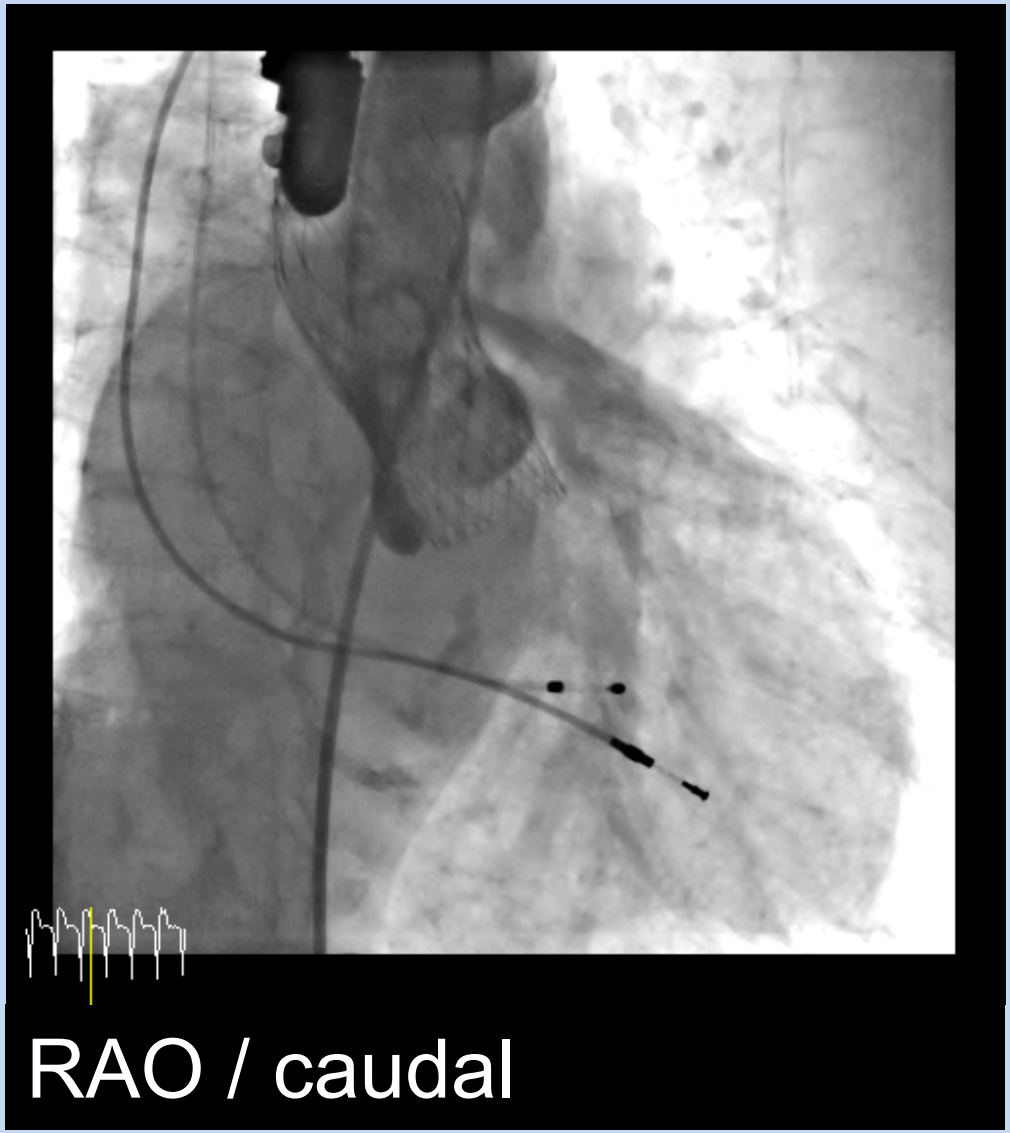


Case 1

Valve position on angiography



RAO / caudal



RAO / caudal

Case 2

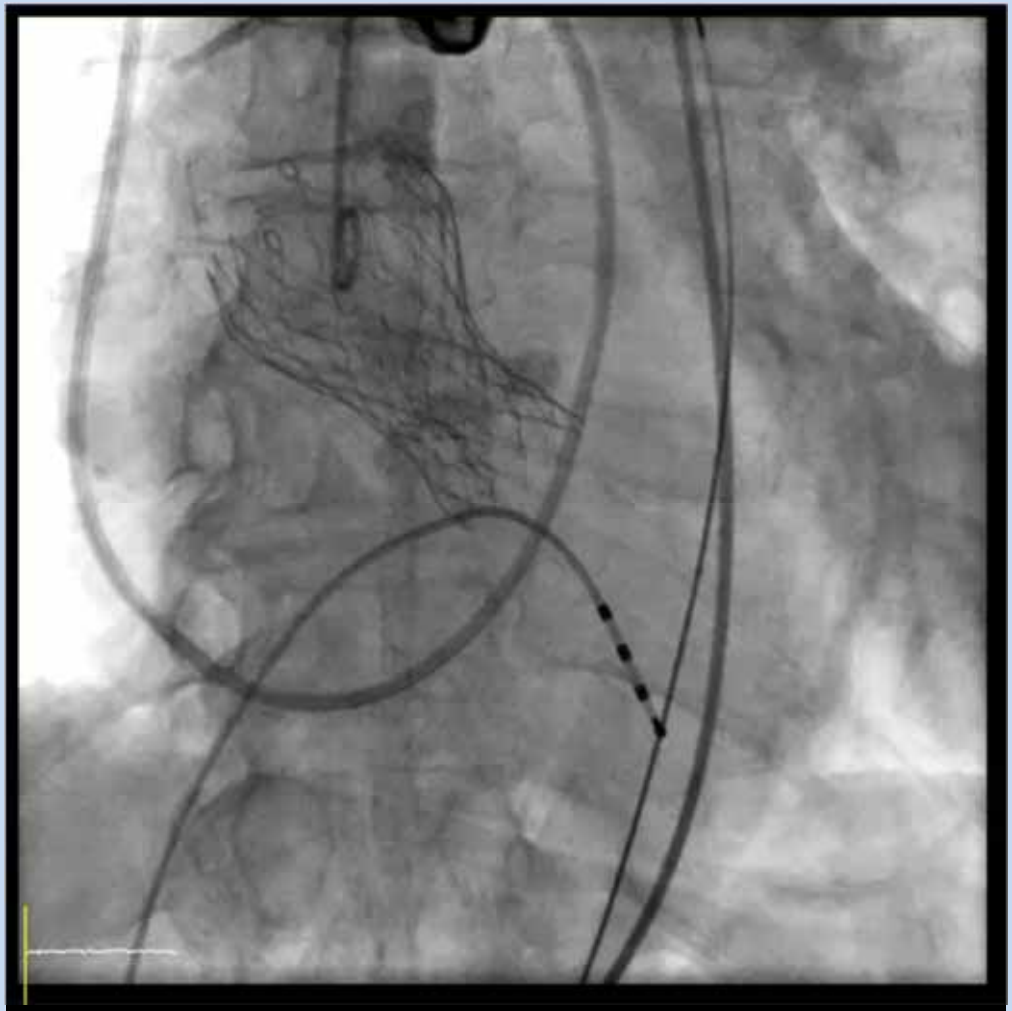
- Brief history: M/77
  - Chief complaint: aggravation of dyspnea
  - COPD
- Cardiovascular risk factors
  - diabetes mellitus/hypertension/dyslipidemia (-/-/+)
- Laboratory findings
  - ECG: NSR, LVH
  - Echocardiography
    - normal LV size with depressed LVEF (42%)
    - AV mean pressure gradient 45 mmHg, AV area 0.62 cm^2
    - Diastolic dysfunction with increased LV filling pressure (E/e' = 35)
- Logistic EuroSCORE: 30.3%

Case 2

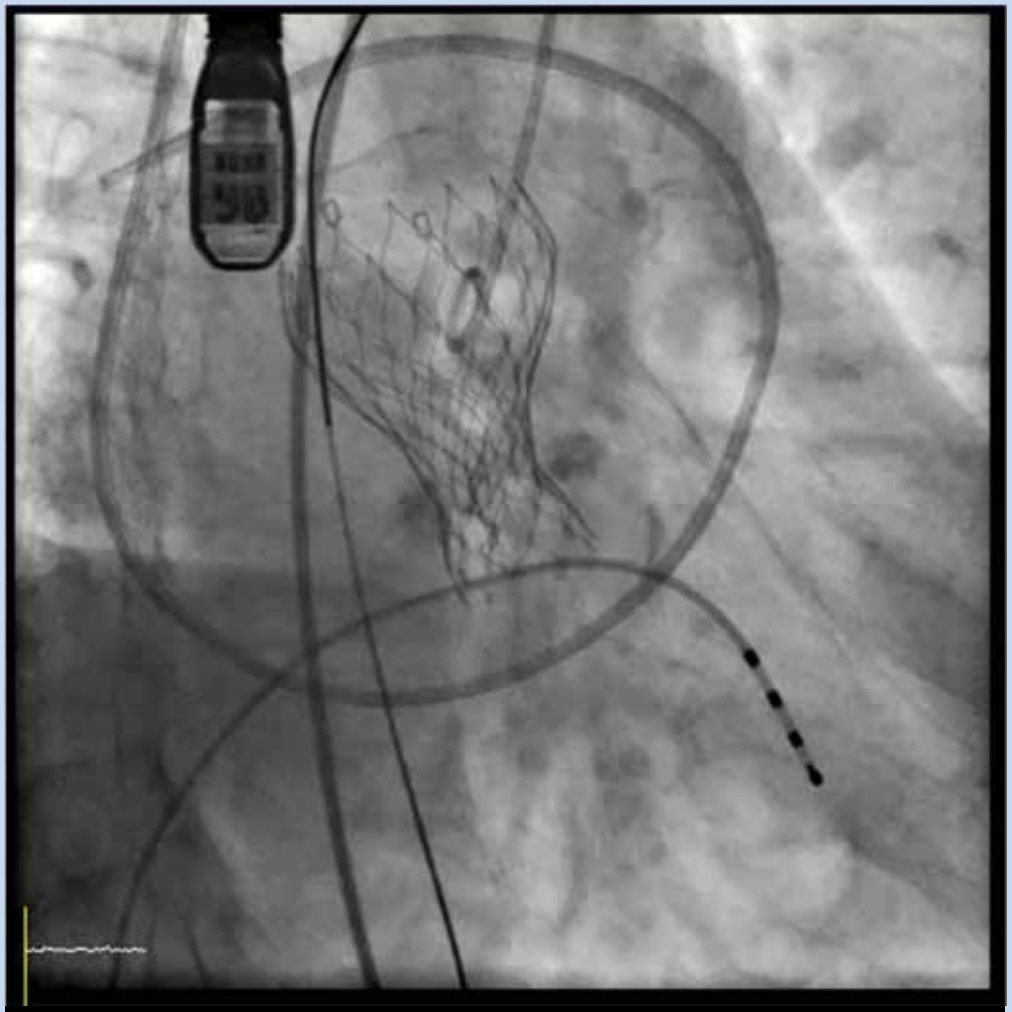
Calcification on MDCT

Case 2

PVL on angiography (CoreValve 31 mm)



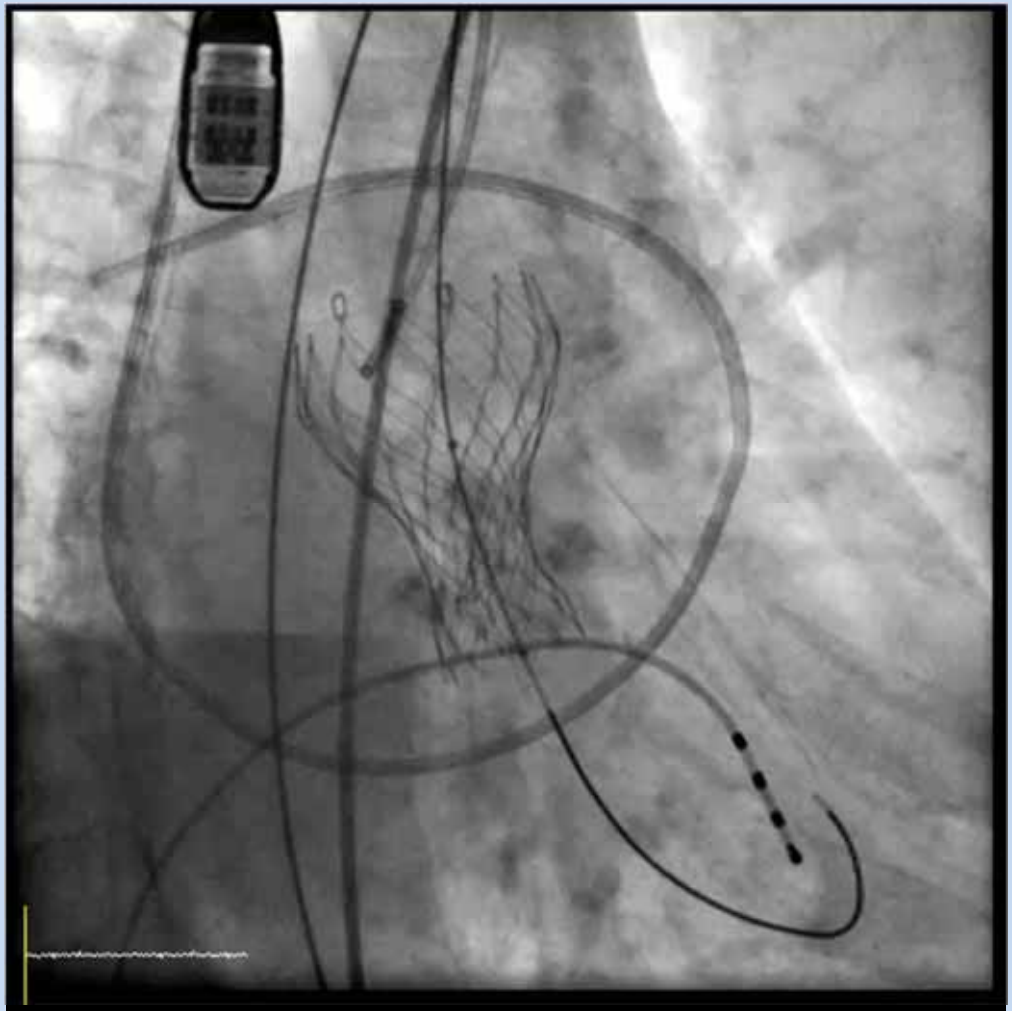
LAO / caudal



RAO / caudal

Case 2

PVL on angiography (after post-dilatation)



