Durability of TAVR vs. SAVR Pathology Insights

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

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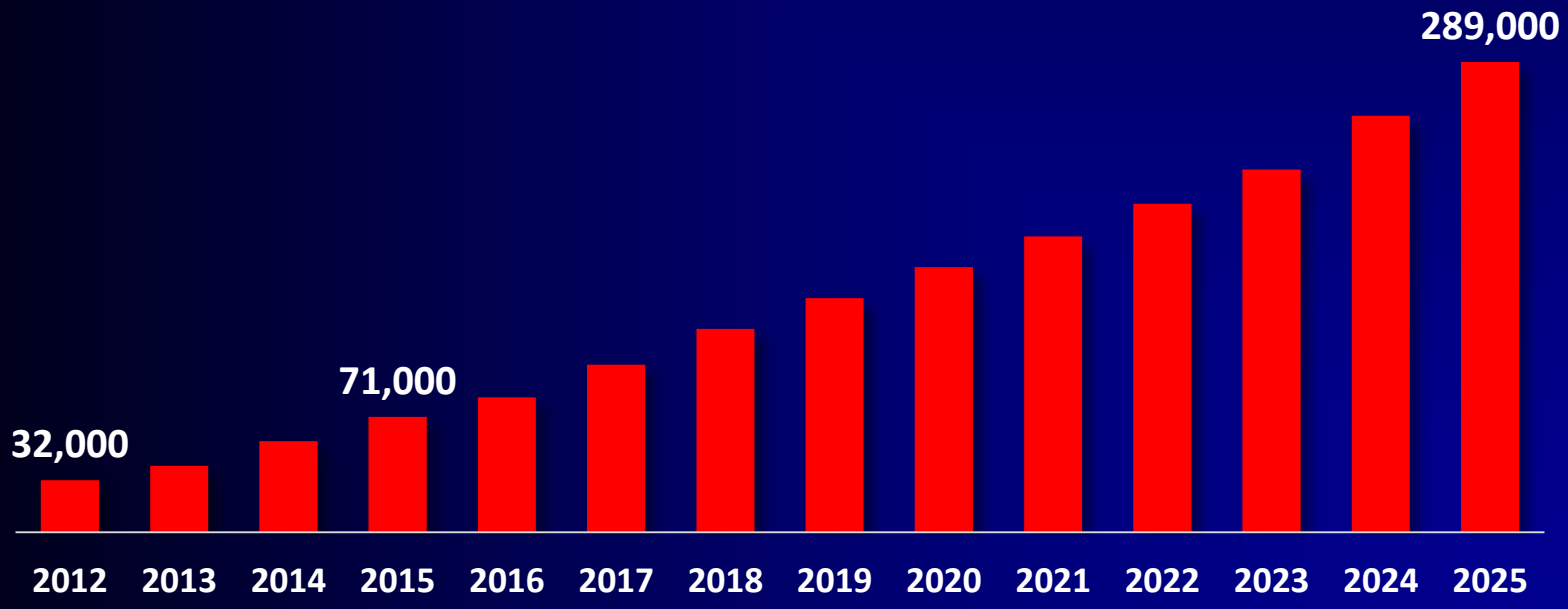
Speaker's Bureau
Abbott Vascular; Biosensors; Boston Scientific; Celonova; Cook Medical; CSI; Lutonix Bard; Sinomed; Terumo Corporation.

Consultant/Advisory Boards
Amgen; Abbott Vascular; Boston Scientific; Celonova; Cook Medical; Lutonix Bard; Sinomed.

Owner of a healthcare company: No
Stockholder of a healthcare company: No

Estimated Global TAVR Procedure Growth

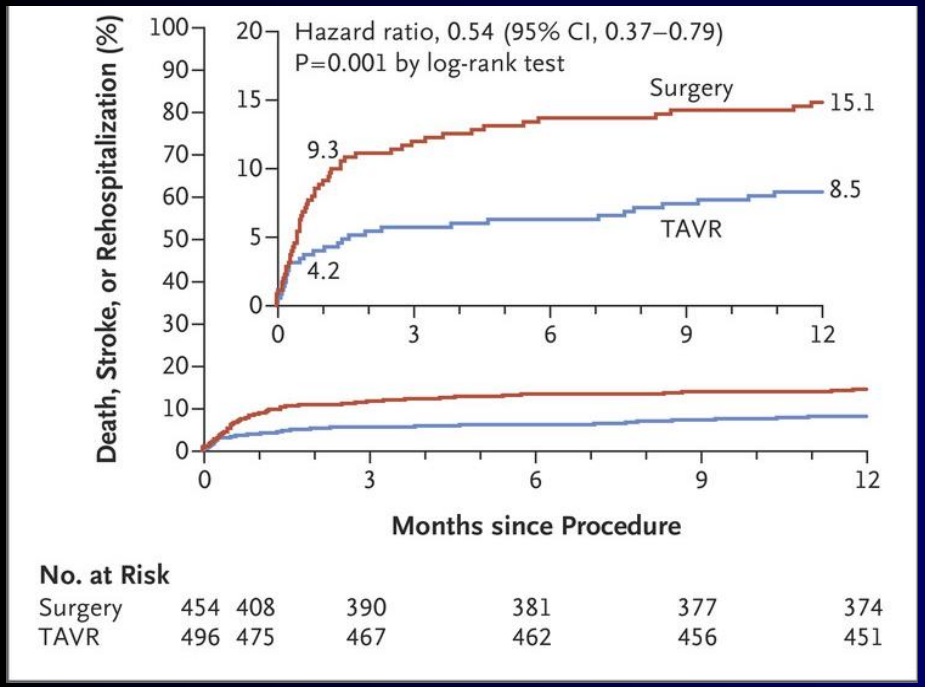
- In 2015, TAVR accounted for 32% of all Medicare AV replacements in the US
- Globally, TAVR is expected to grow approximately 4-fold in the next 10 years



Courtesy of Dr M. Leon TVT 2016; Adapted from Credit Suisse TAVI Comment – January 2015

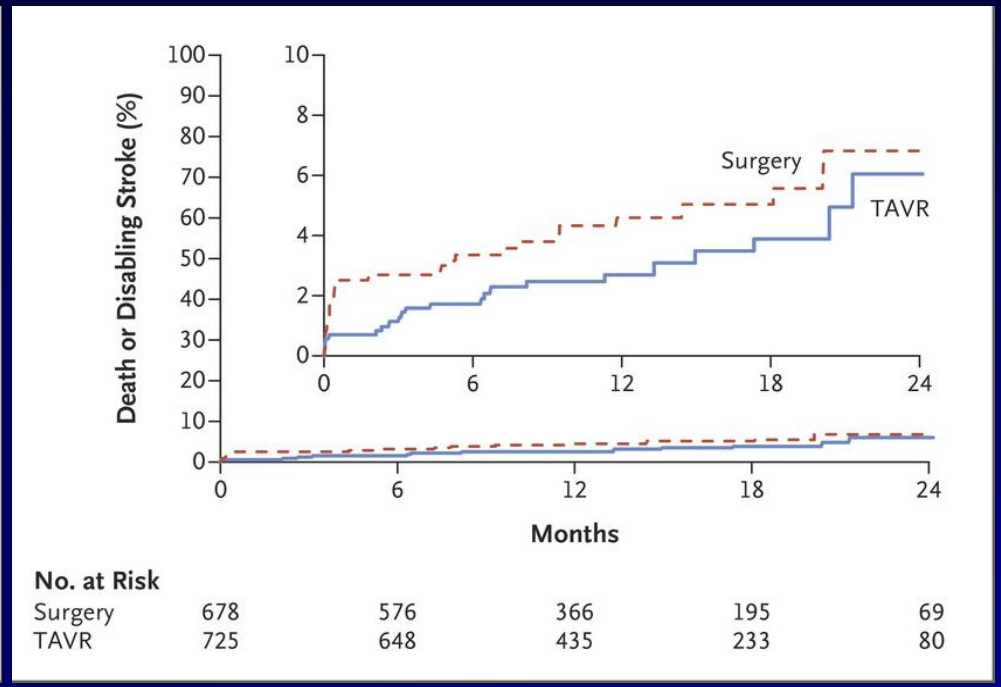
TAVR can be considered an alternative treatment for low-risk patients

PARTNER 3



N Engl J Med. 2019 Mar 17. doi: 10.1056/NEJMoa1814052. [Epub ahead of print]

Evolute Low Risk Trial



N Engl J Med. 2019 Mar 17. doi: 10.1056/NEJMoa1816885. [Epub ahead of print]

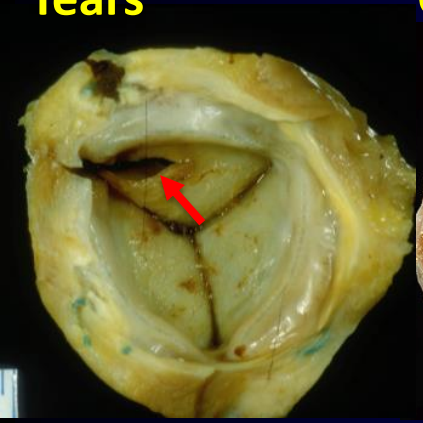
Long term durability data are warranted

TAVR and SAVR
What is the similarities?

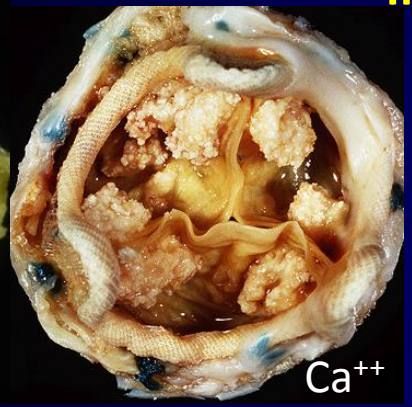
Surgically Implanted Bioprosthetic Valve: Summary

Disadvantages: Limited durability beyond 10 years especially in younger patients: cusp degeneration or tears, Ca^{++}, pannus formation and endocarditis (1–4% of patients during the 1st year, and in approximately 1% per year thereafter.)

