Nothing is Complete Unless You Put Standard in Your Demand: Superior to Surgery in LR, PVL, PPI

Jung-Hee Lee, MD, PhD

Division of Cardiology, Yeungnam University Medical Center, Daegu, Korea

Disclosure

- I have nothing to disclose

TAVR vs. Surgery in Low-Risk

TAVR in Low Risk (LR) Patients with AS

Review of PARTNER 3

- Previous PARTNER studies have shown that TAVR was **superior to standard therapy in extreme-risk patients** and **non-inferior to surgery in high- and intermediate-risk patients**.

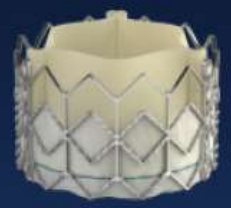
- Over the past decade, technology enhancements and procedural refinements have reduced complications and improved clinical outcomes after TAVR

- PARTNER 3 trial was performed to compare the safety and effectiveness of the **SAPIEN 3 TAVR** vs. **conventional surgery** in patients with severe AS at ***low surgical risk***.

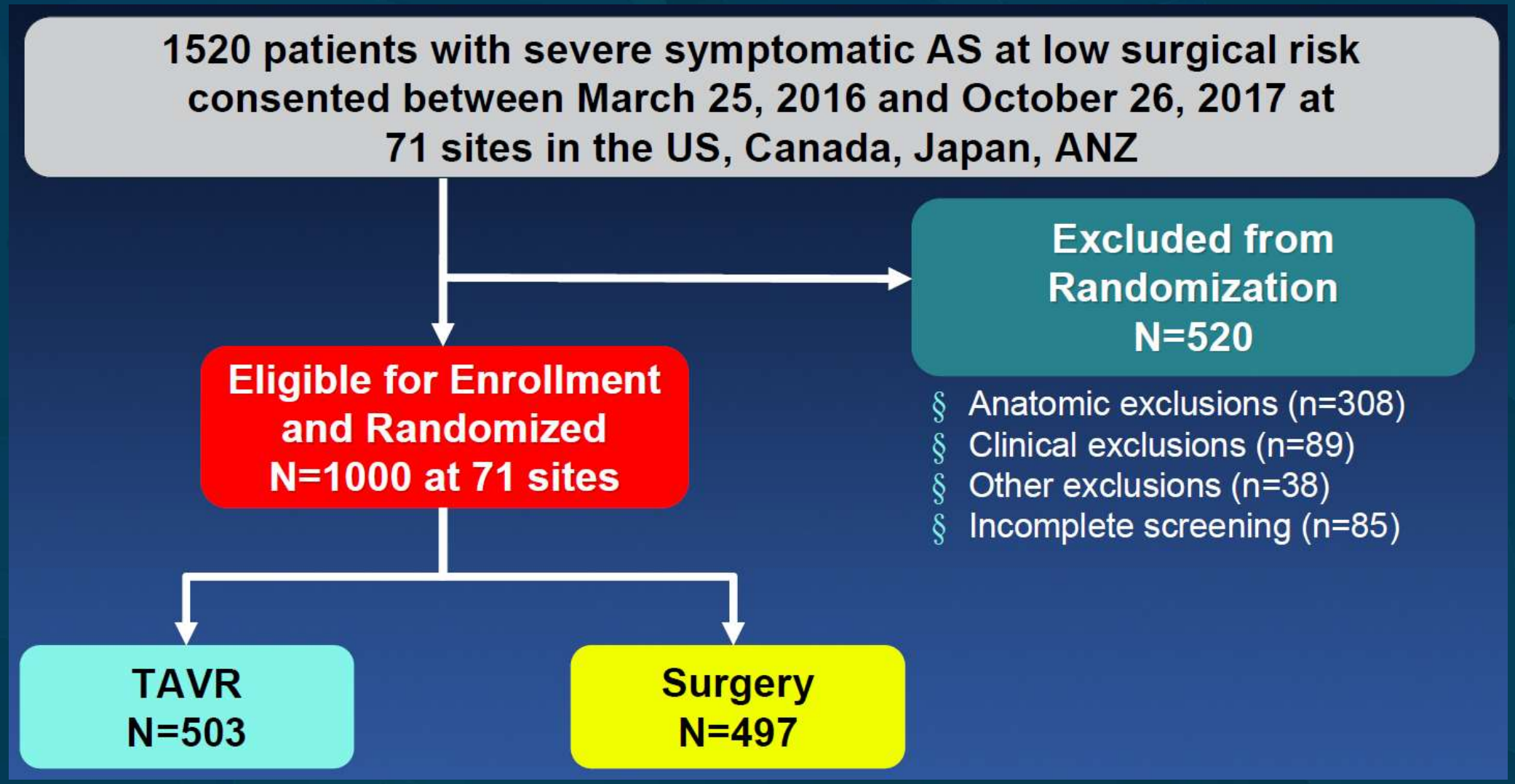
Key Inclusion Criteria of PARTNER 3

- **Severe Calcific Aortic Stenosis**
  - AVA ≤ 1.0 cm^2 or AVA index ≤ 0.6cm^2/m^2
  - Jet velocity ≥ 4.0 m/s or mean gradient ≥ 40 mmHg, AND
    - NYHA Functional Class ≥ 2, OR
    - Abnormal exercise test with severe SOB, abnormal BP response, or arrhythmia, OR
    - Asymptomatic with LVEF < 50%
- **Low Surgical Risk**
  - Determined by multi-disciplinary heart team
  - STS < 4%
  - Adjudicated by case review board

SAPIEN Valve Evolution