NuMED 25 x 40 mm

RAO / caudal

Case 2

AR index by catheterization

265 / [17:00] LEFT VENTRICLE

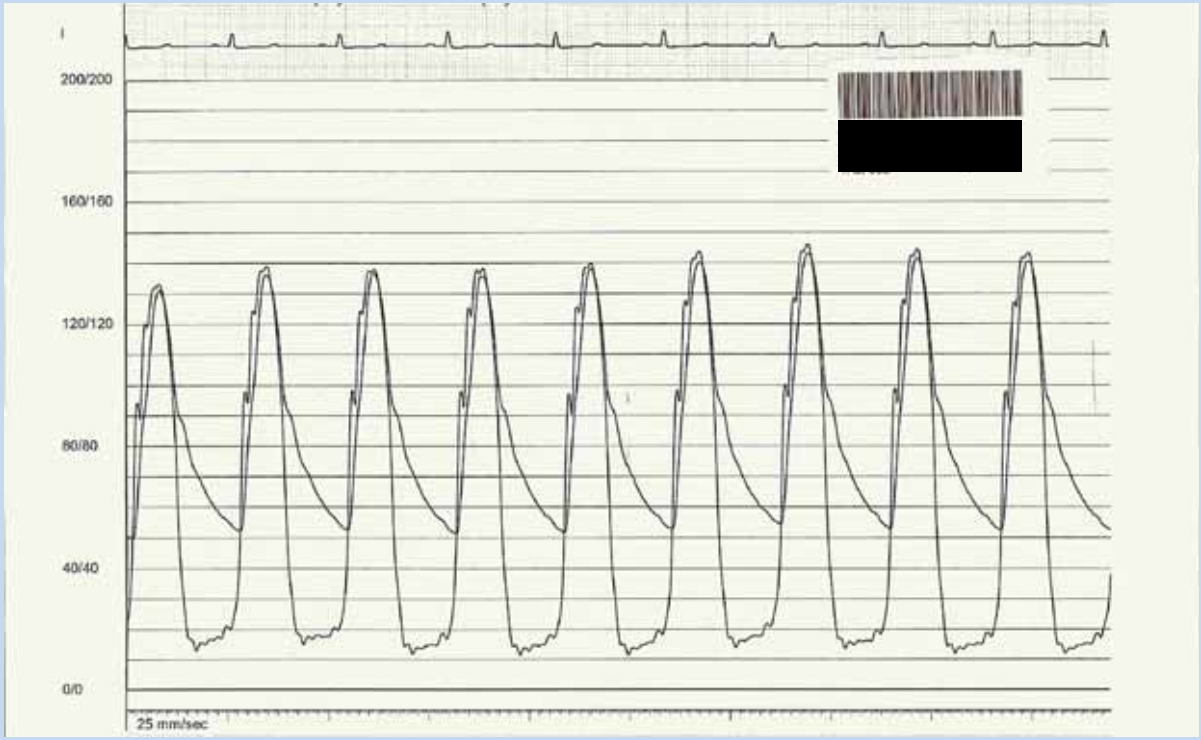
HEART RATE	55	[bpm]
LV BDP	16	[mmhg]
LV EDP	22	[mmhg]
LV PEAK SYST	141	[mmhg]
LV MEAN SYST	92	[mmhg]
LV MEAN DIAS	17	[mmhg]
LV MAX DP/DT	1441	[mmhg/sec]
LV MIN DP/DT	-1099	[mmhg/sec]
LV PEAK VCE	23.2	[/sec]
LV V MAX	38.9	[/sec]

265 / [17:00] AORTA

HEART RATE	55	[bpm]
AO PEAK SYST	139	[mmhg]
AO MIN DIAS	52	[mmhg]
AO MEAN PRESSURE	84	[mmhg]

265 / [17:00] AORTIC VALVE

AOV LAG TIME	0	[msec]
AOV SEP	17	[sec/min]
AOV PEAK GRAD	2.6	[mmhg]
AOV MEAN GRAD	14.7	[mmhg]

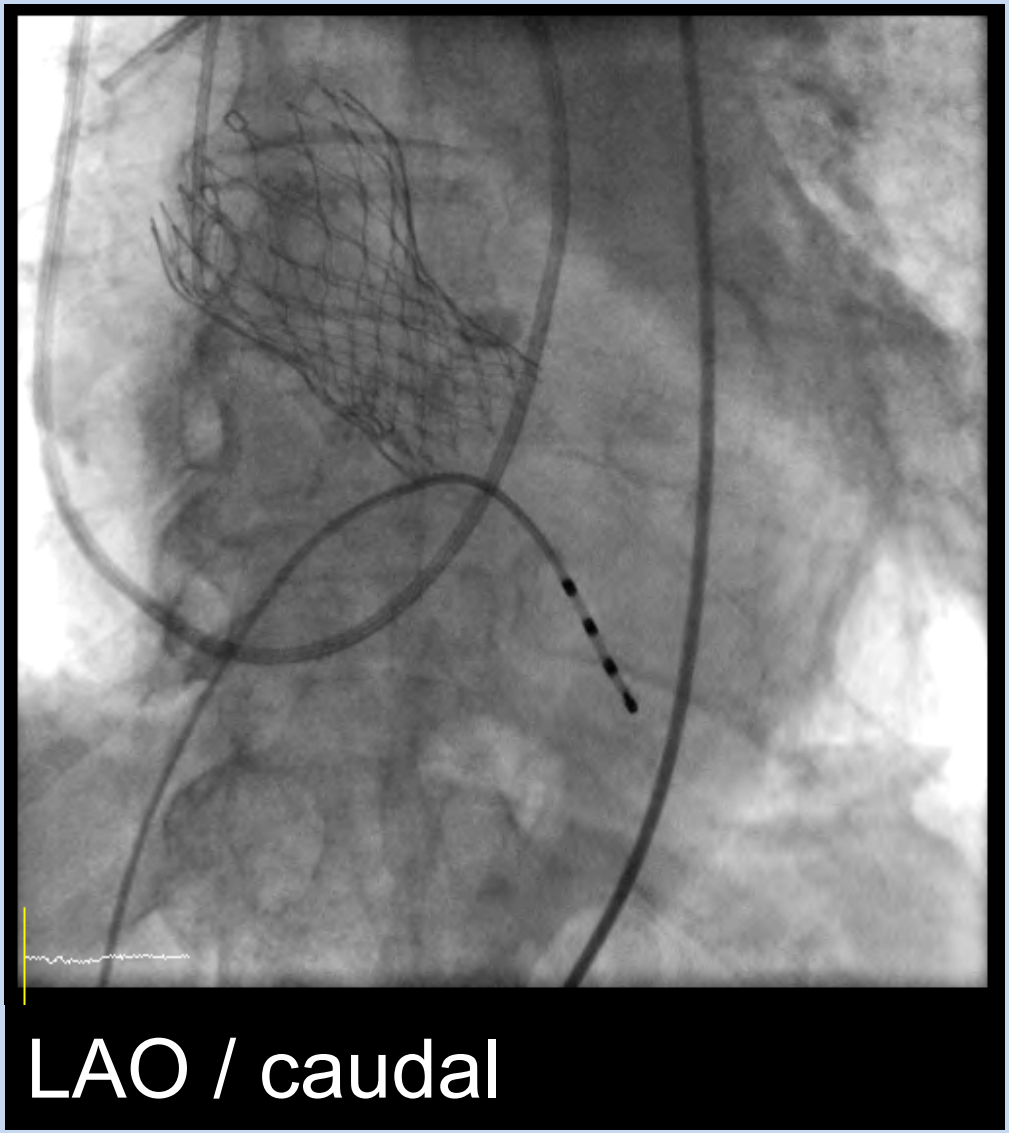


AR index = (52 – 22) / 139 x 100 = 22

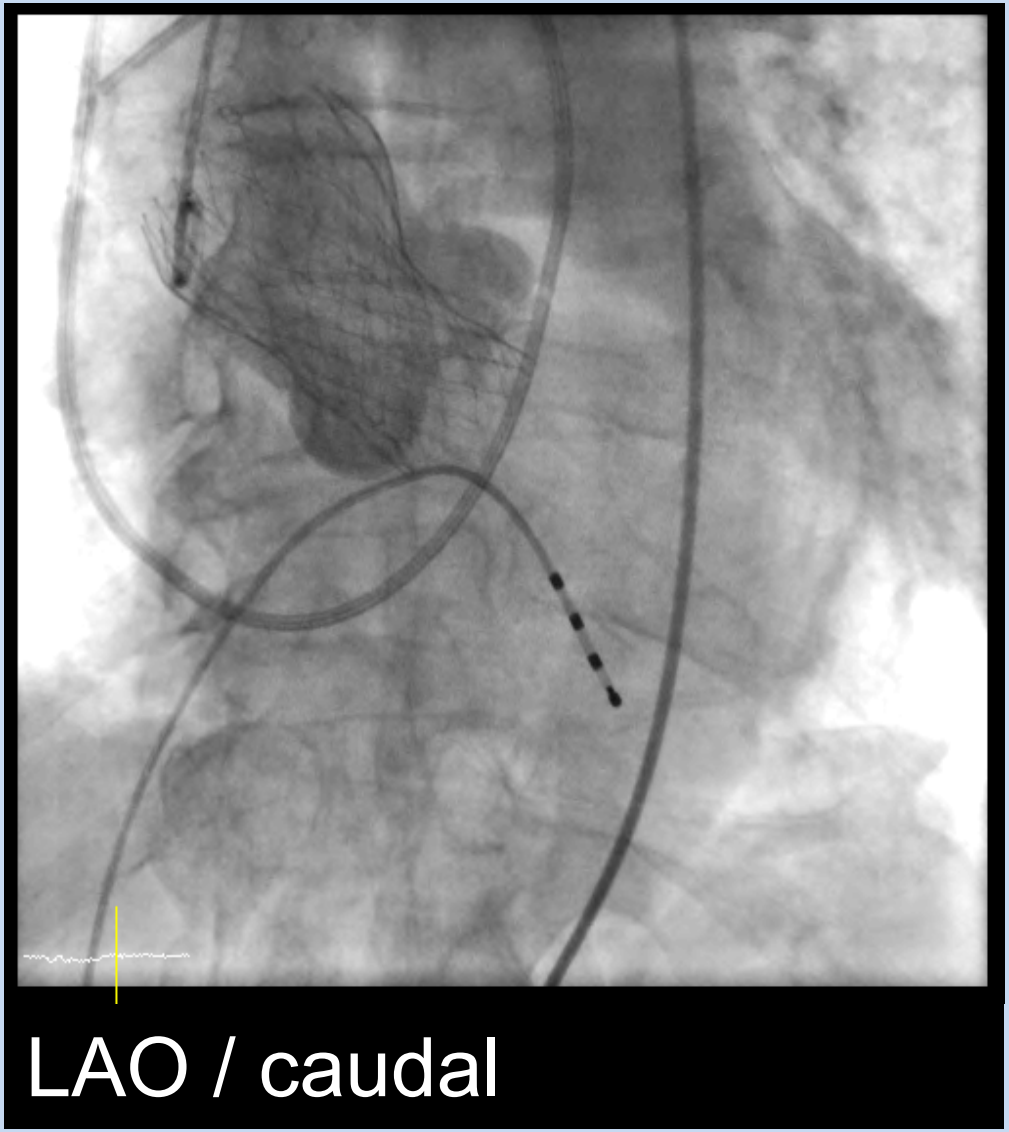
*Caution in interpretation of AR index:
Underlying diastolic dysfunction with elevated LVEDP (E/e' = 35)