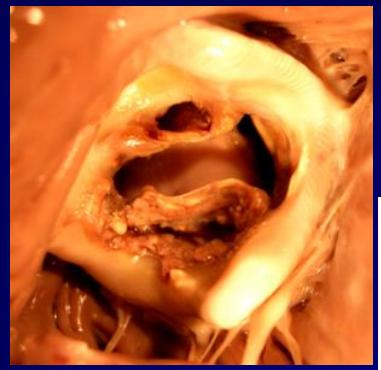
Tears



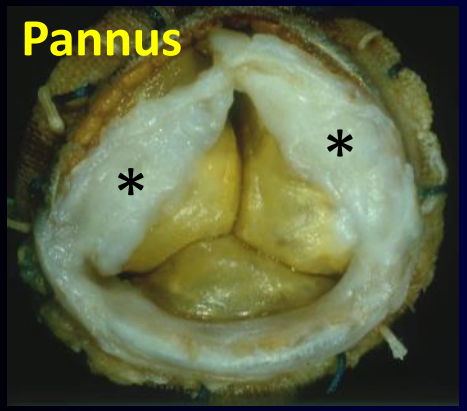
Calcification



Infective endocarditis

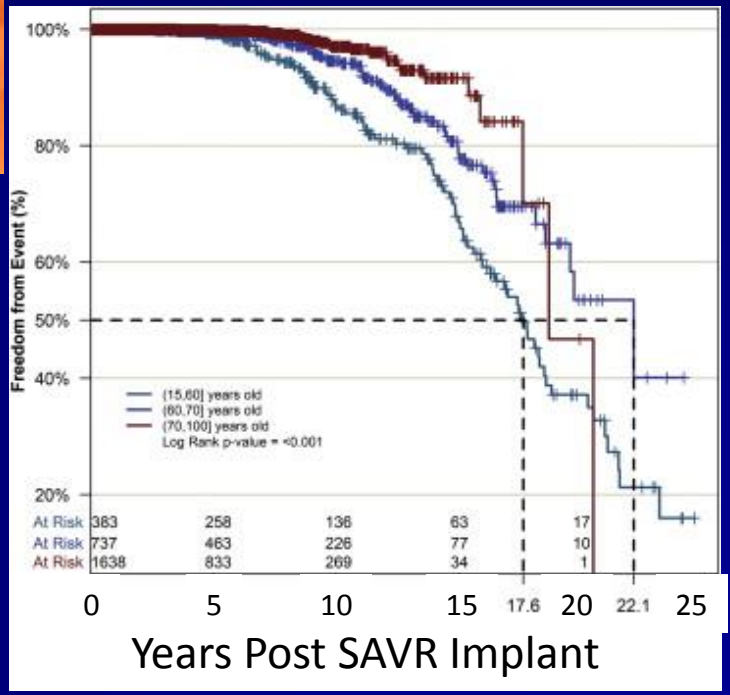


Pannus



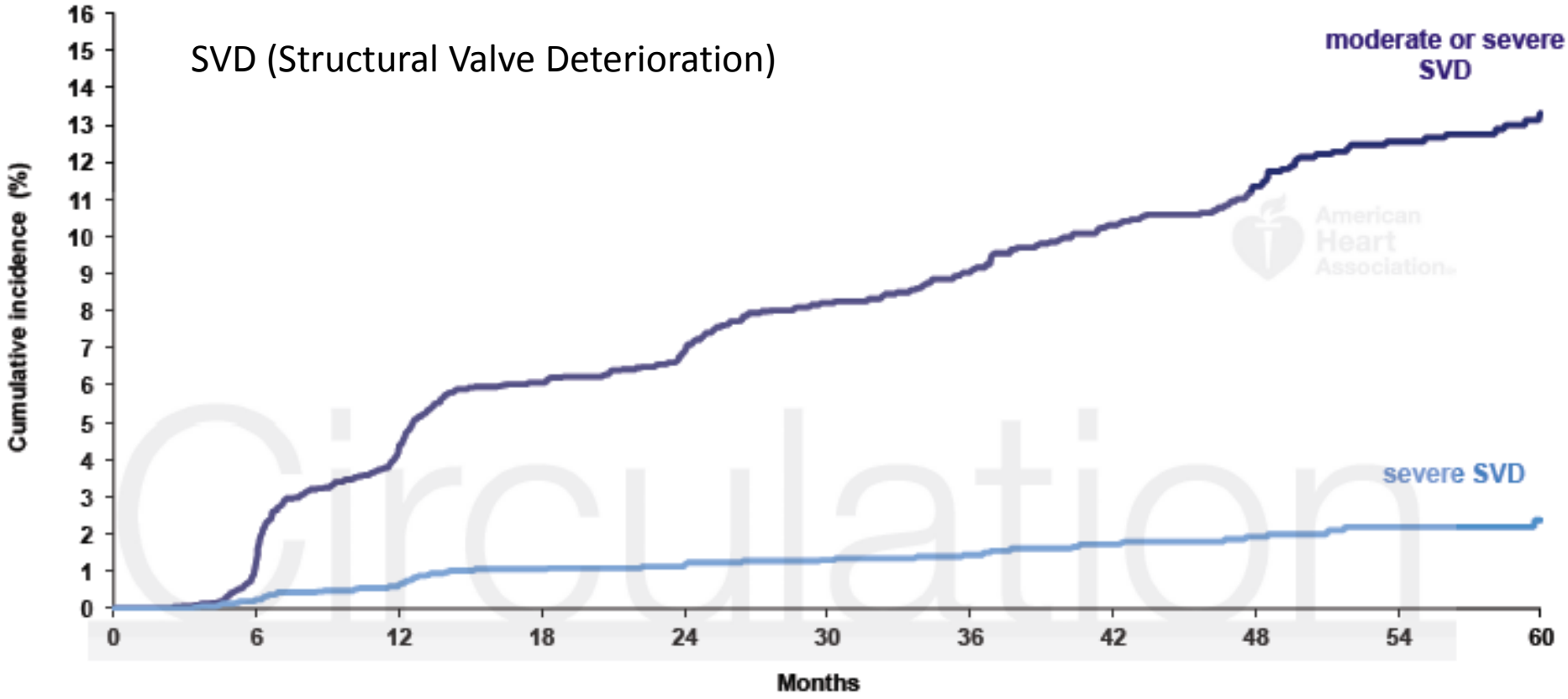
Thrombus

Freedom from Event (Severe AS/AR or Redo)



Bourguignon T et al. Ann Thorac Surg. 2015;99(3):831-7.

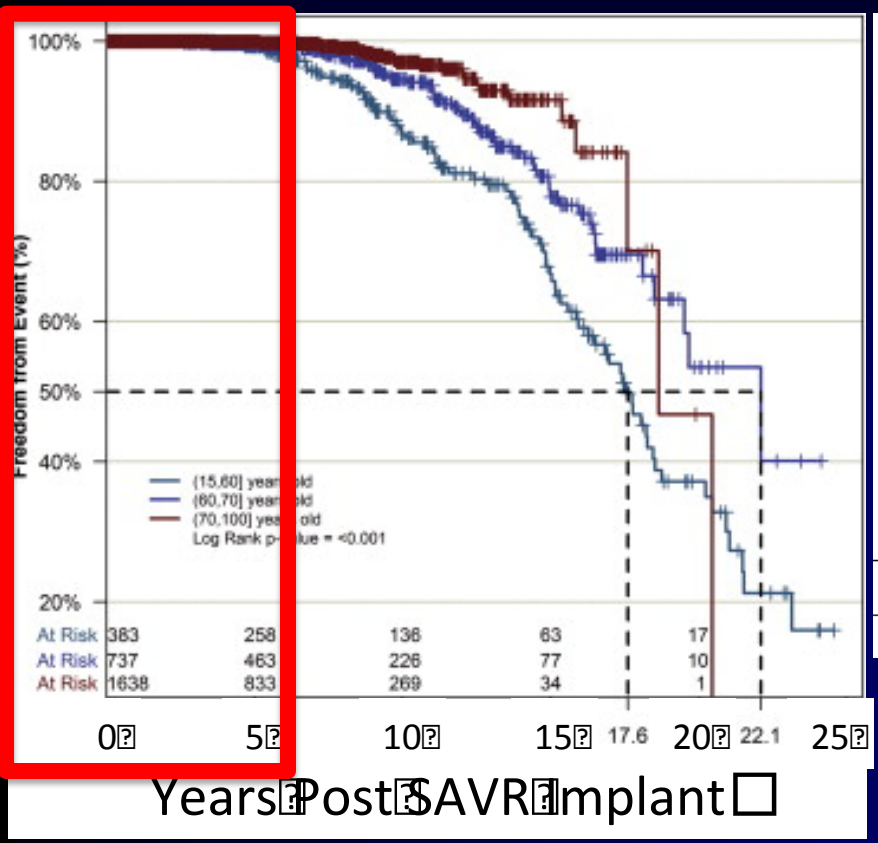
Long term f/u of TAVR
FRENCH 2 Registry 5-year f/u

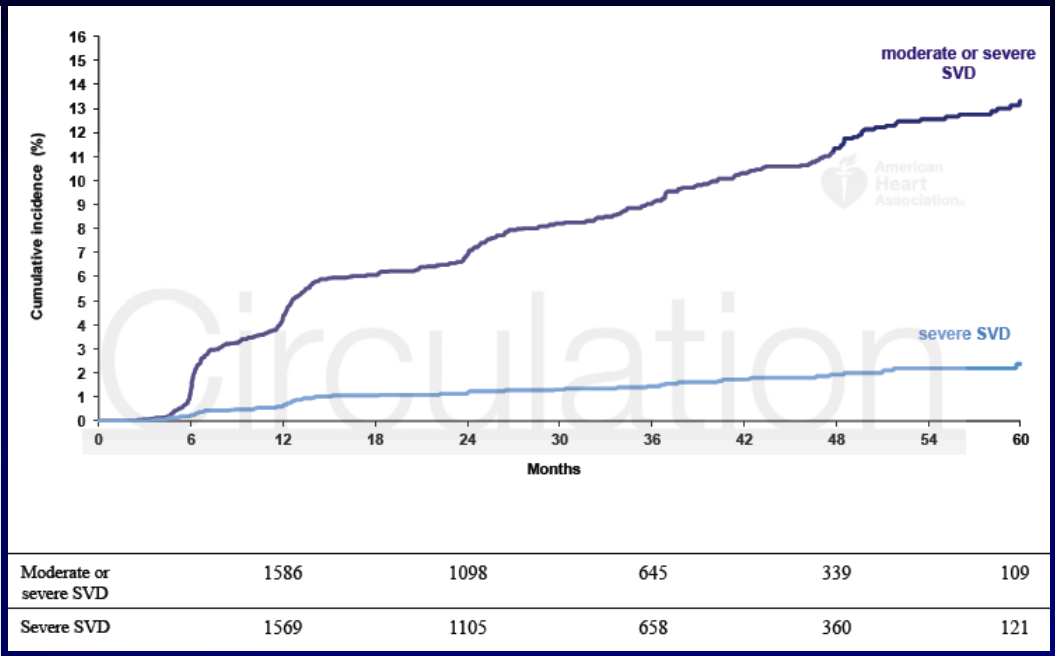


Moderate or severe SVD	1586	1098	645	339	109
Severe SVD	1569	1105	658	360	121

Romain Didier, et al. Circulation. 2018 Dec 4;138(23):2597-2607

Long term duration of SAVR and TAVR is similar?