	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility			
Available Valve Sizes	 23 mm 26 mm	 23 mm 26 mm 29 mm	 20 mm 23 mm 26 mm 29 mm
FDA Approval of Valve:	PARTNER 1 2011	PARTNER 2 2014	PARTNER 3 2015

Study Flow



N Engl J Med 2019;380:1695-705.

Baseline Patient Characteristics

Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)	Other Co-Morbidities	TAVR (N=496)	Surgery (N=454)
Age (years)	73.3 ± 5.8	73.6 ± 6.1	Diabetes	31.3%	30.2%
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI – kg/m^2	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	1.9 ± 0.7	1.9 ± 0.6	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	27.7%	28.0%	Atrial Fibrillation (h/o)	15.7%	18.8%
Prior CABG	3.0%	1.8%	Permanent Pacemaker	2.4%	2.9%
Prior CVA	3.4%	5.1%	Left Bundle Branch Block	3.0%	3.3%
Peripheral Vascular Disease	6.9%	7.3%	Right Bundle Branch Block	10.3%	13.7%

N Engl J Med 2019;380:1695-705.

Procedural & Hospital Findings

Variable	TAVR (N=496)	Surgery (N=454)	P-value
Conscious Sedation	65.1%	NA	NA
Procedure Time (min)	58.6 ± 36.5	208.3 ± 62.2	<0.001
Fluoroscopy Time (min)	13.9 ± 7.1	NA	NA
Aortic Cross-Clamp Time (min)	NA	74.3 ± 27.8	NA
Total CPB Time (min)	NA	97.7 ± 33.8	NA
Median ICU Stay (days)	2.0	3.0	<0.001
Median Total LOS (days)	3.0	7.0	<0.001
Discharge to Home/Self-care	96.0%	73.1%	<0.001
Concomitant Procedures	7.9%	26.4%	<0.001

N Engl J Med 2019;380:1695-705.