Case 2

Valve position on angiography



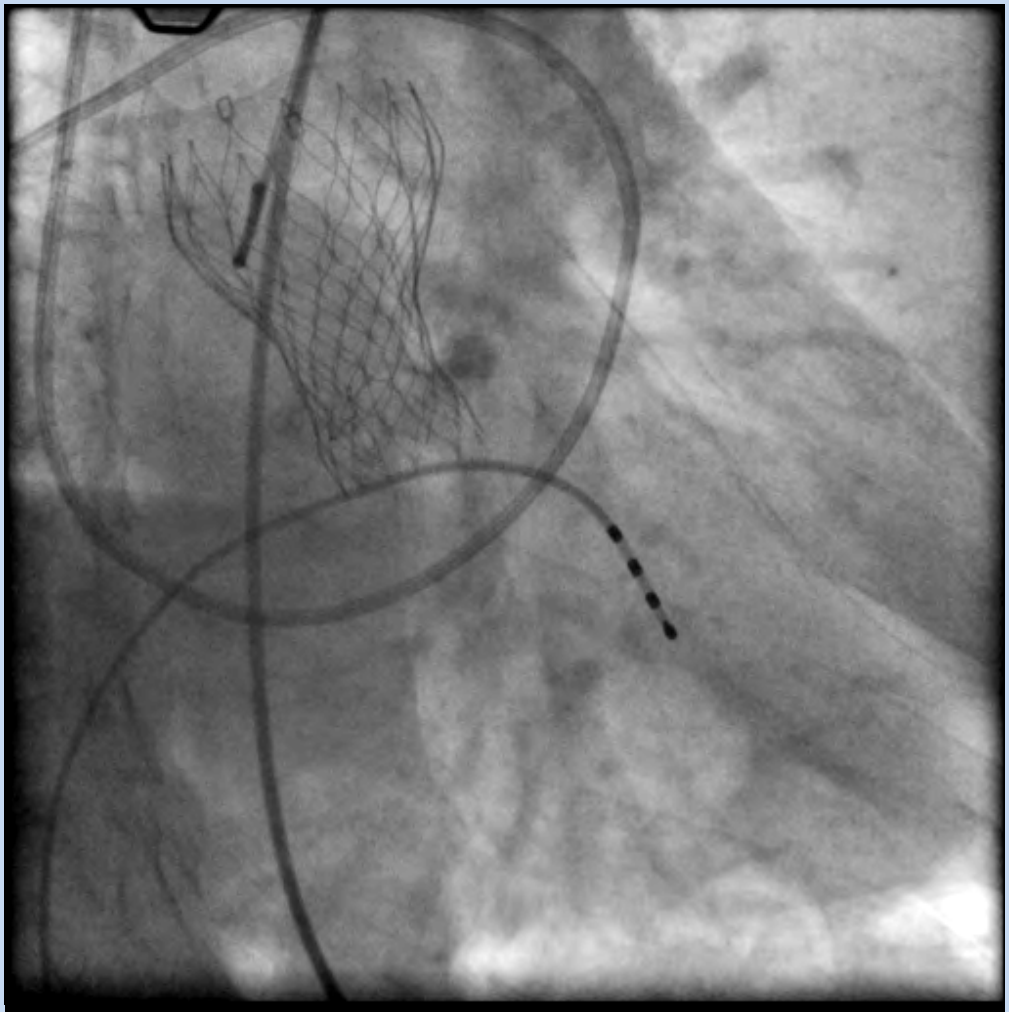
LAO / caudal



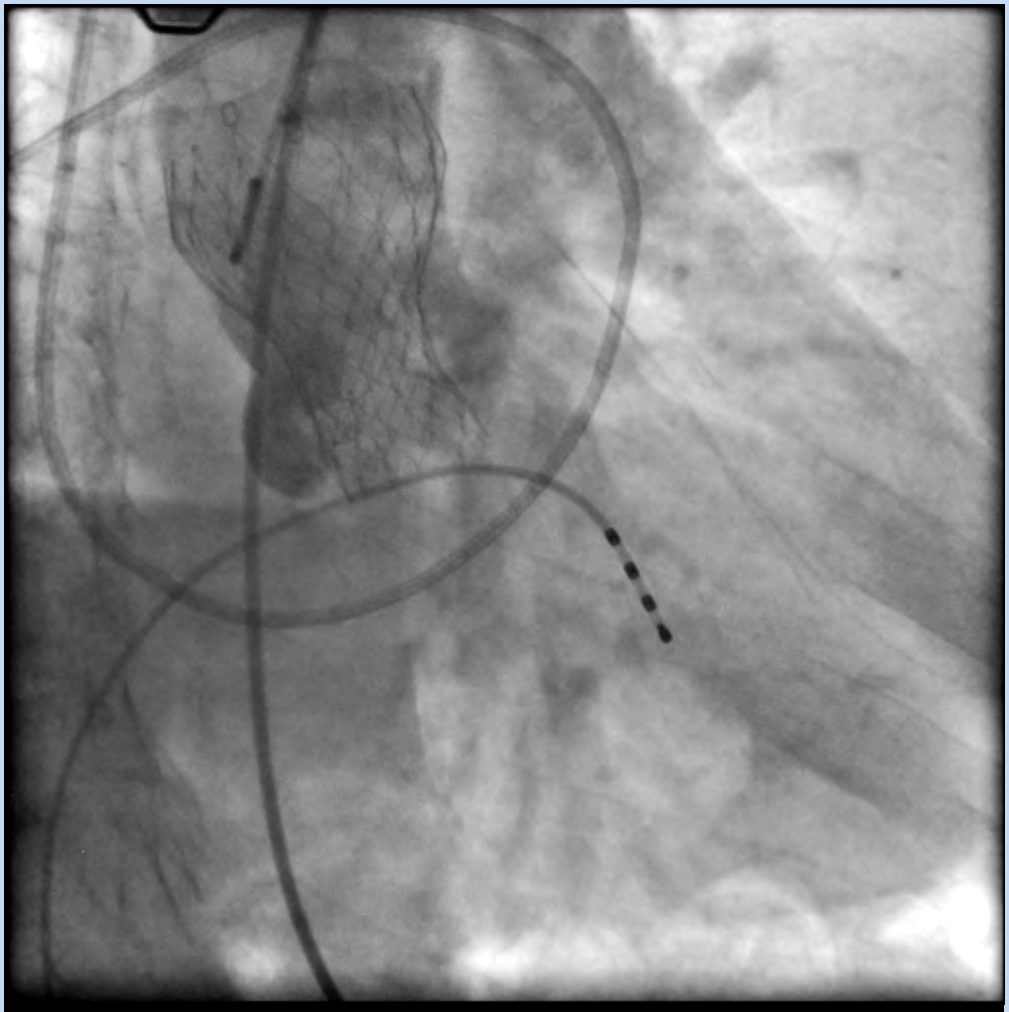
LAO / caudal

Case 2

Valve position on angiography



RAO / caudal



RAO / caudal

Case 3

- Brief history: M/86
  - Chief complaint: aggravation of dyspnea
  - 2VD, s/p PCI
  - History of stroke
  - SSS on pacemaker
- Cardiovascular risk factors
  - diabetes mellitus/hypertension/dyslipidemia (-/+/+)
- Laboratory findings
  - ECG: pacemaker rhythm
  - Echocardiography
    - normal LV size with normal LVEF (69%)
    - AV mean pressure gradient 55 mmHg, AV area 0.73 cm^2
- Logistic euroSCORE: 4.3%

Case 3

Calcification on MDCT

Case 3

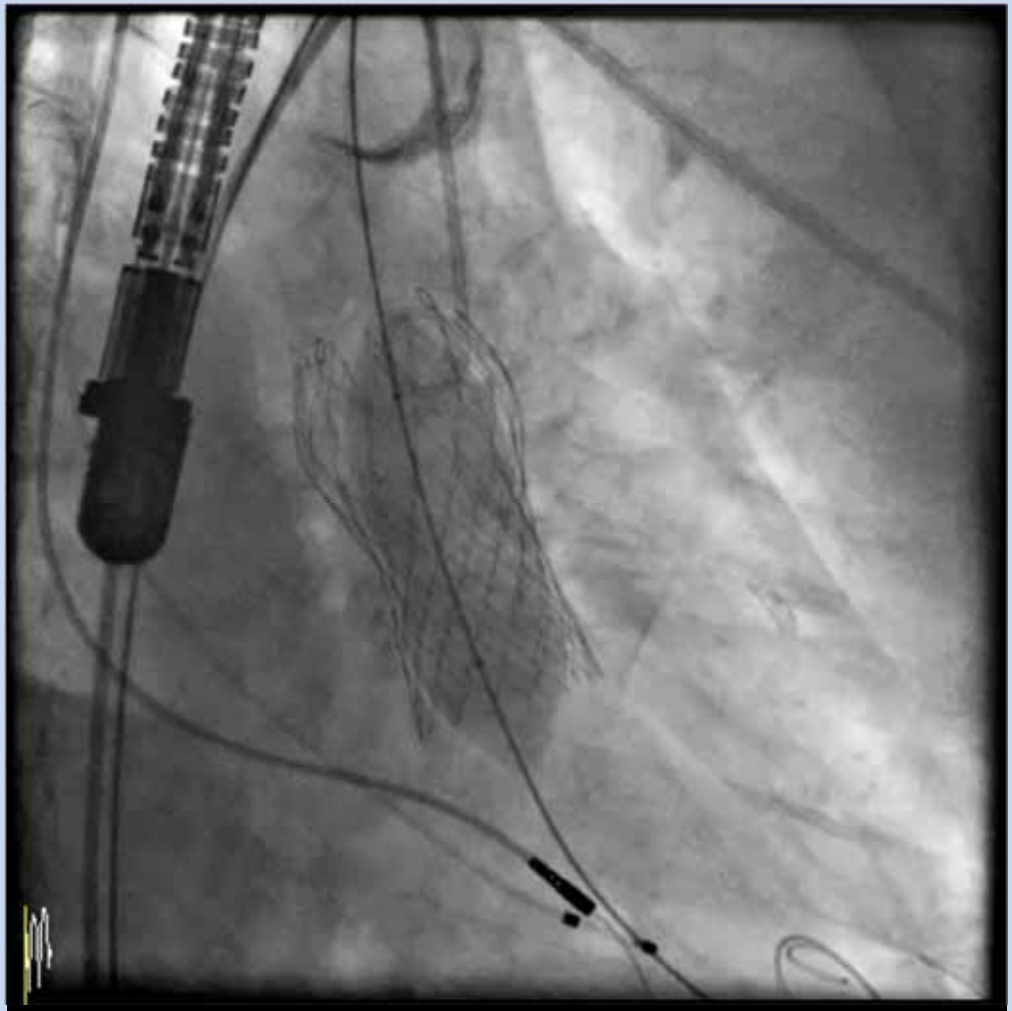
PVL on angiography (CoreValve 29 mm)

AP / caudal

RAO /caudal

Case 3

PVL on angiography (after post-dilatation)



NuMED 23 x 40 mm

RAO / caudal

Case 3

AR index by catheterization

96 / [13:20] LEFT VENTRICLE

HEART RATE	68	[bpm]
LV BDP	3	[mmhg]
LV EDP	23	[mmhg]
LV PEAK SYST	161	[mmhg]
LV MEAN SYST	97	[mmhg]
LV MEAN DIAS	17	[mmhg]
LV MAX DP/DT	1252	[mmhg/sec]
LV MIN DP/DT	-1160	[mmhg/sec]
LV PEAK VCE	20.2	[/sec]
LV V MAX	35.1	[/sec]

96 / [13:20] AORTA

HEART RATE	68	[bpm]
AO PEAK SYST	147	[mmhg]
AO MIN DIAS	54	[mmhg]
AO MEAN PRESSURE	91	[mmhg]

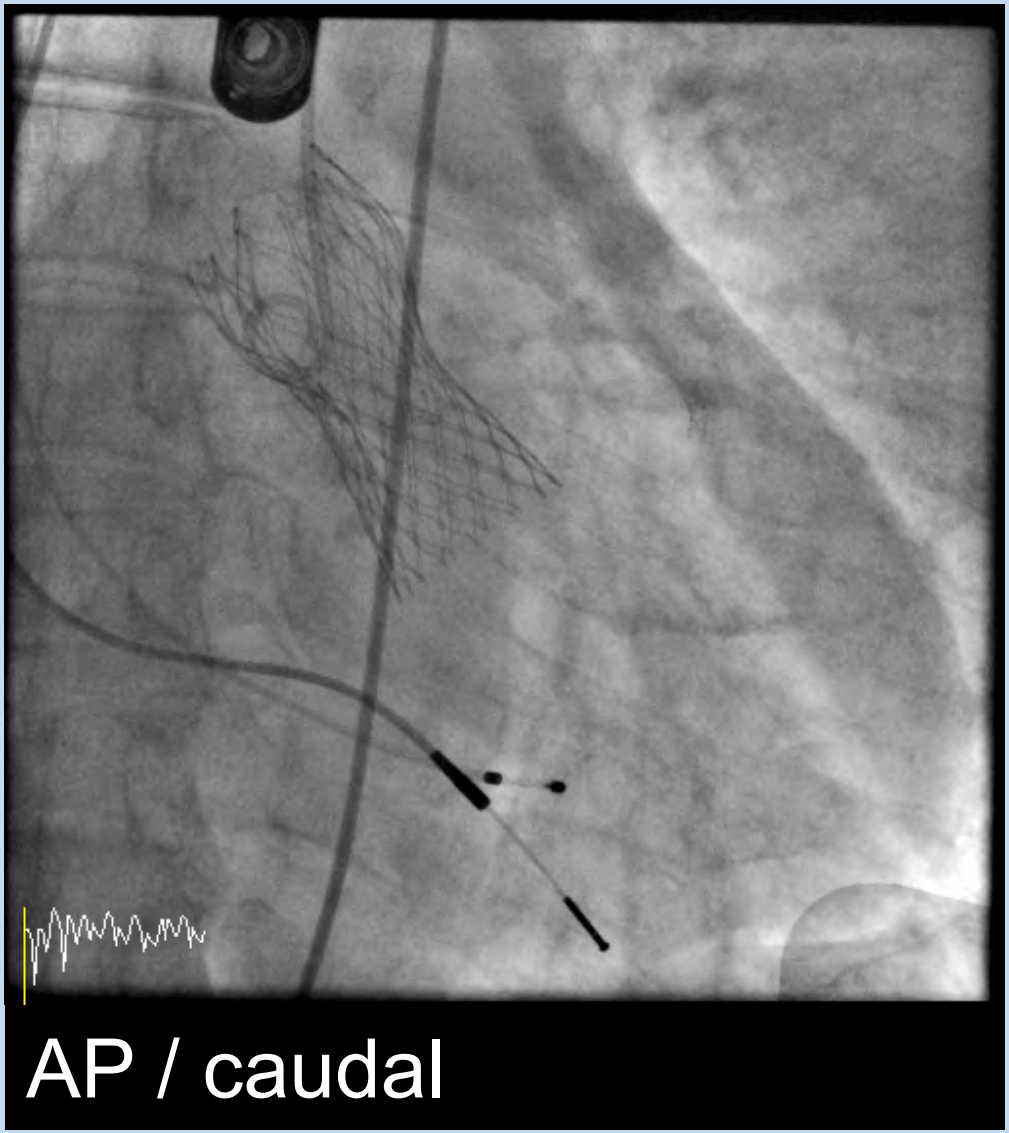
96 / [13:20] AORTIC VALVE

AOV LAG TIME	62	[msec]
AOV SEP	19	[sec/min]
AOV PEAK GRAD	13.0	[mmhg]
AOV MEAN GRAD	6.9	[mmhg]