Moderate or severe SVD	1586	1098	645	339	109
Severe SVD	1569	1105	658	360	121

SAVR
Freedom from Event (Severe AS/AR or Redo) 99%/5Y

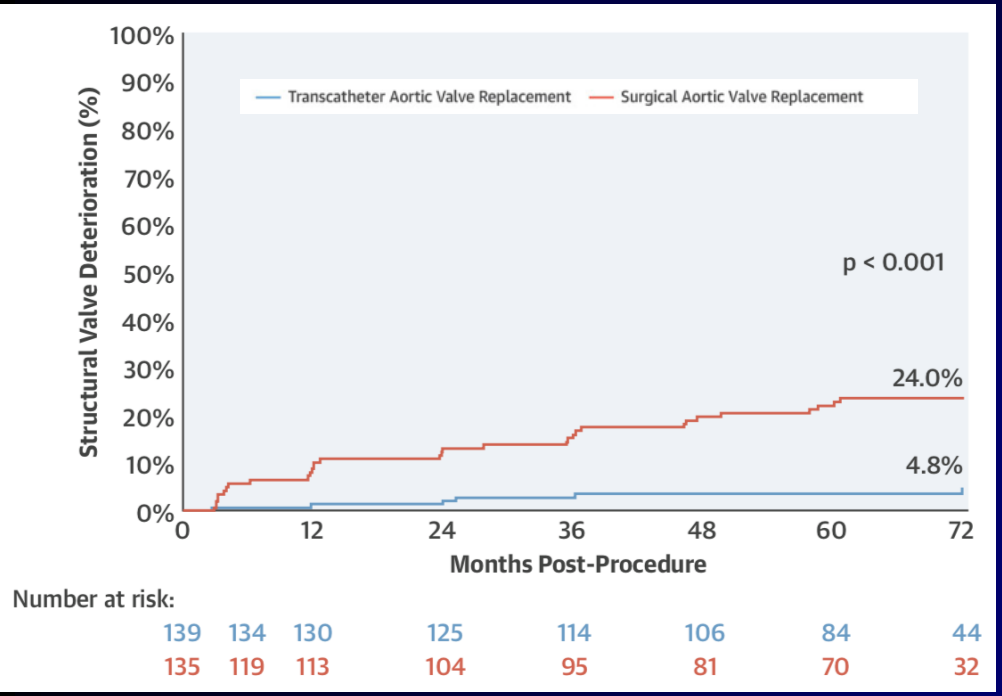
Bourguignon T et al. Ann Thorac Surg. 2015;99(3):831-7.

TAVR
severe SVD
1%/5Y

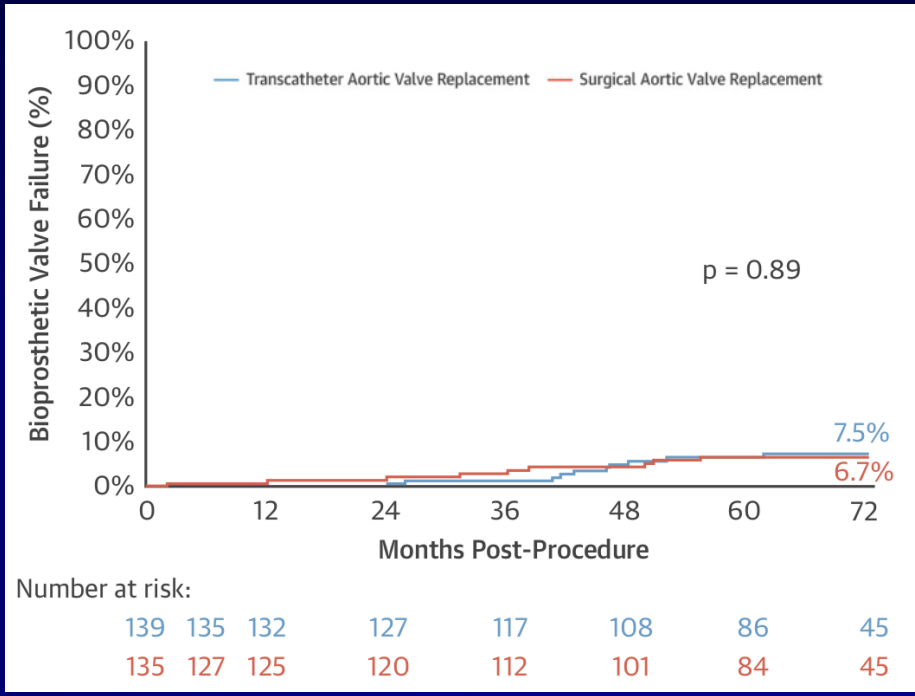
Romain Didier, et al. Circulation 2018 10.1161/CIRCULATIONAHA.118.0368

Long term f/u of TAVR
NOTION Trial 6-year f/u

Structural Valve Deterioration (SVD)



Bioprosthetic Valve Failure (BVF)

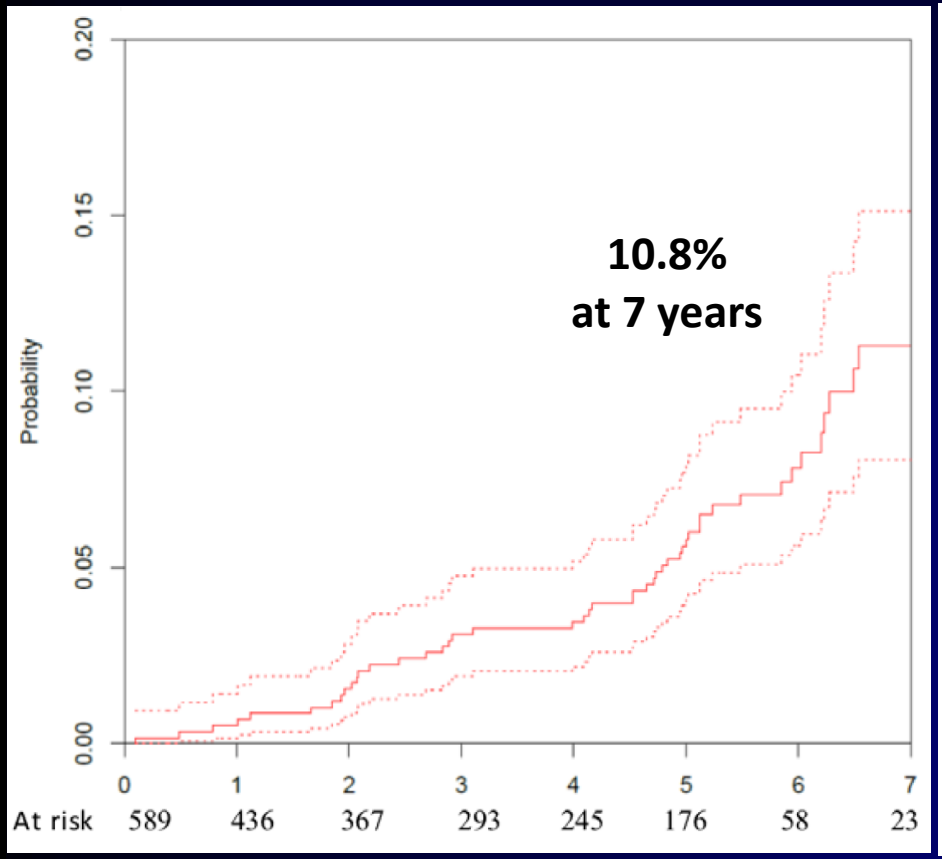


BVF (Valve-related Death, AV reintervention, severe SVD) rate were low and similar for both groups

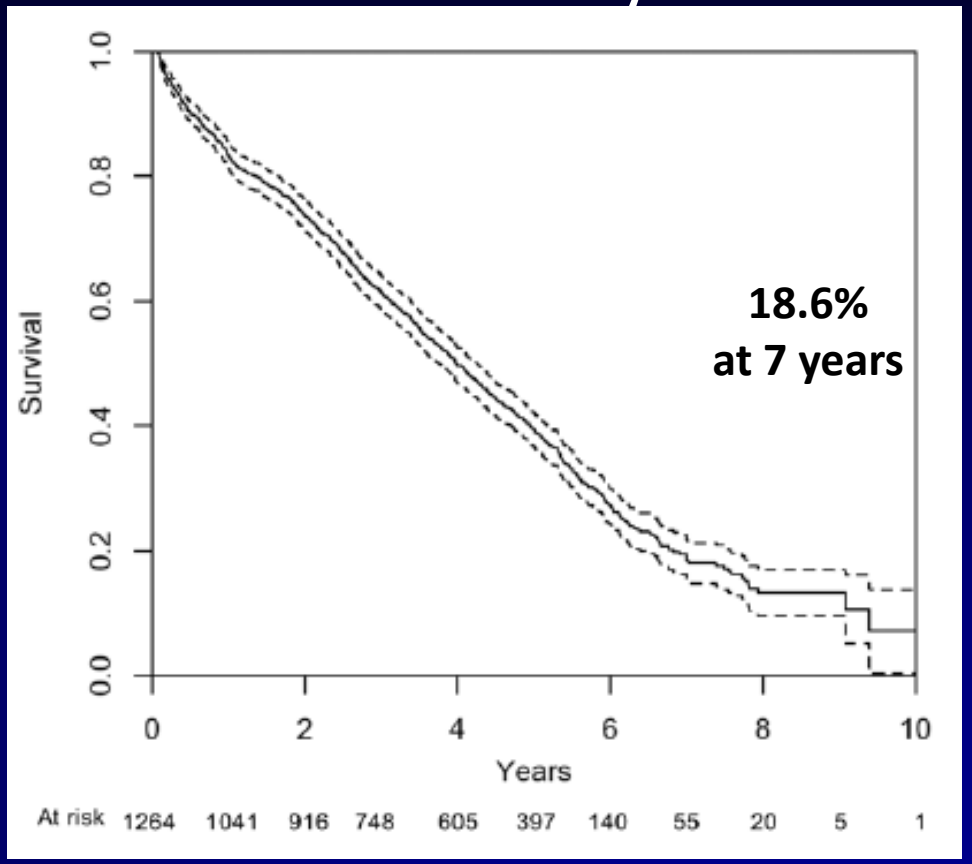
Søndergaard L et al. J Am Coll Cardiol. 2019 Feb 12;73(5):546-553.