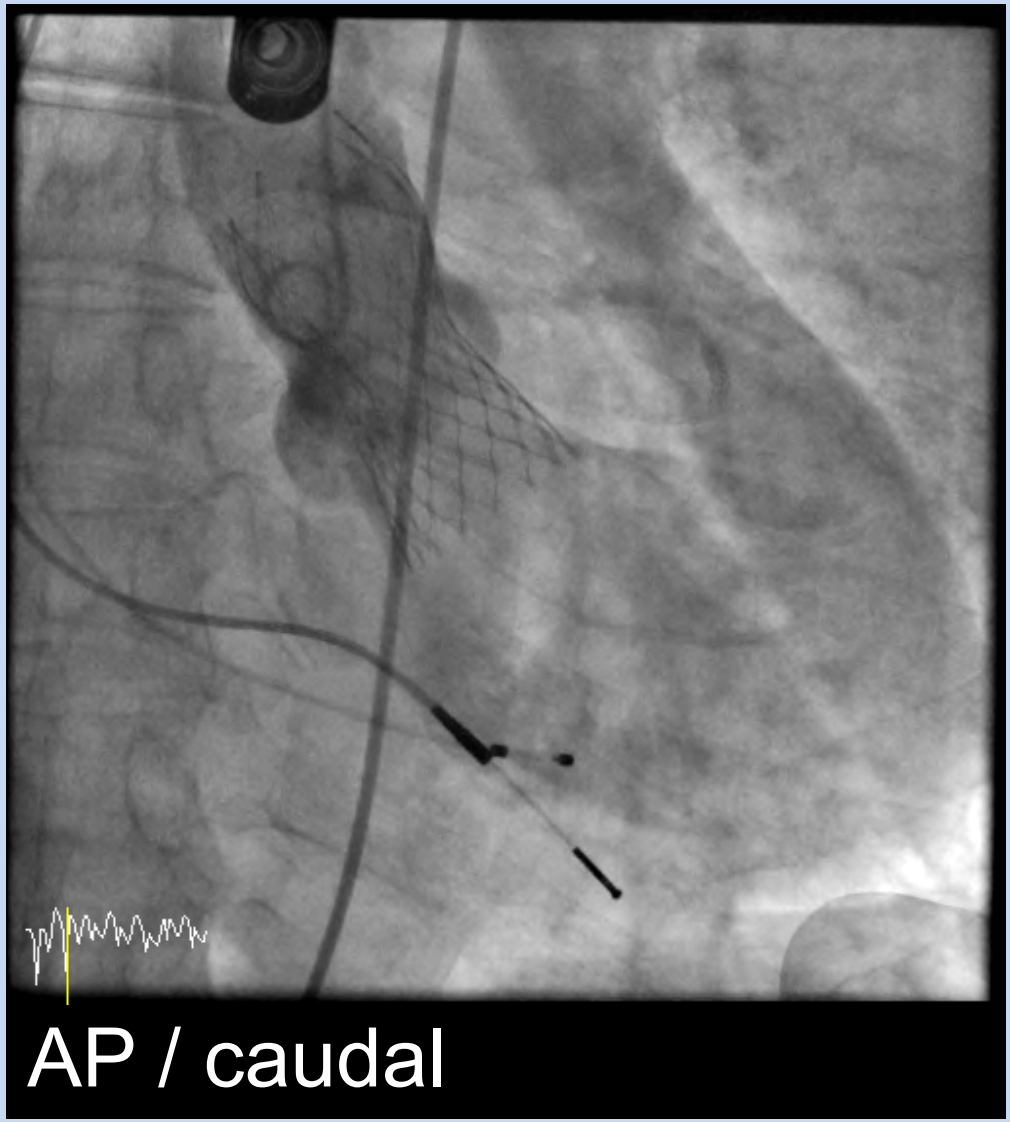
AR index = (54 – 23) / 147 x 100 = 20

Case 3

Valve position on angiography



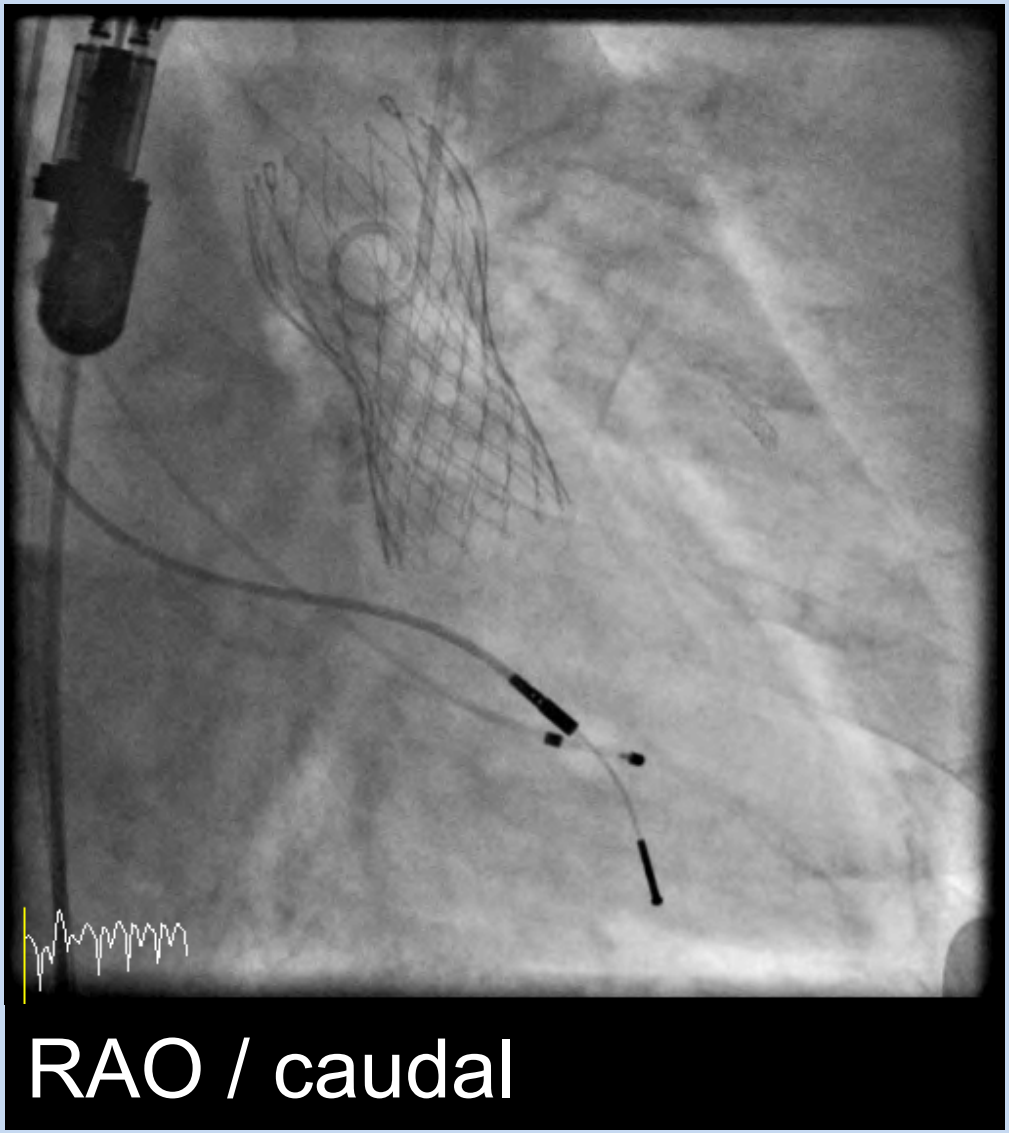
AP / caudal



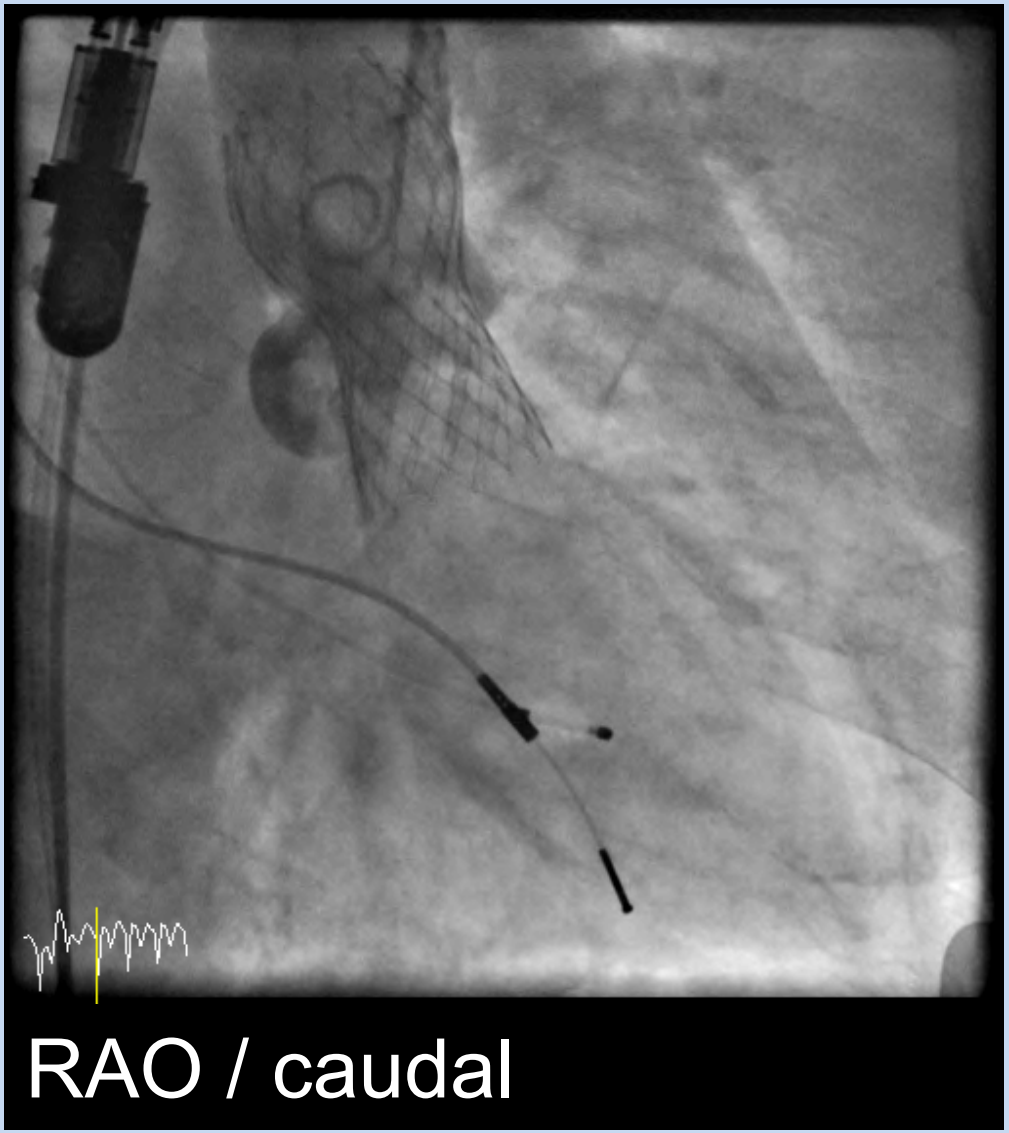
AP / caudal

Case 3

Valve position on angiography



RAO / caudal



RAO / caudal

Case 4

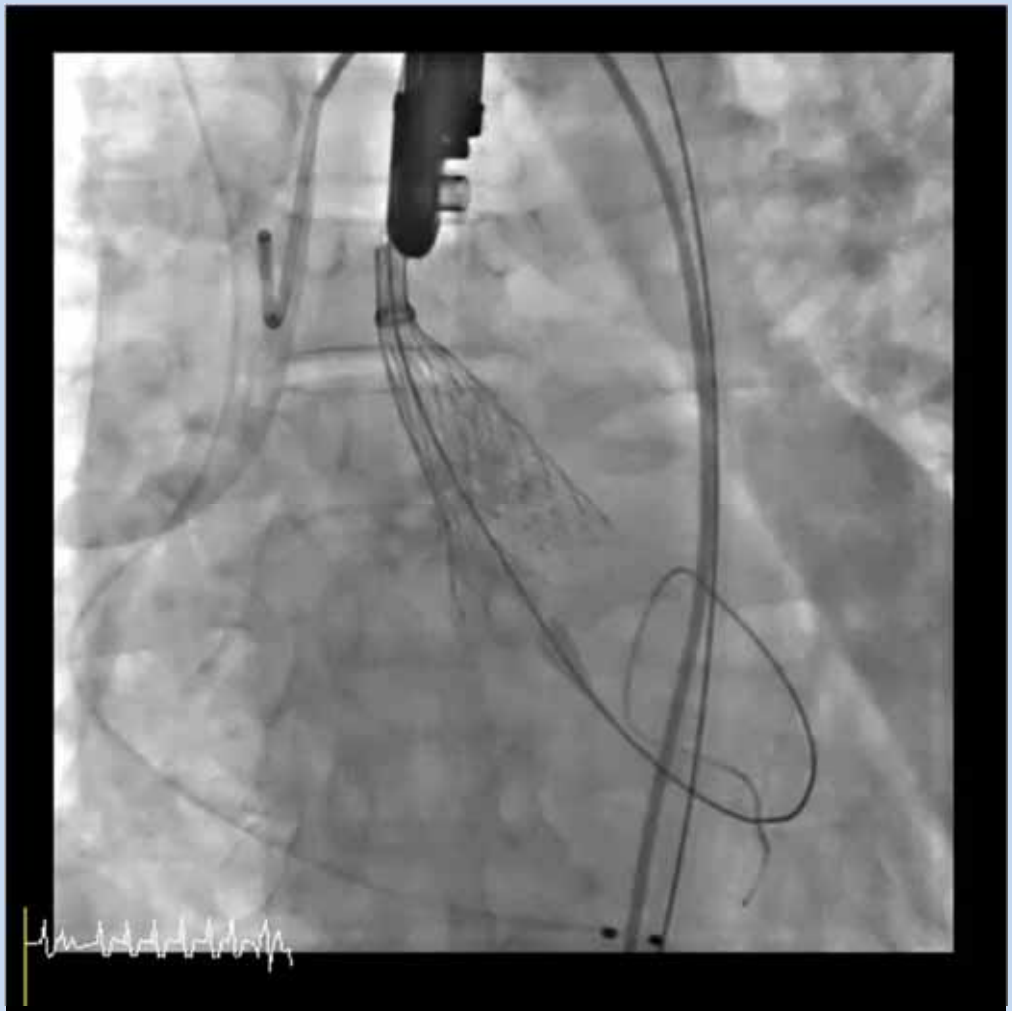
- Brief history: M/83
  - Chief complaint: aggravation of dyspnea
  - Colon cancer
- Cardiovascular risk factors
  - diabetes mellitus/hypertension/dyslipidemia (-/-/-)
- Laboratory findings
  - ECG: NSR
  - Echocardiography
    - normal LV size with depressed LVEF (53%)
    - AV mean pressure gradient 75 mmHg, AV area 0.68 cm^2
- Logistic euroSCORE: 5.8%