Longest follow-up data TAVR French Registry

Cumulative incidence of moderate and severe Structural valve deterioraton



Survival analysis

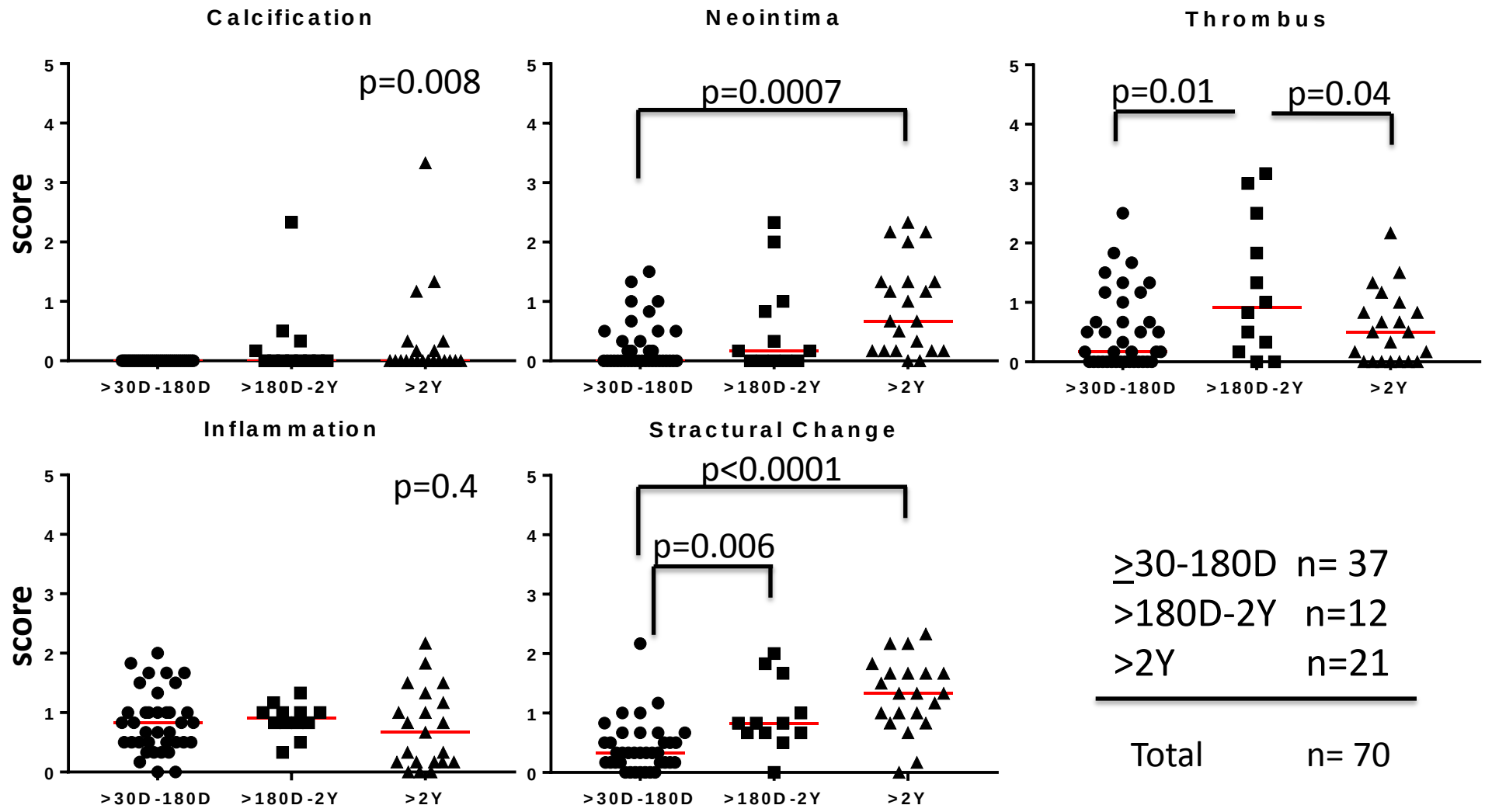


The rate of structural valve deterioration was low, however, long-term assessment was limited by the poor survival rate

Durand E et al. Circ Cardiovasc Interv 2019 Apr;12(4):e007597

Histologic changes of leaflets from TAVR valves by duration of implant

Medtronic and Edwards TAVR valve	≥30 days, n=83
Age, years (Median [IQR; range])	81 (76-88)
Male sex	50 (60%)
Following TAVR, days (Median [IQR; range])	252 (67-850 [30-1825])
Medtronic / Edwards	64 / 22
CoreValve / Evolut R / Sapien / Sapien XT / Sapien 3	63 / 2 / 9 / 6 / 3
IE, % (n) *excluded from the analysis	16% (13)

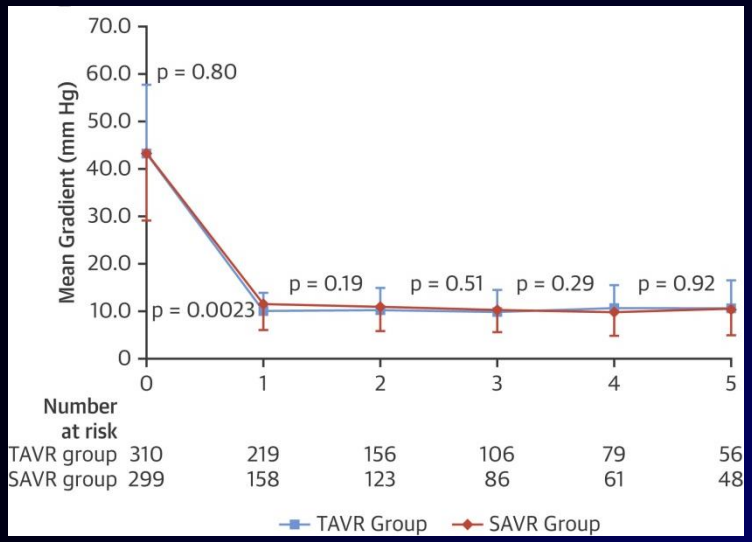


≥30-180D n= 37
>180D-2Y n=12
>2Y n=21

Total n= 70

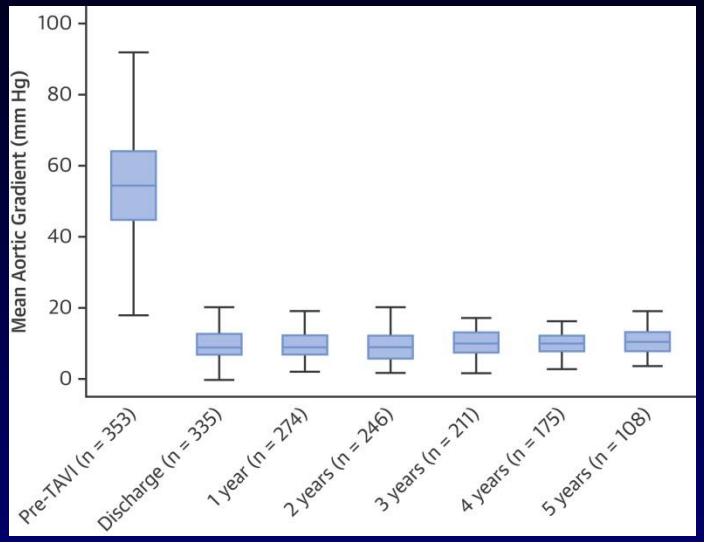
Transcatheter Valve Durability

PARTNER 5-year Echocardiographic performance (SAPIEN)

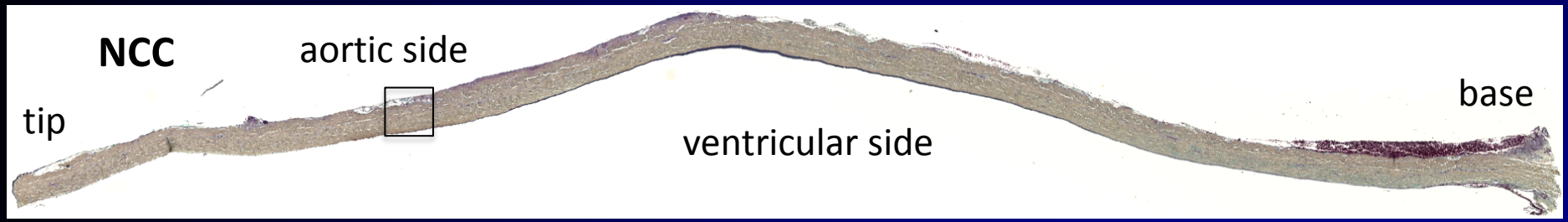


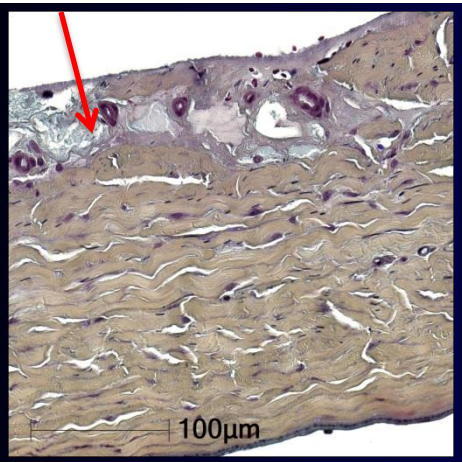
Mack MJ. et al. Lancet. 2015;20;385(9986):2477-84.

CoreValve 5-year Follow-up (registry)



Rodriguez-Gabella, T. et al. J Am Coll Cardiol. 2017;70(8):1013-28.