Case 4

Calcification on MDCT

Case 4

Valve deployment (CoreValve 26 mm)

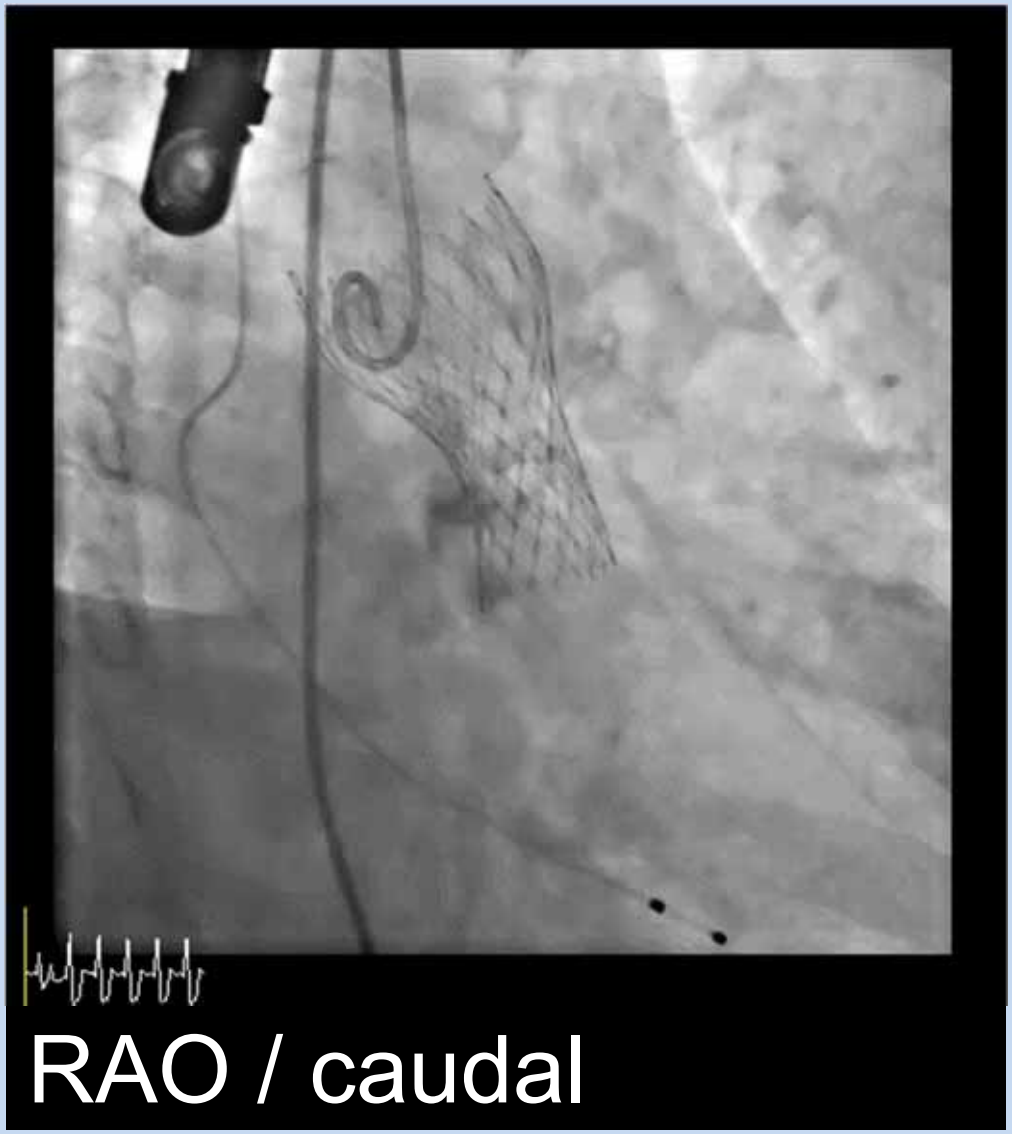


LAO / caudal

*Incomplete valve expansion at the portion of severe eccentric calcification

Case 4

PVL on angiography (CoreValve 26 mm)



We did not perform post-dilatation in this case:

High risk of complication, such as distal embolization or coronary obstruction

Relatively low benefit of procedure

Case 4

AR index by catheterization

107 / [14:16] LEFT VENTRICLE

HEART RATE	62	[bpm]
LV BDP	11	[mmhg]
LV EDP	22	[mmhg]
LV PEAK SYST	133	[mmhg]
LV MEAN SYST	86	[mmhg]
LV MEAN DIAS	16	[mmhg]
LV MAX DP/DT	799	[mmhg/sec]
LV MIN DP/DT	-829	[mmhg/sec]
LV PEAK VCE	14.5	[/sec]
LV V MAX	22.1	[/sec]

107 / [14:16] AORTA

HEART RATE	62	[bpm]
AO PEAK SYST	123	[mmhg]
AO MIN DIAS	49	[mmhg]
AO MEAN PRESSURE	74	[mmhg]

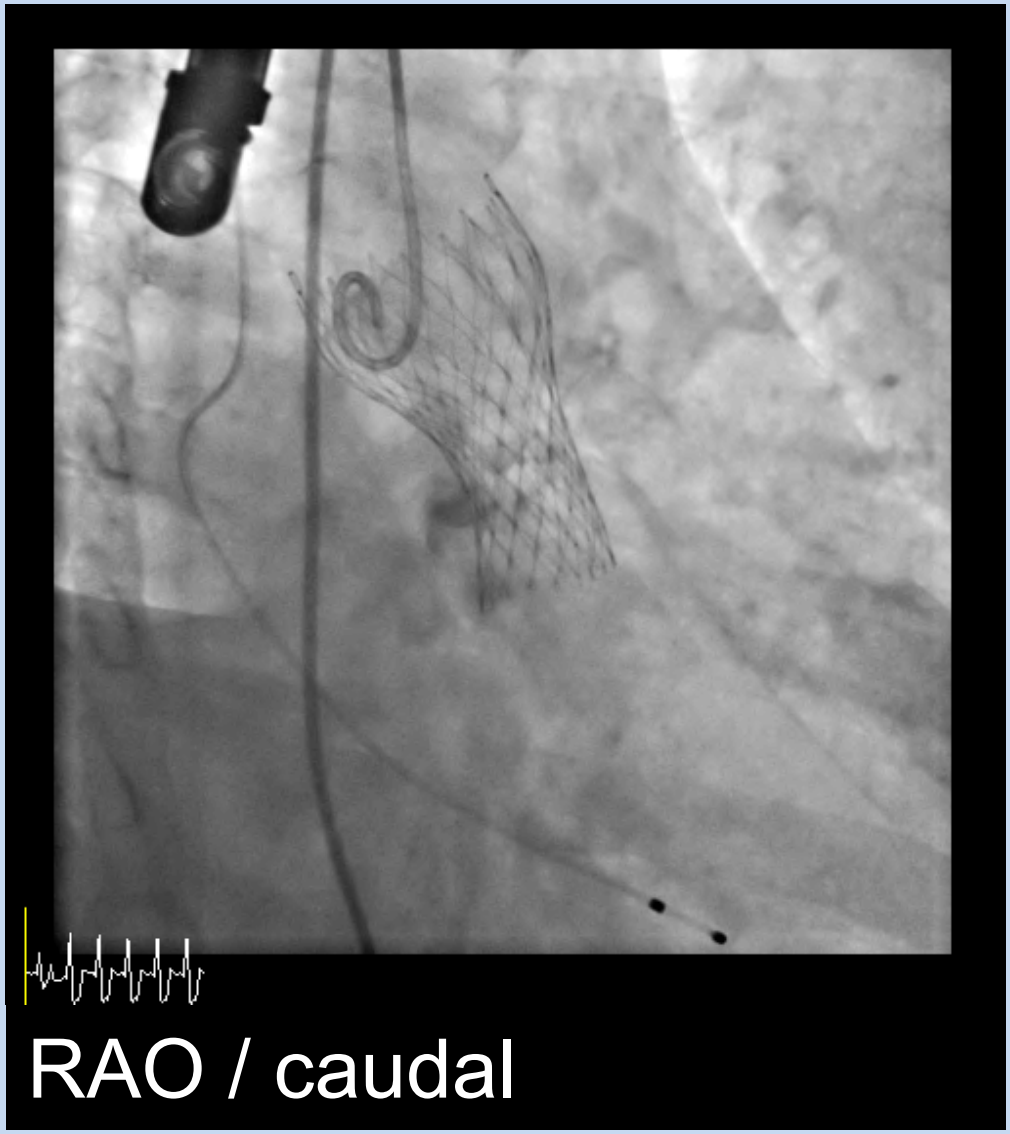
107 / [14:16] AORTIC VALVE

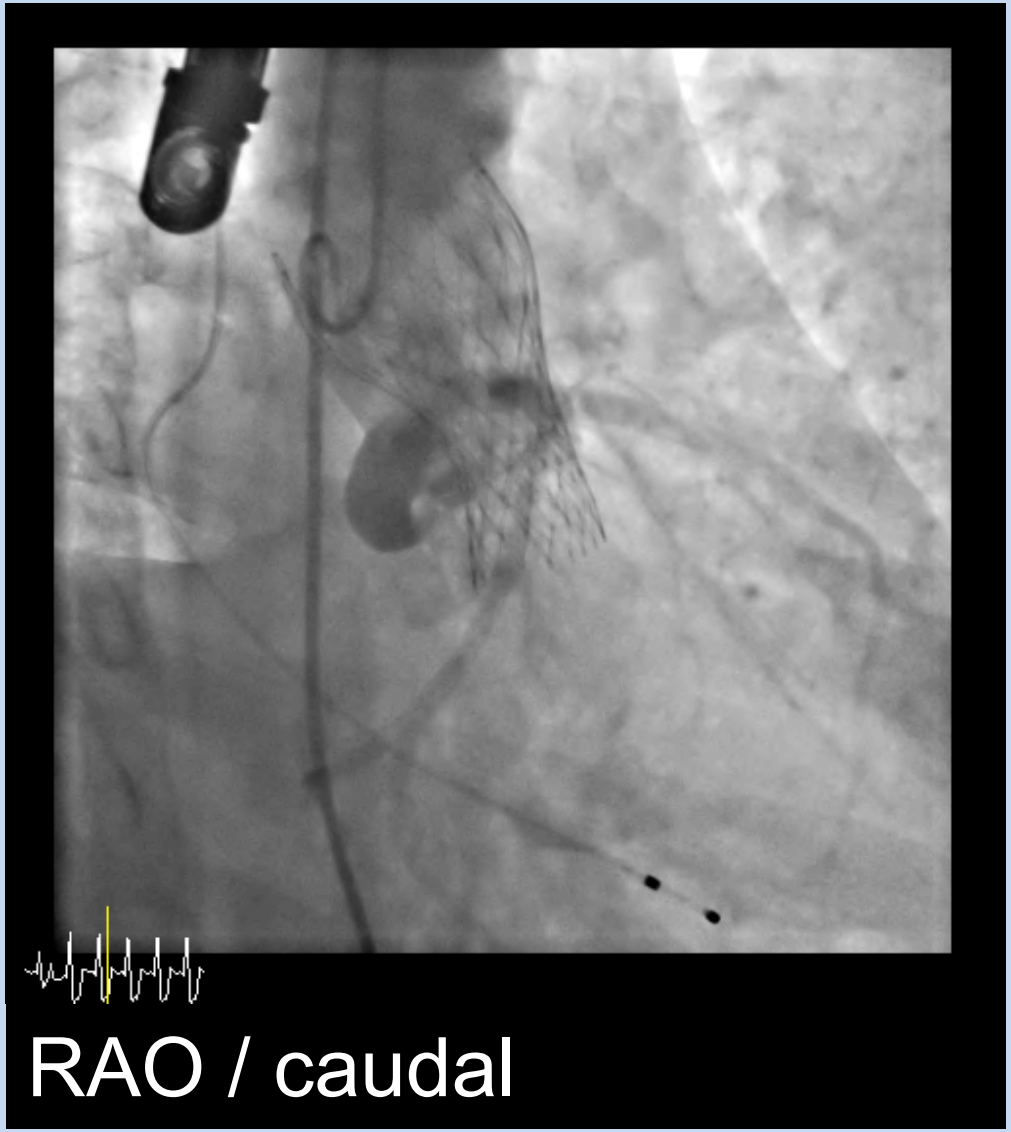
AOV LAG TIME	29	[msec]
AOV SEP	15	[sec/min]
AOV PEAK GRAD	9.9	[mmhg]
AOV MEAN GRAD	22.1	[mmhg]