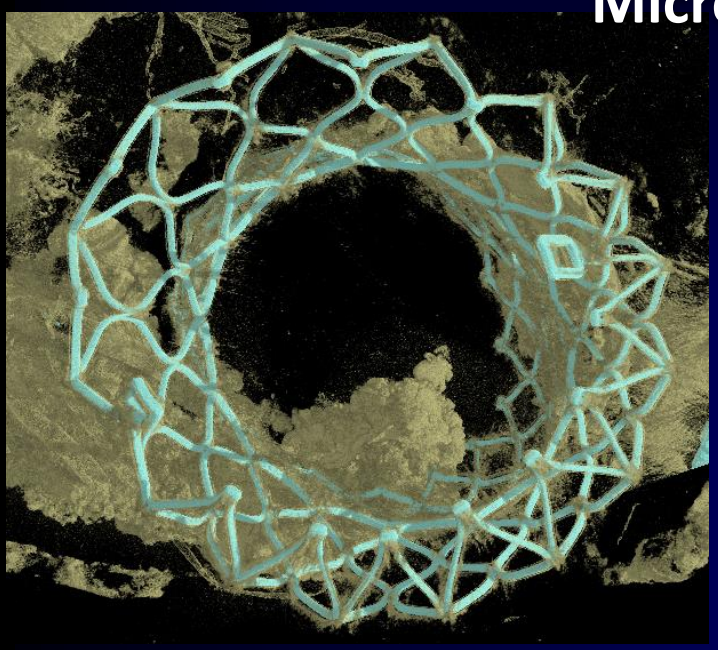


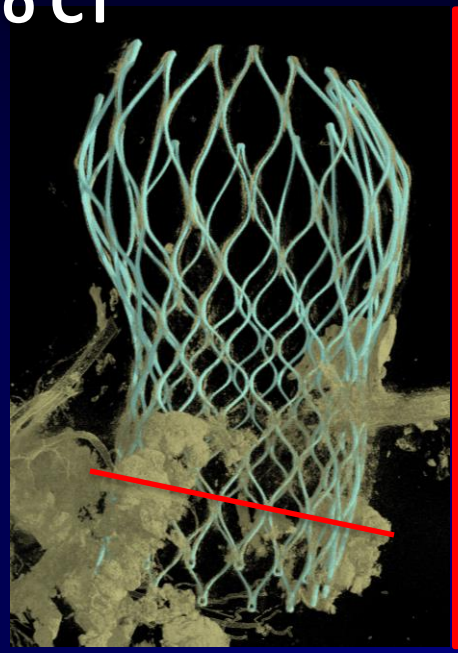
A case with mild structural changes

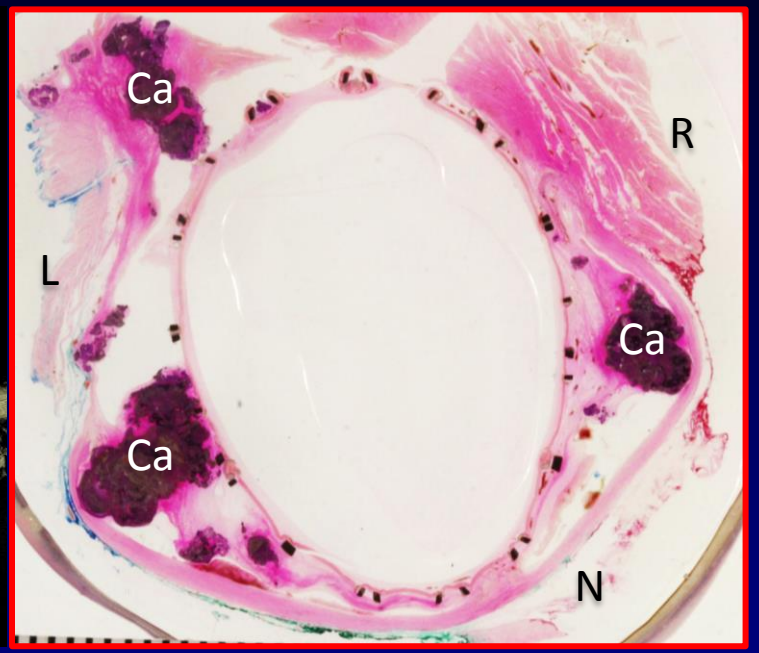
89 y.o. female, with a history of AS, DM, HLP, HTN, and CHF
Died due to congestive heart failure, **1477**days (**4** years) after TAVR implantation

Structural and procedural difference between TAVR and SAVR valve

Micro CT





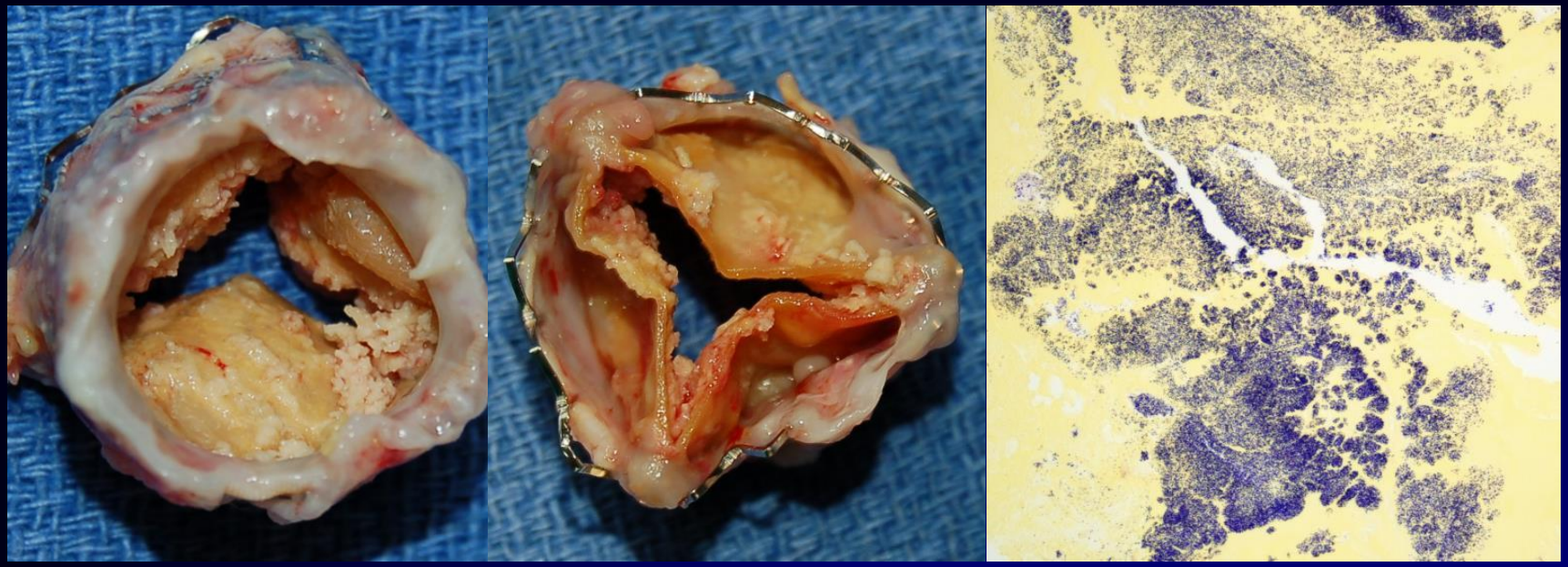


- Thinner leaflets for transcatheter delivery (TAVR 0.25mm, SAVR 0.4 mm)
- Native aortic valve calcification and oval-shaped annulus hamper circular and symmetric stent deployment
- Higher stress and strain are burdened into a prosthesis during procedure

Martin C et al. J Biomech 2015 Sep 18;48(12):3026-34.
Hwang IC et al. Circ J. 2019 Apr 5. [Epub ahead of print]

Long-term durability is not the same?

Bioprosthetic valve failure: Endocarditis



Endocarditis: CVPath Registry

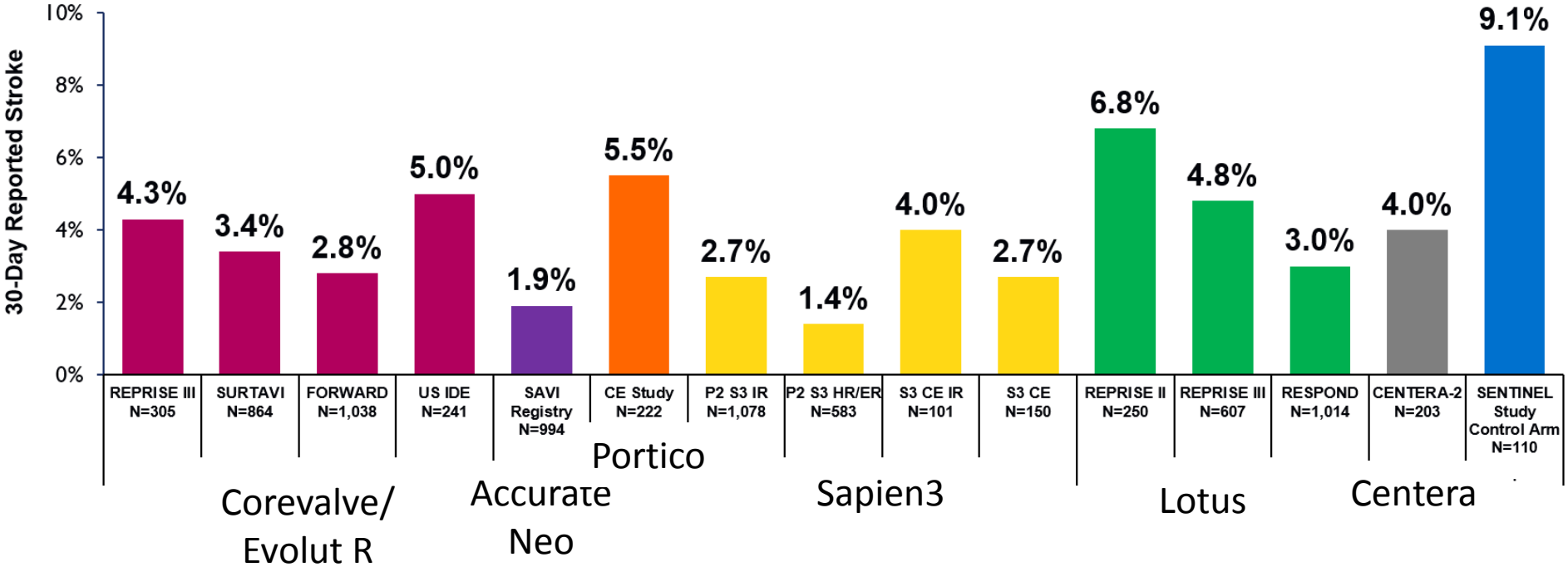
	Cases with Endocarditis N=12 (15%)
Age	80 (74-87)
Sex (male), %	67%
Duration, days	340 (111-962)

Regueiro A, et al. JAMA 2016:316(10):1083-92

TAVR and subsequent Infective endocarditis incidence is 1.1%per person-year (age 80, 64% men)

TAVR Stroke Rates with Contemporary Devices

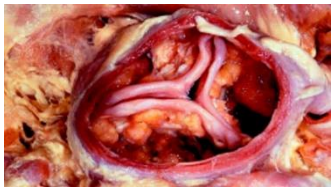
- Stroke remains an issue (~4.4% average rate) in contemporary TAVR studies.
- TAVR device trials tend to emphasize only the major/disabling stroke rates.



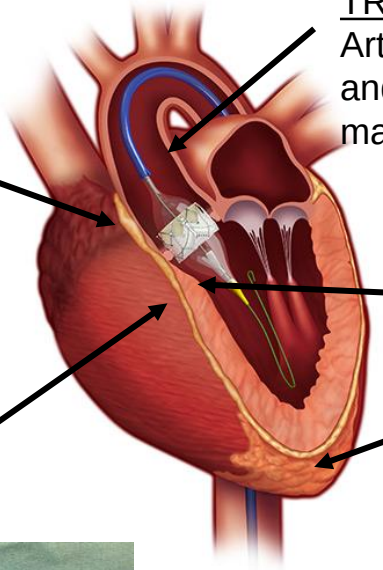
[1] Feldman, et al., EuroPCR 2017; [2]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67; [3]Moellman, et al., PCR London Valves 2015; [4]Grube, et al., EuroPCR 2017; [5]Kodali, et al., *Eur Heart J* 2016; [6]Vahanian, et al., EuroPCR 2015; [7]Webb, et. al. *J Am Coll Cardiol Intv* 2015; 8: 1797-806; [8]DeMarco, et al, TCT 2015; [9]Meredith, et al., PCR London Valves 2015; [10]Falk, et al. Eur Heart J 2017; [11]Kodali, TCT 2016; [12]Reardon, M *NEJM* 2017; [13]Reichenspurner H, et al., *JACC* 2017; [14]Popma et al, JACC:CVInt 2017;10(3):268-75

Sources of Debris During TAVR

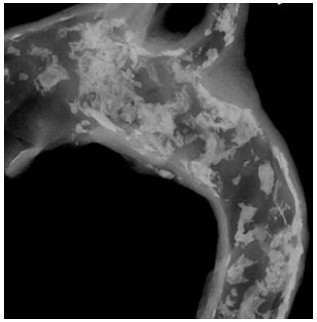
ASCENDING ARCH
Arterial wall, calcific and atherosclerotic material



STENOTIC VALVE
Leaflet tissue and calcific deposits

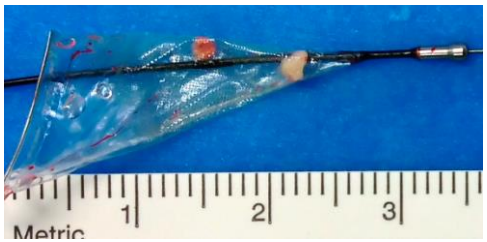


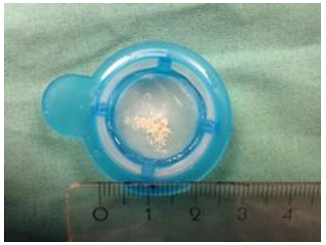
TRANSVERSE ARCH
Arterial wall, calcific and atherosclerotic material

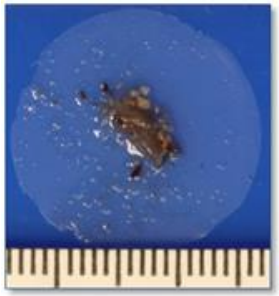


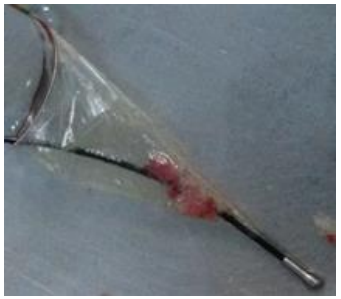
TAVI DEVICES
Foreign material

NATIVE HEART
Myocardium

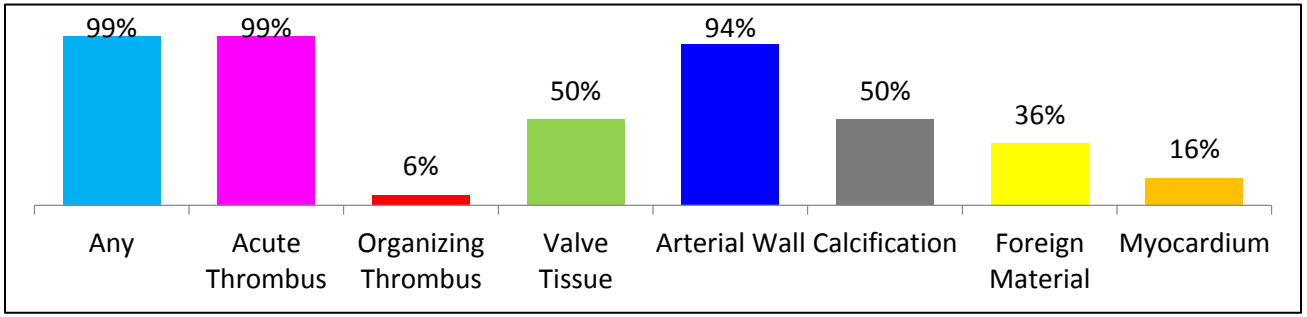








Patients with captured debris



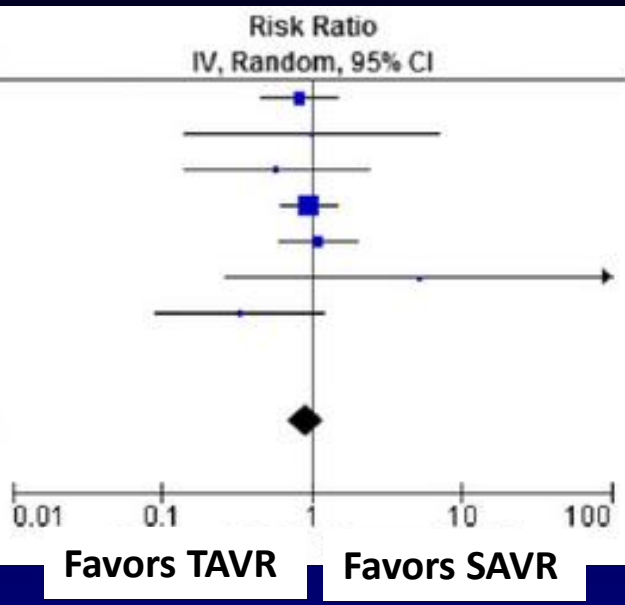
According to the meta-analysis…

All cause mortality @ 1M

Study or Subgroup	TAVR Events	TAVR Total	SAVR Events	SAVR Total	Weight	Risk Ratio IV, Random, 95% CI
ITALIAN OBSERVANT	20	650	24	650	23.5%	0.83 [0.47, 1.49]
Latib	2	111	2	111	2.1%	1.00 [0.14, 6.97]
NOTION	3	139	5	135	4.0%	0.58 [0.14, 2.39]
PARTNER 2A	39	1011	41	1021	43.3%	0.96 [0.63, 1.48]
Piazza	20	255	18	255	21.3%	1.11 [0.60, 2.05]
STACCATO	2	34	0	36	0.9%	5.29 [0.26, 106.27]
TAVIK	3	216	9	216	4.8%	0.33 [0.09, 1.21]
US PIVOTAL	0	202	0	181		Not estimable
Total (95% CI)		**2618**		**2605**	**100.0%**	**0.91 [0.68, 1.20]**
Total events	89		99			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.59$, $df = 6$ ($P = 0.60$); $I^2 = 0\%$

Test for overall effect: $Z = 0.67$ ($P = 0.50$)

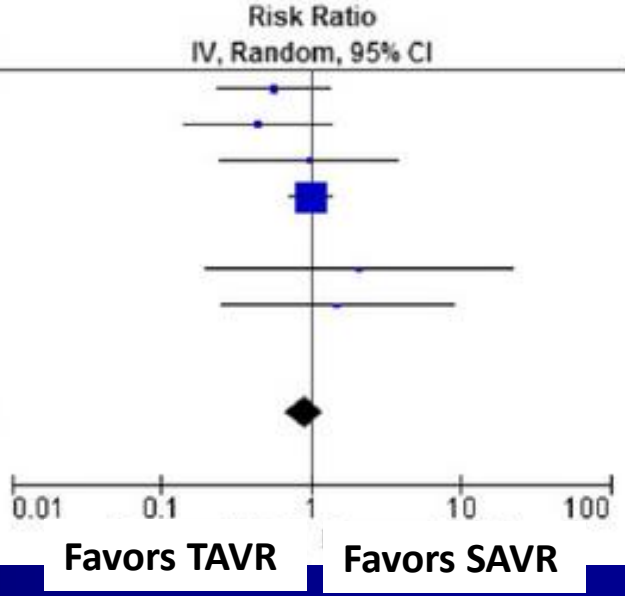


Cerebrovascular (CVA) incidence @ 1M

Study or Subgroup	TAVR Events	TAVR Total	SAVR Events	SAVR Total	Weight	Risk Ratio IV, Random, 95% CI
ITALIAN OBSERVANT	8	650	14	650	11.1%	0.57 [0.24, 1.35]
Latib	4	111	9	111	6.3%	0.44 [0.14, 1.40]
NOTION	4	139	4	135	4.4%	0.97 [0.25, 3.81]
PARTNER 2A	64	1011	65	1021	74.1%	0.99 [0.71, 1.39]
Piazza	0	255	0	255		Not estimable
STACCATO	2	34	1	36	1.5%	2.12 [0.20, 22.30]
TAVIK	3	216	2	216	2.6%	1.50 [0.25, 8.89]
US PIVOTAL	0	202	0	181		Not estimable
Total (95% CI)		**2618**		**2605**	**100.0%**	**0.91 [0.68, 1.21]**
Total events	85		95			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.69$, $df = 5$ ($P = 0.59$); $I^2 = 0\%$

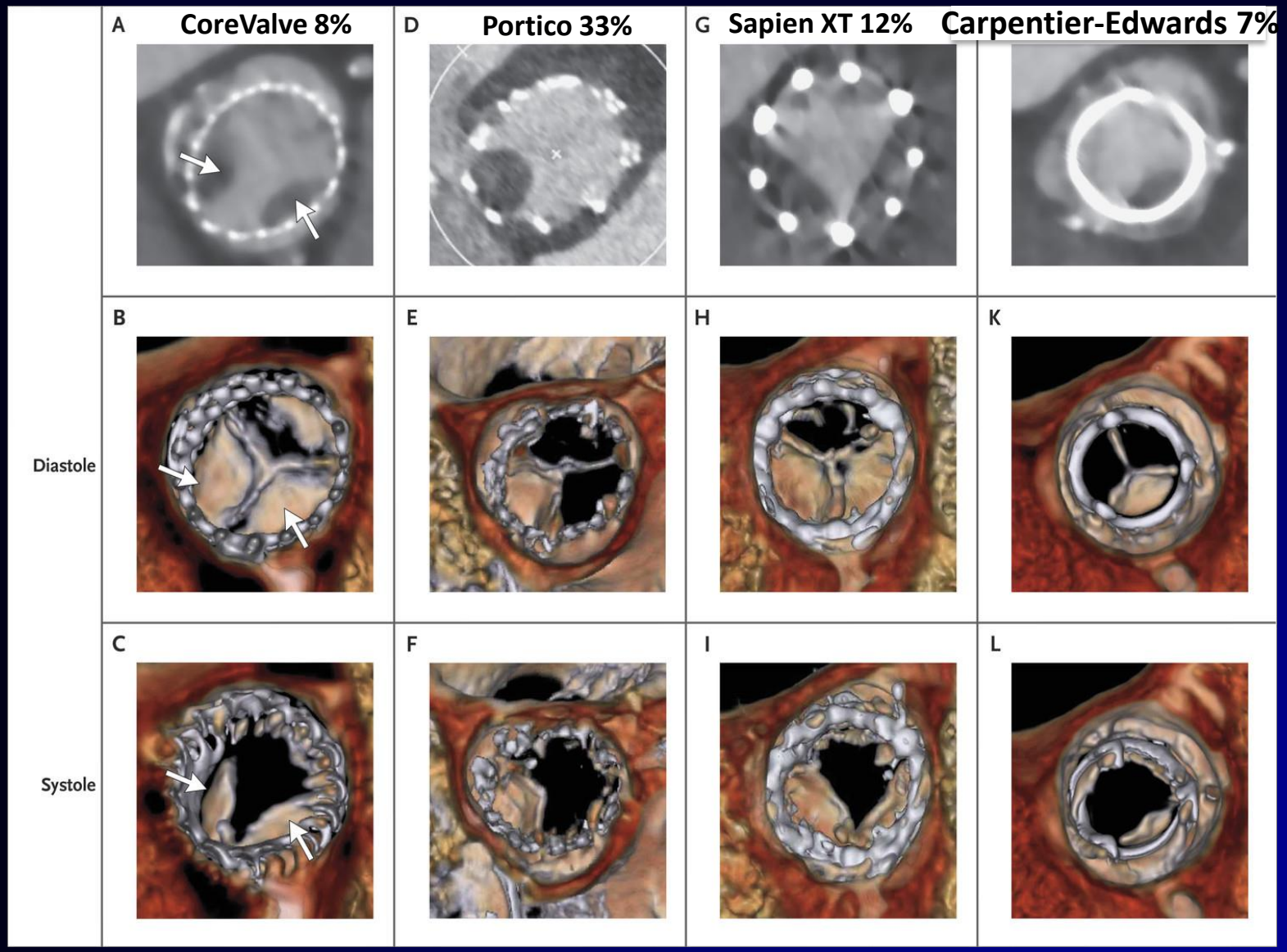
Test for overall effect: $Z = 0.66$ ($P = 0.51$)