AR index = (49 – 22) / 123 x 100 = 22

Case 4

Valve position on angiography





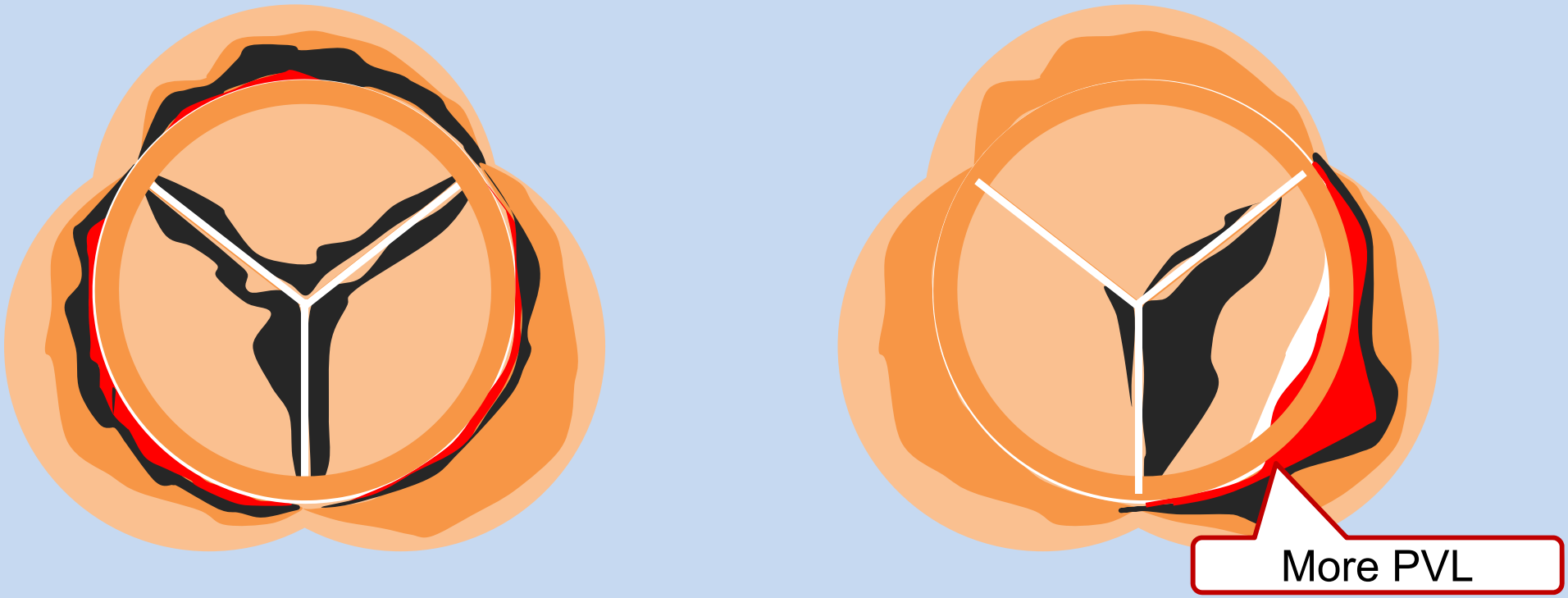
Summary of Cases

	Degree of calcification	Distribution of calcification	PVL
Case 1	Mild		Trivial
Case 2	Severe	Concentric	Mild
Case 3	Severe	**Eccentric**	**Moderate**
Case 4	Severe	**Eccentric** (+ LVOT calcification)	**Moderate**

Hypothesis based on These Observations

Symmetric calcification

Asymmetric calcification



Asymmetric calcification portends higher risk of PVL

Three-Centers' Study on Calcification & PVL

Calcification

1) severity of calcification (quantitative)
   distribution of calcification (symmetric vs. asymmetric)
2) angle between the axis of ascending aorta and the LVOT axis

PVL (paravalvular leakage after CoreValve TAVI)

1) assessed immediately after procedure
2) measured by left ventriculography (+ echocardiography)
3) cutoff: grade ≥3

Total number of patients = 66 CoreValve

1) SNU hospital
2) AMC
3) Singapore National Heart Center

Calcification & PVL

	All (n=63)	Grade <3 (n=48)	Grade ≥3 (n=15)	*p* value
Total calcium score (mean, IQR)	710±539 (569, 342-915)	578±420 (437, 305-851)	1246±647 (1032, 831-1361)	<0.001
Δ calcium score (mean, IQR)	268±300 (215, 92-381)	181±141 (166, 59-261)	620±482 (484, 414-607)	<0.001
Angle (mean, IQR)	160±10 (160, 154-165)	160±10 (160, 154-165)	158±9 (162, 150-166)	0.729

Values given as mean ± SD or number (percentage), unless otherwise indicated. Comparisons of continuous and categorical data were made by the Mann-Whitney U test and Fisher exact test, respectively.

Unpublished data

Predictor of PVL (bivariate analysis)

Grade ≥3 PVL

	Odds ratio	*P* value	95% CI
Age, per year	0.961	0.366	0.880-1.048
Gender	0.825	0.757	0.245-2.785
DM	0.162	0.092	0.019-1.347
Smoker	5.000	0.070	0.879-28.440
STS	0.733	0.114	0.498-1.077
Mean PG, *per increase of 5 mmHg*	1.200	0.024	1.005-1.071
Procedure time	1.024	0.195	0.988-1.061
Total calcium score, *per increase of 100*	1.286	0.002	1.048-1.227
Δ calcium score, *per increase of 100*	3.893	<0.001	1.371-2.839
Angle	0.963	0.222	0.905-1.023

Unpublished data

Application on Aforementioned Cases

	Degree of calcification (Total calcium score)	Distribution of calcification (Calcium score difference)	PVL
Case 1	**Mild (49.1)**	**Concentric (32.9)**	Trivial
Case 2	**Severe (1130.1)**	**Concentric (81.64)**	Mild
Case 3	**Severe (689.8)**	**Eccentric (354.0)**	**Moderate**
Case 4	**Severe (1943.0)**	**Eccentric (565.6)**	**Moderate**

Calcification & PVL

- The degree of eccentric calcification is a better parameter to predict the risk of PVL than that of total calcification.
- Baseline clinical variables do not predict the risk of grade ≥3 PVL.
- The ∠LVOT-Aorta angle is not a significant predictor of PVL in patients undergoing TAVI with CoreValve. (maybe due to the long height of device)

Endovascular & **Co**ronary **Re**vascularization in **Seoul**

ENCORE SEOUL 2014

SEPTEMBER 24(WED) ~ 26(FRI), 2014

COEX CONVENTION CENTER, SEOUL, KOREA

Course Directors

·Hyeon-Cheol Gwon, MD

·Taehoon Ahn, MD

·Yangsoo Jang, MD

·Hyo-Soo Kim, MD

Take home massages for PVL

1. Comprehensive assessment of calcification
- Severity, location, eccentricity

2. Proper sizing for procedure
- 3-D reconstruction (MDCT, 3D-EchoCG)
- Modest over-sizing

3. Optimal positioning
- Landmark (eq. NCC)

4. Identification or quantification of PLV
- Supra-skirtal or true paravalvular regurgitation
- TEE, Aortography, and Ao-Pulse Pr. (ARi)

5. Correction
- Balloon post-dilatation, valve-in-valve technique

Baseline clinical characteristics (1)

	All (n=66)	Grade <3 (n=53)	Grade ≥3 (n=13)	*p* value
Age, yrs	78.6±7.0	78.9±7.4	77.0±5.0	0.196
Female, n (%)	33 (50.0%)	27 (50.9%)	6 (46.2%)	0.757
Weight, kg	57.1±10.7	57.4±11.2	55.7±8.2	0.545
Height, cm	156.7±9.6	156.8±9.8	156.4±9.0	0.961
BSA, cm^2	1.53±0.20	1.53±0.21	1.56±0.14	0.758
DM, n (%)	19 (28.8%)	18 (34.0%)	1 (7.7%)	0.088
HTN, n (%)	51 (77.3%)	42 (79.2%)	9 (69.2%)	0.471
Dyslipidemia, n (%)	45 (68.2%)	38 (71.7%)	7 (53.8%)	0.319
Smoker, n (%)	6 (9.1%)	3 (5.7%)	3 (23.1%)	0.085
IHD, n (%)	33 (50.0%)	28 (52.8%)	5 (38.5)	0.537
Prev. PCI, n (%)	26 (39.4%)	20 (37.7%)	6 (46.2%)	0.753
Carotid ds, n (%)	3 (4.5%)	3 (5.7%)	0 (0%)	1.000
PAD, n (%)	6 (9.1%)	4 (7.5%)	2 (15.4%)	0.337
NYHA class (median, IQR)	2.7±0.7 (3, 2-3)	2.7±0.7 (3, 2-3)	2.5±0.7 (3, 2-3)	0.452

Baseline clinical characteristics (2)

	All (n=66)	Grade <3 (n=53)	Grade ≥3 (n=13)	*p* value
EuroSCORE (median, IQR)	16.6±12.2 (13.5, 7.5-24.4)	17.0±12.9 (12.6, 7.9-25.0)	15.1±8.9 (17.4, 5.6-22.7)	0.809
STS (median, IQR)	9.8±10.1 (5.9, 3.5-12.4)	11.0±10.8 (6.5, 3.9-14.1)	4.2±1.3 (4.0, 2.7-5.4)	0.037

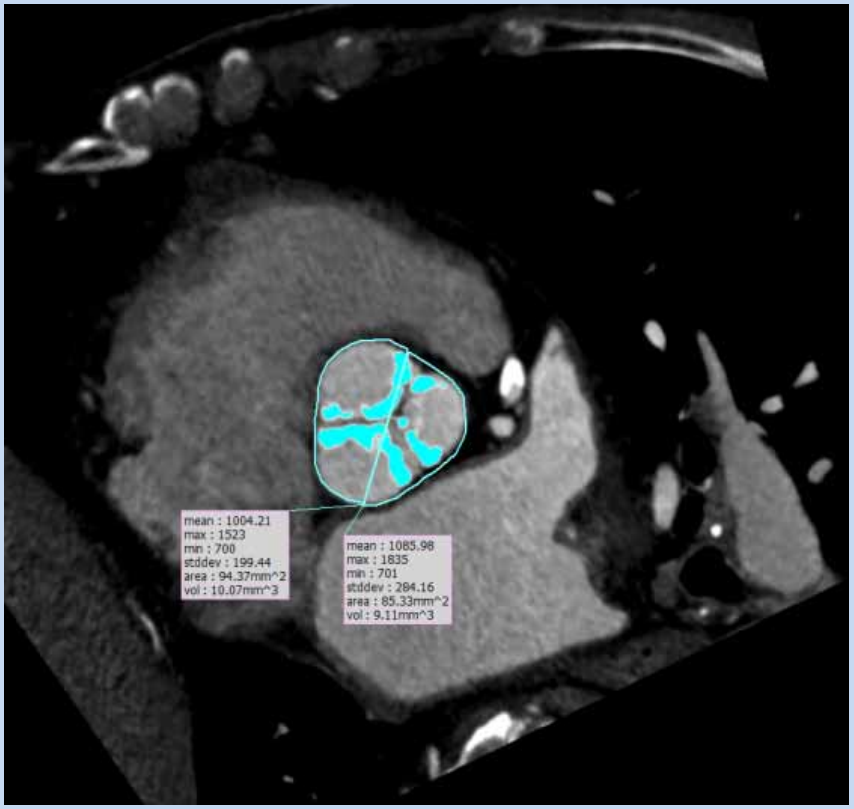
Values given as mean ± SD or number (percentage), unless otherwise indicated. Comparisons of continuous and categorical data were made by the Mann-Whitney U test and Fisher exact test, respectively.