Enezate TH et al. Cardiovasc Revasc Med. 2017;18(5S1):S40-S48.

TAVR and SAVR
What is the differences?

Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types.

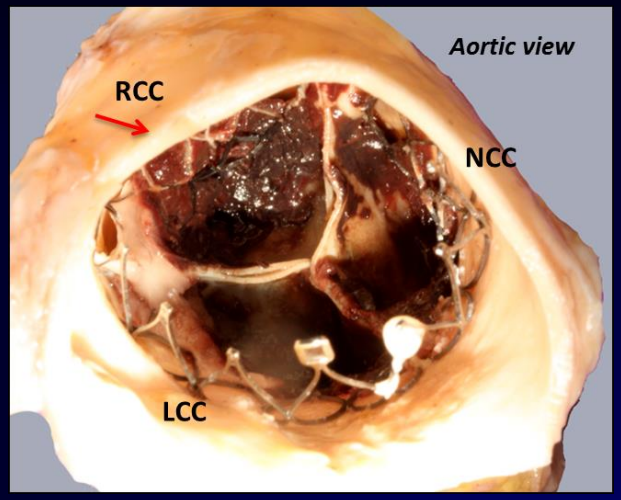


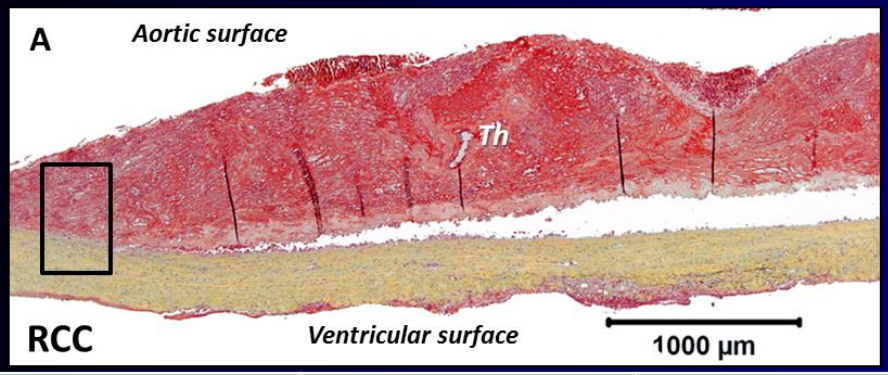
Makkar R, et al. N Engl J Med 2015;373(21):2015-24

Transcatheter aortic valve failure: Severe Thrombosis (5%)

CoreValve: 15 days

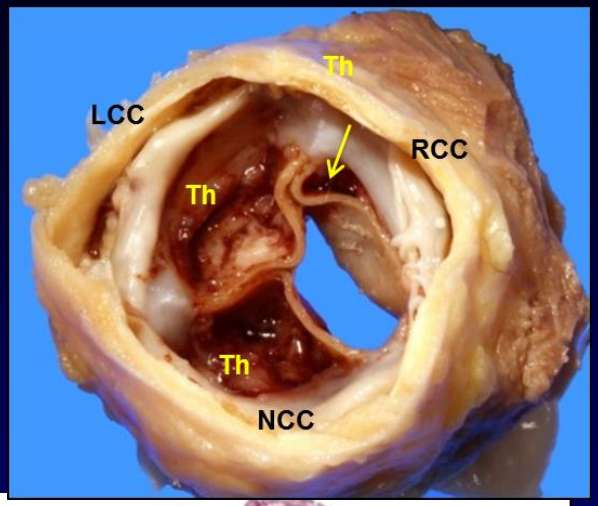
De Marchena E, R Virmani, et al. JACC Cardiovasc Interv. 2015 Apr 27;8(5):728-39.

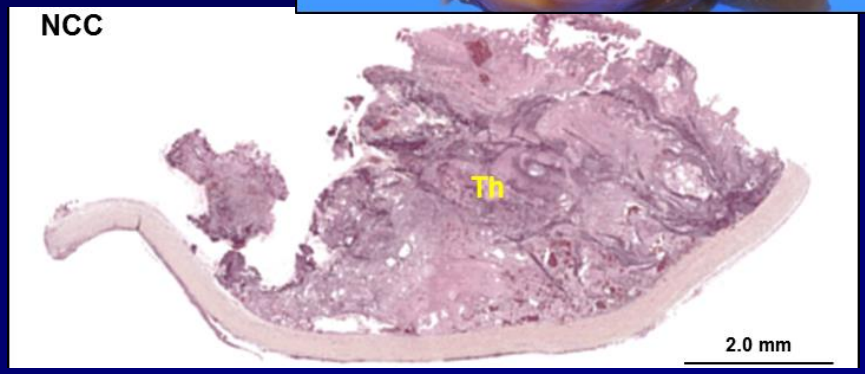




SAPIEN: 495 days

Yahagi K, et al. Catheter Cardiovasc Interv. 2017 15;90(6):1048-1057.



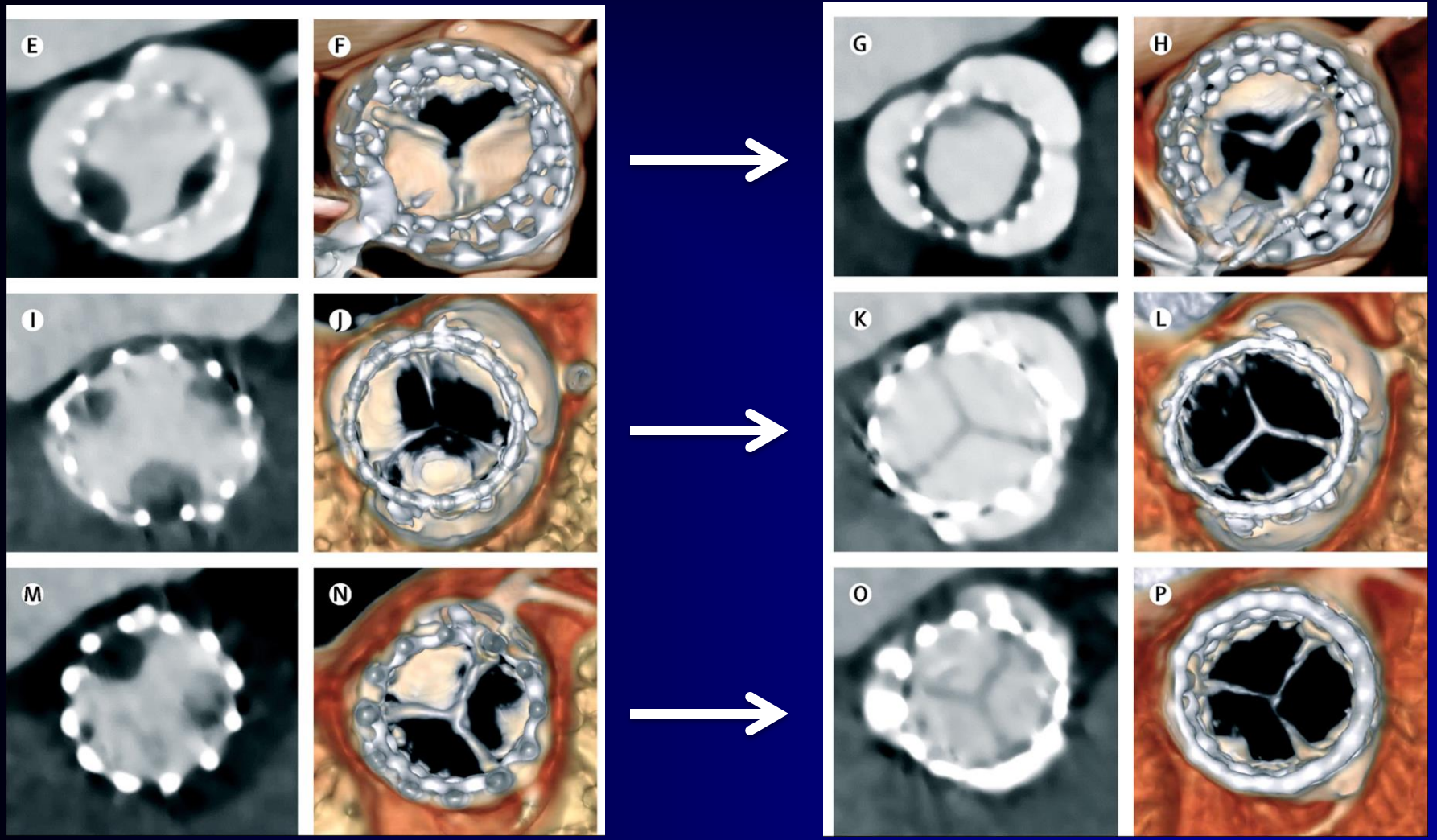


	Overall N=66	Cases with Severe thrombus N=12 (18%)	Cases without Severe thrombus N=54 (82%)	P value
Age	81 (76-88)	85 (76-89)	81 (76-88)	0.7
Sex (male), %	65%	50%	67%	0.3
Duration, days	252 (67-850)	257 (86-857)	104 (54-776)	0.3

Oral anticoagulation therapy (OAC), but not DAPT, was effective in prevention or treatment of subclinical leaflet thrombosis.

Reduced leaflet motion
in a patient receiving **DAPT** after TAVR

Resolution of reduced leaflet
motion following 3 months of **OAC**



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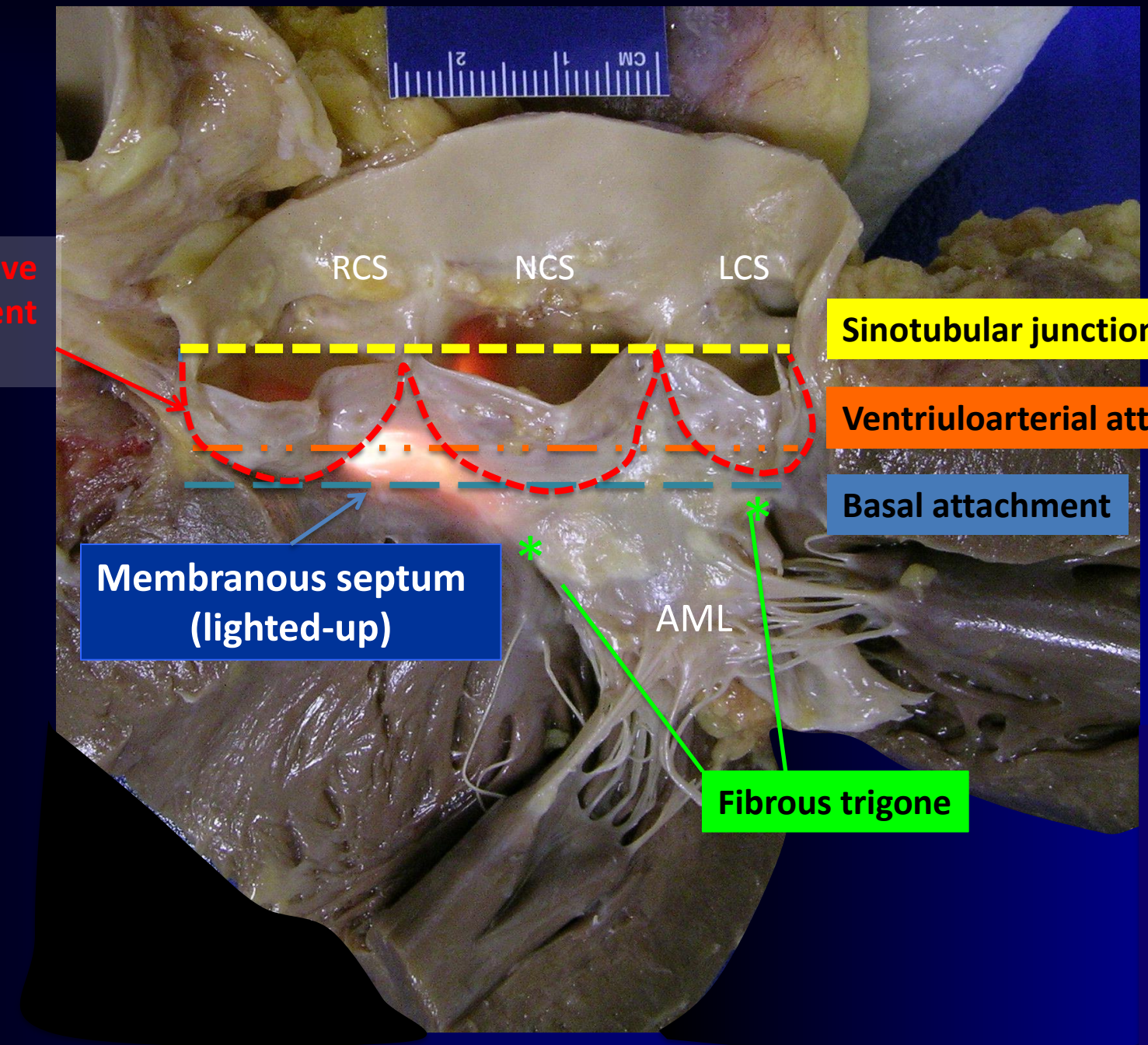
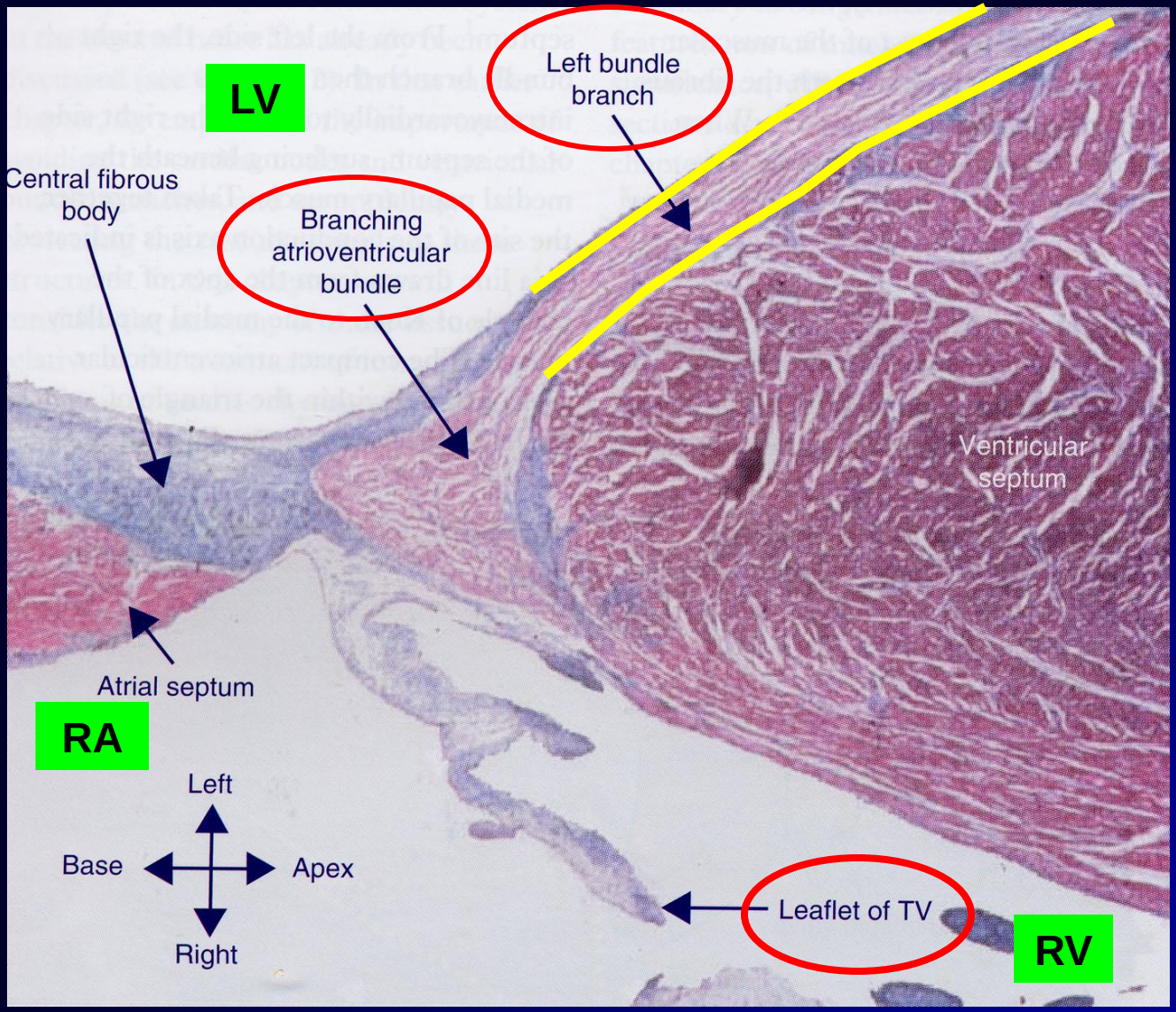
Aortic Outflow Tract



Left Bundle Branch



A 82 Years Old Case Treated with a Pacemaker Implant after TAVR with CoreValve

Association between implantation depth assessed by computed tomography and new-onset conduction disturbances after TAVR

MDCT measurements before and after TAVR

MDCT	Total (N = 138)	Conduction disturbances (N = 63)	No conduction disturbances (N = 75)	*p*-value
Pre-interventional				
Annulus area (mm^2)	444 ± 84	449 ± 77	440 ± 91	0.520
Annulus eccentricity (%)	25.4 ± 8.9	25.5 ± 10.6	25.3 ± 7.3	0.913
Cover index (%)	18.4 ± 12.9	21.6 ± 12.1	15.6 ± 12.9	0.007
Oversizing (by nominal prosthesis area, %)	25.6 ± 20.1	30.6 ± 20.0	21.4 ± 19.4	0.009
Aortic valve complex calcium (mm^3)	184 ± 297	184 ± 273	178 ± 311	0.666
Left ventricle outflow tract calcium (mm^3)	11 ± 35	6 ± 17	16 ± 45	0.235
Post-interventional				
Transcatheter aortic valve area (mm^2)	407 ± 70.2	420 ± 63	396 ± 74	0.049
Expansion (%)	72.9 ± 18.0	67.4 ± 14.0	77.2 ± 16.0	0.001
Eccentricity index (%)	10.2 ± 9.9	11.6 ± 8.0	8.7 ± 9.8	0.042
Implantation depth (mm)	7.0 ± 2.8	7.7 ± 2.9	6.4 ± 2.6	0.006

Univariate and multivariate logistic regression analysis to identify independent associations with Conduction Disturbances

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age	0.99	0.95–1.04	0.752			
Male gender	1.40	0.72–2.74	0.327			
Chronic obstructive pulmonar disease	2.47	1.07–5.71	0.034	3.14	1.26–7.84	0.014
Self-expandable prosthesis	2.33	1.16–4.68	0.018			
Oversizing	1.02	1.01–1.04	0.01	1.02	1.00–1.04	0.02
Expansion	0.96	0.93–0.99	0.008			
Eccentricity index	1.04	0.99–1.09	0.096			
Implantation depth	1.20	1.05–1.36	0.004	1.16	1.01–1.33	0.035

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Summary

- Indication of TAVR for low-risk patients are expanding, long-term data of prosthetic valve durability are warranted.
- Up to this point, clinical BVF rate seems similar between TAVR and SAVR.
- Structural changes of the leaflet are likely the main causation of late (>5 year) bioprosthetic valve failure.
- Major structural changes for the most part were not seen in our pathological evaluation of TAVR devices though the duration of these implants is limited
- Meta analysis shows cerebrovascular event at 1 month is similar, however, cerebrovascular outcome of TAVR may improve with distal emboli in the future.
- Pathological severe thrombosis, that may cause reduced leaflet motion; was seen in 12% in CVPath TAVR registry. Oral anticoagulation therapy, but not DAPT, is effective in prevention or treatment of subclinical leaflet thrombosis.
- Rate of pacemaker implantation is still a concern in TAVR, and implantation depth matters.

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