Baseline echocardiographic and procedural characteristics

	All (n=63)	Grade <3 (n=53)	Grade ≥3 (n=13)	*p* value
Echocardiographic parameter				
EF, %	55.8±12.0	56.1±11.7	54.5±13.3	0.589
AVA, cm2	0.63±0.18	0.64±0.18	0.61±0.17	0.534
MPG, mmHg	59.4±20.1	56.5±18.6	71.2±22.4	0.027
Annulus, mm	21.7±2.2	21.6±2.0	22.2±2.8	0.464
AR (grade ≥3)	8 (12.1%)	6 (11.3%)	2 (15.4%)	0.651
MR (grade ≥3)	7 (10.6%)	7 (13.2%)	0 (0%)	0.329
Procedural parameter				
Procedure time, min	90.9±31.0	85.5±32.5	107.0±20.9	0.088
Valve size, mm	27.7±1.8	27.6±1.7	28.1±2.1	0.473

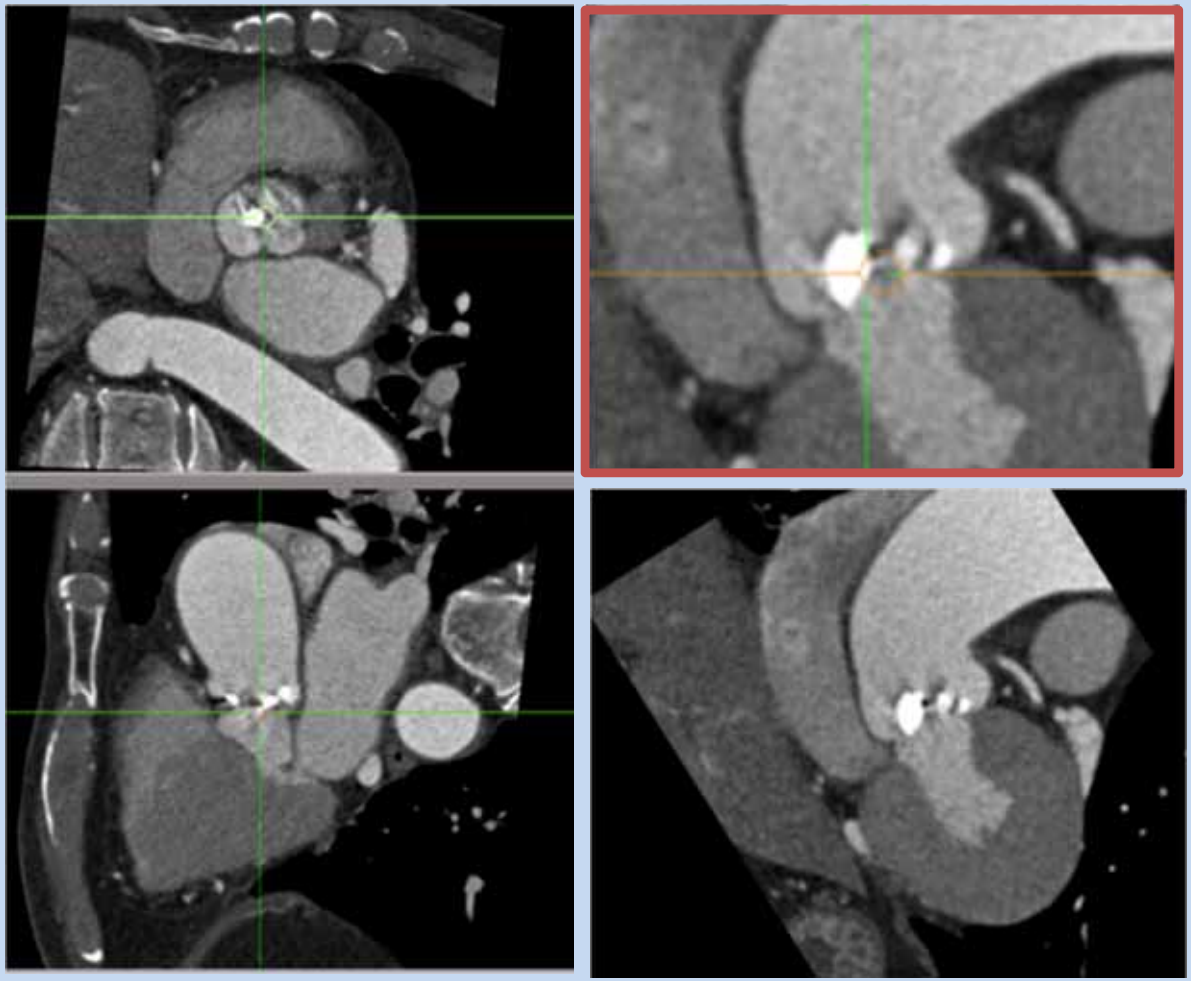
Values given as mean ± SD or number (percentage), unless otherwise indicated. Comparisons of continuous and categorical data were made by the Mann-Whitney U test and Fisher exact test, respectively.

Calcium area measurement



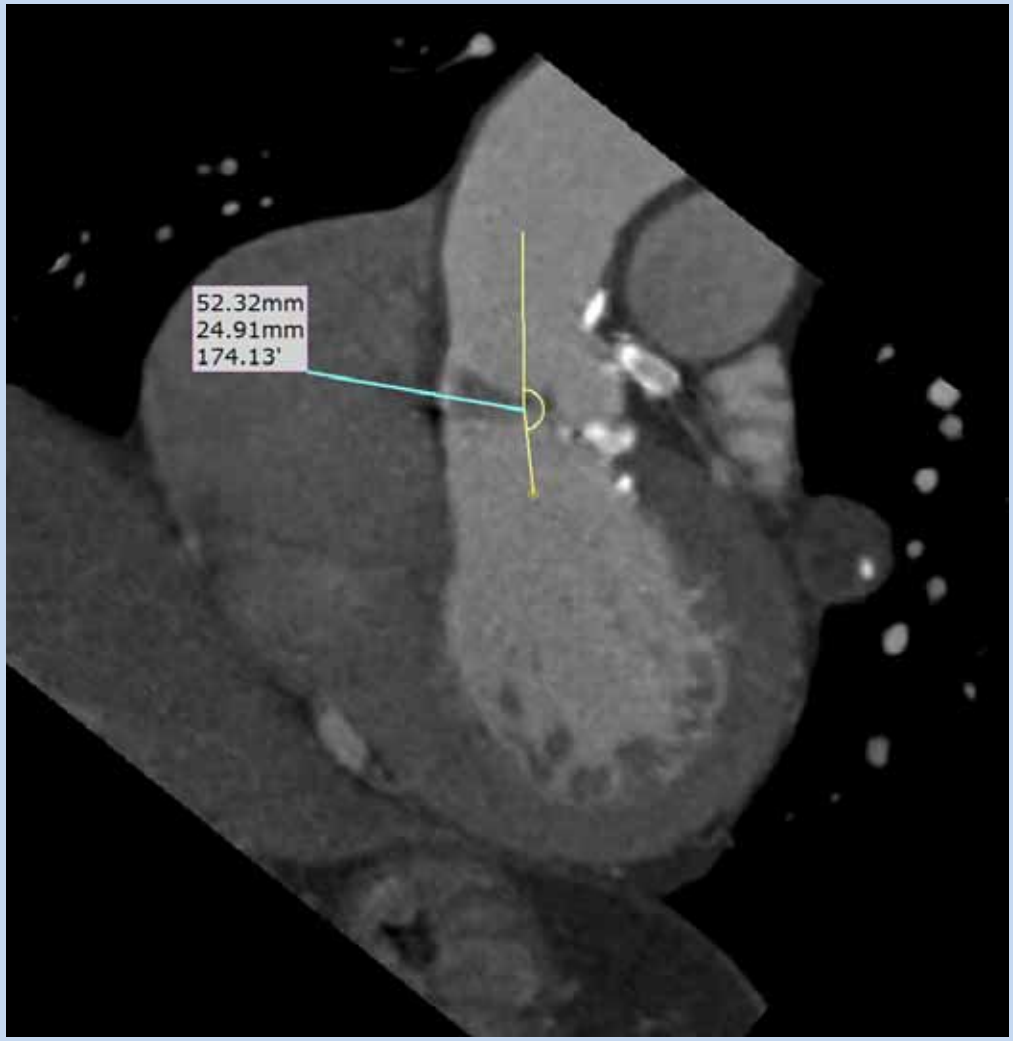
- Threshold of calcification
  : 700 HU on enhancement images
- Area of pixels over threshold
- Each half of the valve

Aortic valve calcification asymmetry assessment



- Stand alone 3D workstation
- Diastole phase images
- Perpendicular planes of aortic root
- Slice thickness 1 mm
- Slice interval 1 mm
- Number of images 30

Angle measurement



- Angle between aortic root axis and LVOT axis
- Measure angle in maximum distorted alignment

Predictor of PVL (multivariate analysis)

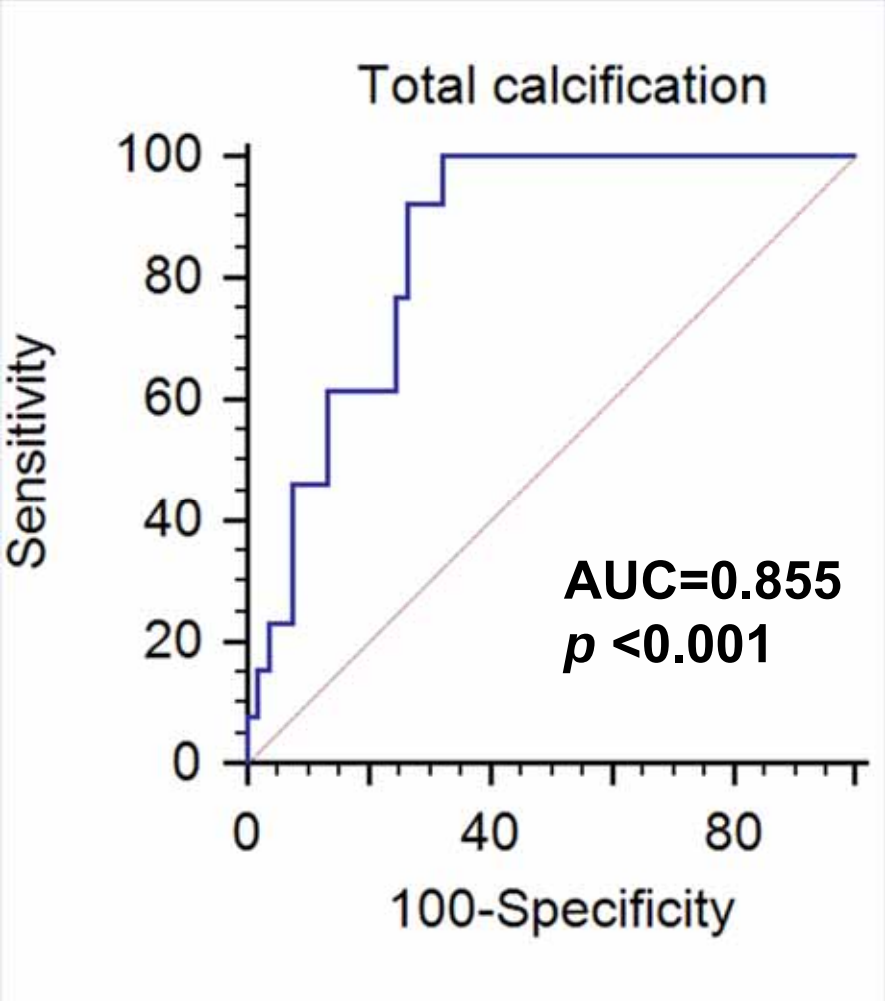
Grade ≥3 PVL

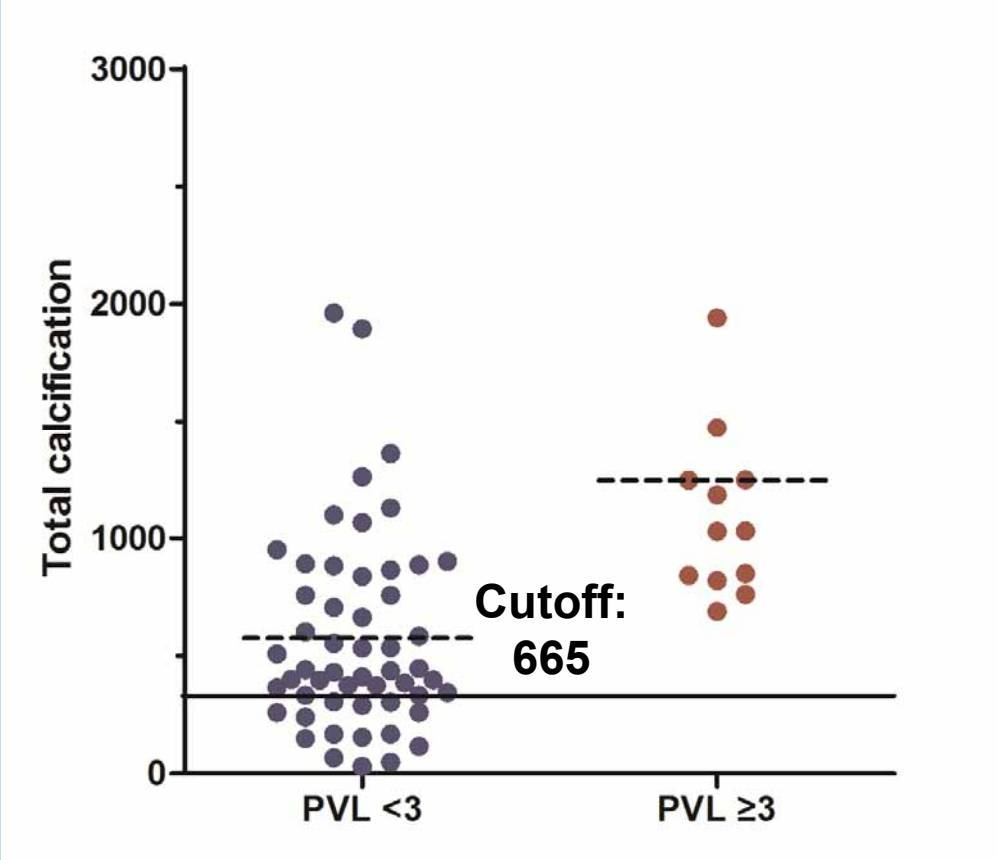
	Odds ratio	*P* value	95% CI
Age, per year	1.014	0.894	0.829-1.240
Gender	0.510	0.620	0.036-7.275
DM	0.290	0.467	0.010-8.143
Smoker	2.858	0.575	0.073-112-300
Mean PG, *per increase of 5 mmHg*	1.054	0.777	0.940-1.087
Total calcification, *per increase of 100*	0.663	0.200	0.594-1.115
Δ calcium score, *per increase of 100*	10.406	0.021	1.195-8.706
Angle	0.980	0.698	0.883-1.087

Unpublished data

Predictive value of total calcium score

Grade ≥3 PVL



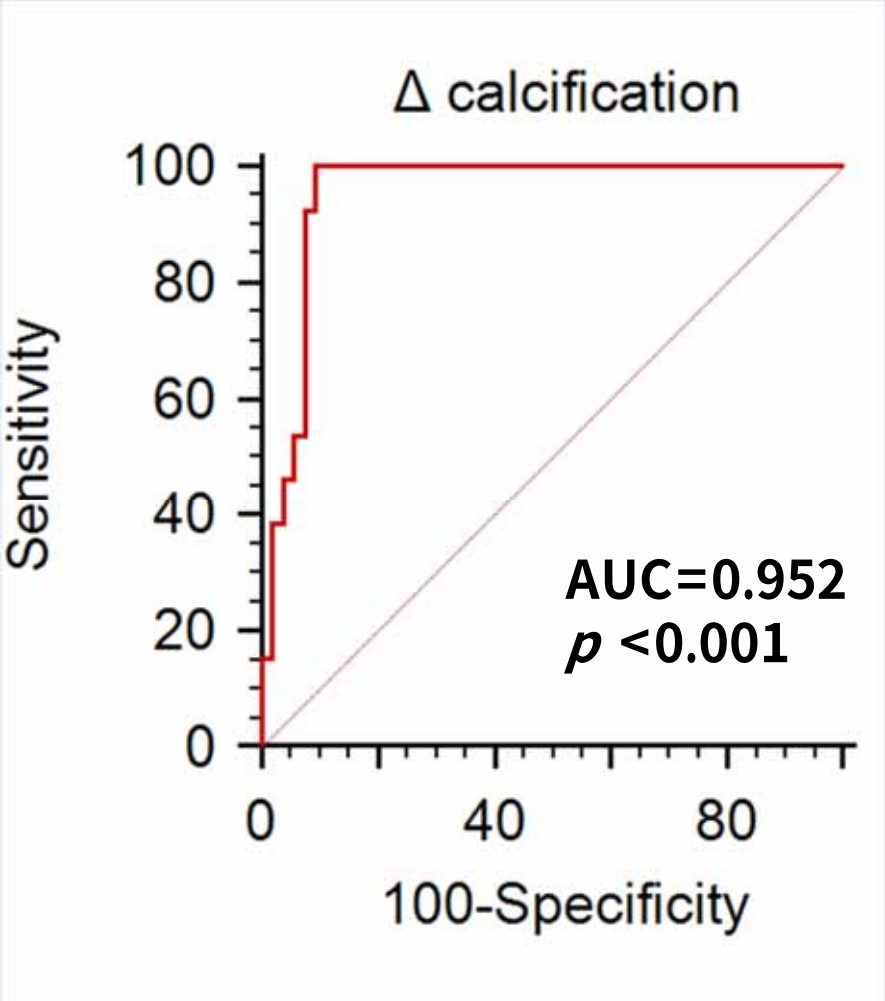


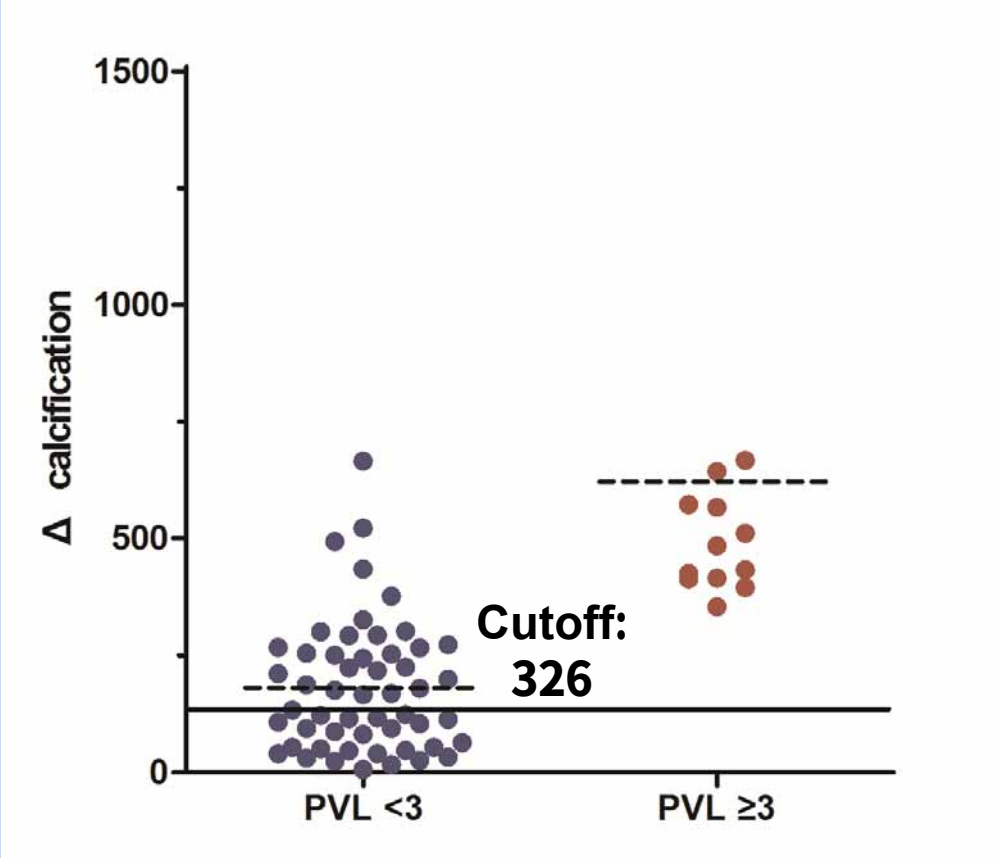
Sensitivity: 100%
Specificity: 68%

Unpublished data

Predictive value of Δ calcium score

Grade ≥3 PVL



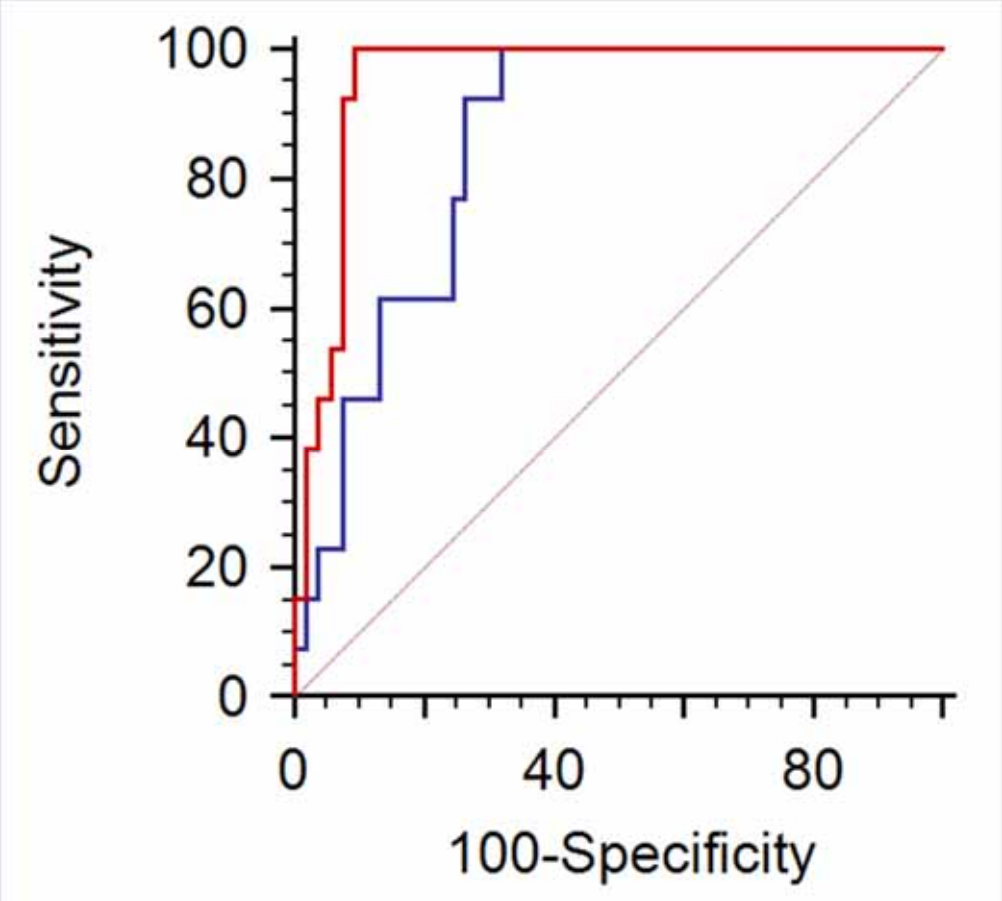


Sensitivity: 100%
Specificity: 91%

Unpublished data

Better predictive ability of Δ calcium score

Grade ≥3 PVL



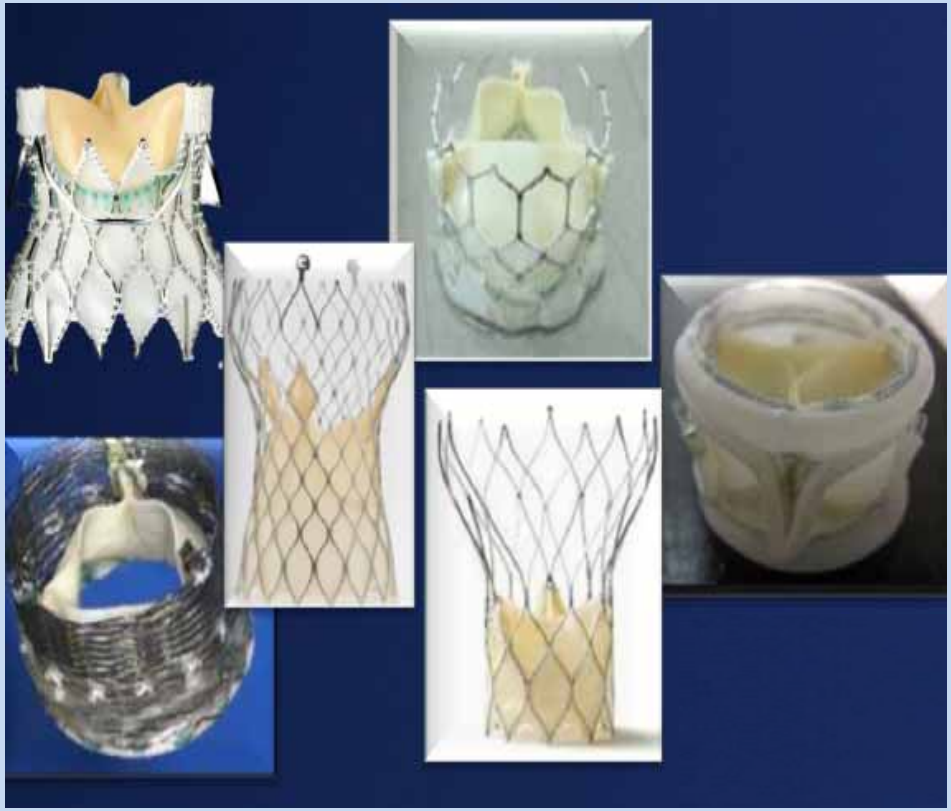
	AUC	95% CI	*P* for difference
Total calcium score	0.855	0.746-0.929	0.011
Δ calcium score	0.952	0.869-0.989	

Unpublished data

New generation device

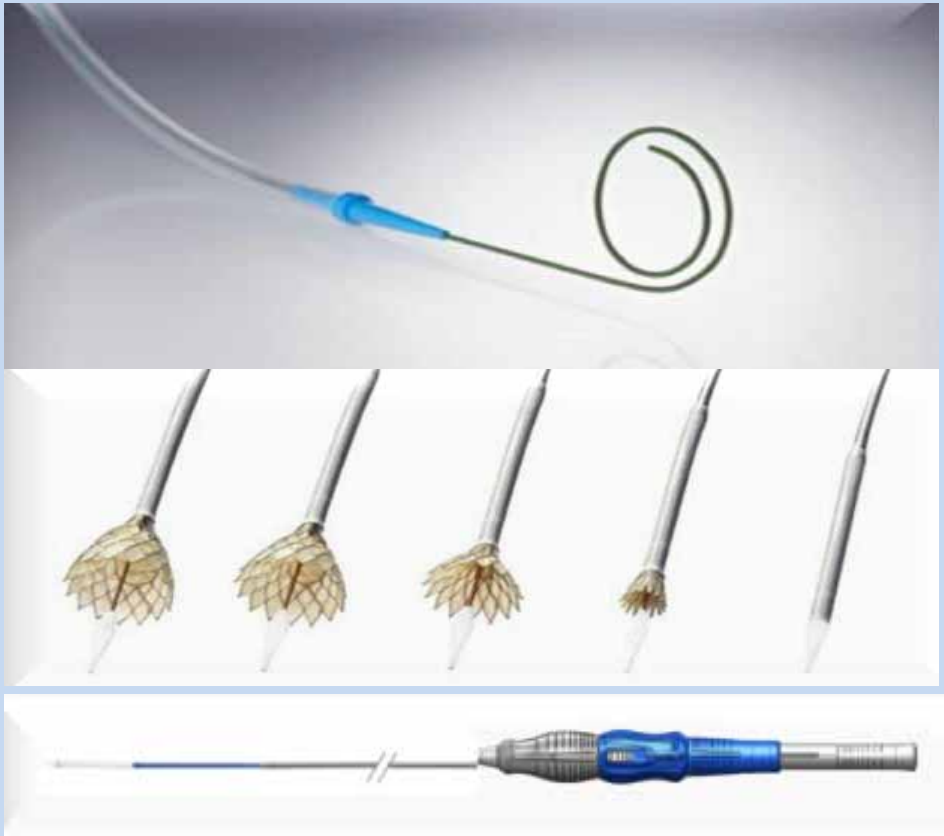
Annular Sealing

- Optimized radial force
- Positioning arms
- Skirt design



Optimal Positioning

- Stable Deployment
- Recapture capability
- Accessories (e.g. guidewire)



Généreux P. et al. J Am Coll Cardiol 2013;61;1125-36