Procedural Complications

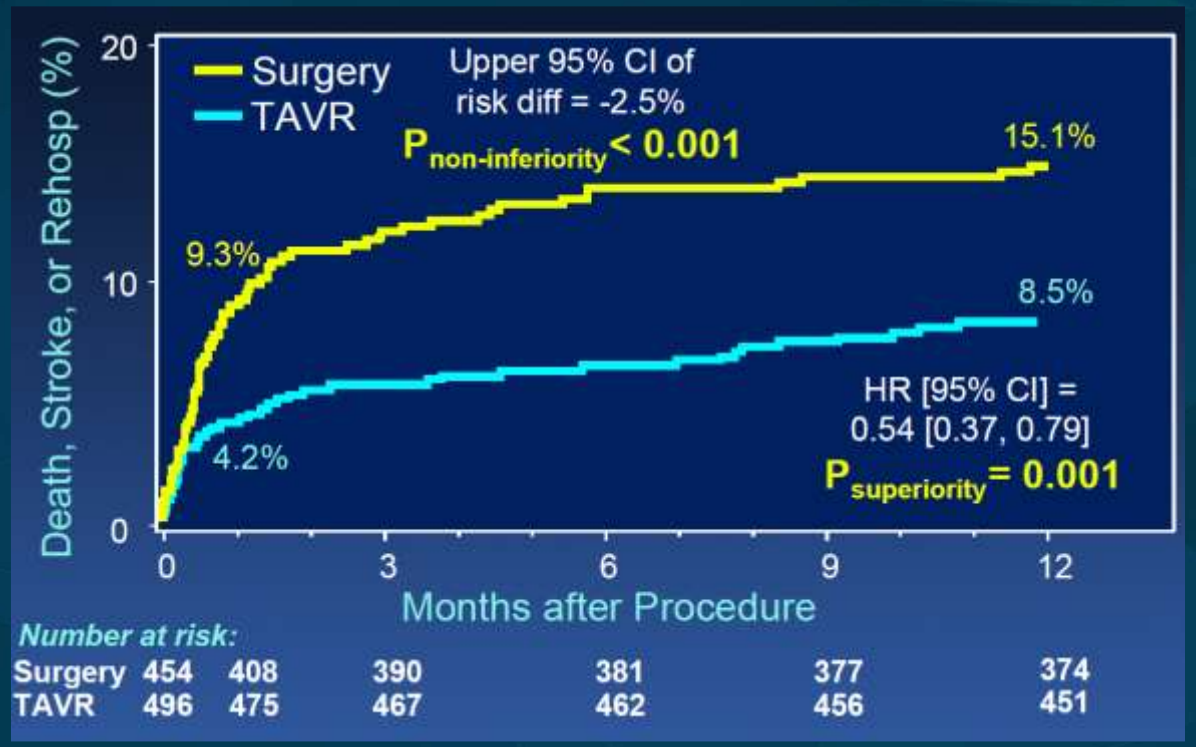
In-Hospital

Complication	TAVR (N=496)	Surgery (N=454)	P-value
In-hospital Death	0.4% (2)	0.9% (4)	0.43
≥ 2 Transcatheter Valves Implanted*	0.2% (1)	NA	NA
Valve Embolization	0	NA	NA
Aortic Dissection	0	NA	NA
Annular Rupture	0.2% (1)	NA	NA
Ventricular Perforation	0.2% (1)	0.4% (2)	0.61
Coronary Obstruction	0.2% (1)	0.4% (2)	0.61
Access Site Infections	0.4% (2)	1.3% (6)	0.16

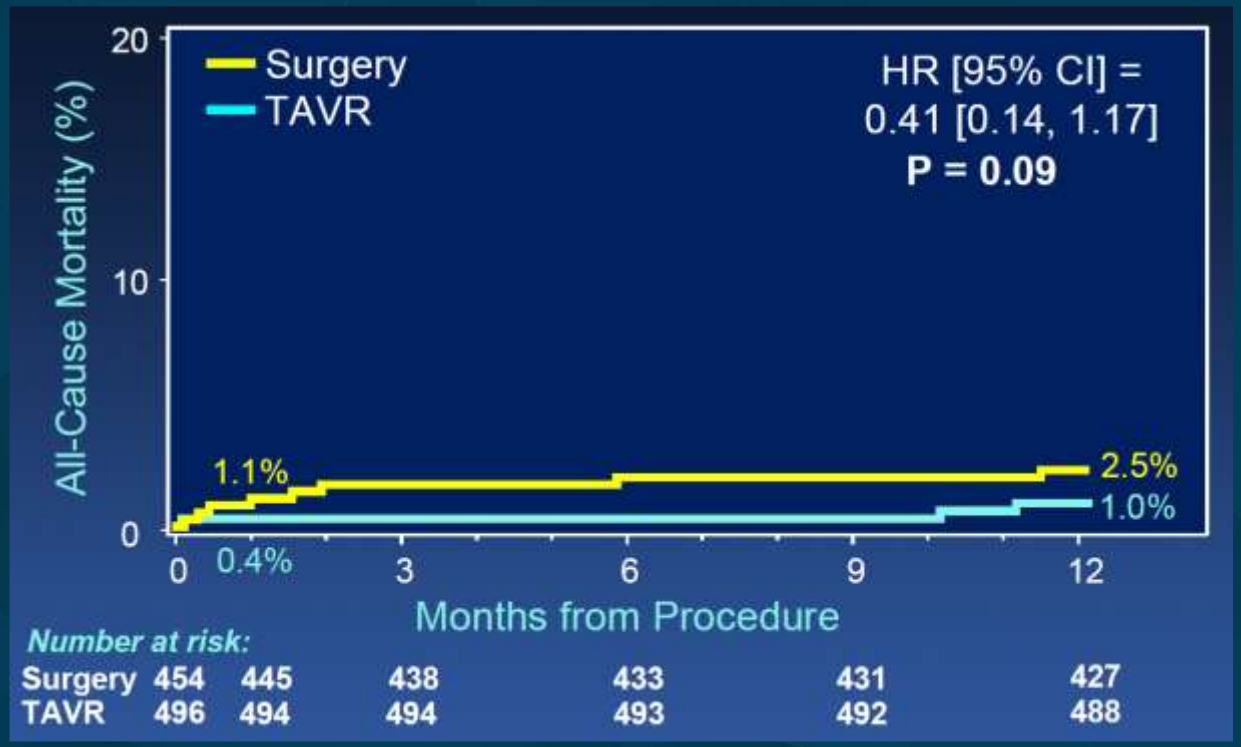
N Engl J Med 2019;380:1695-705.

Clinical Outcomes

Primary Endpoint: All-cause mortality + all strokes + CV re-hospitalization



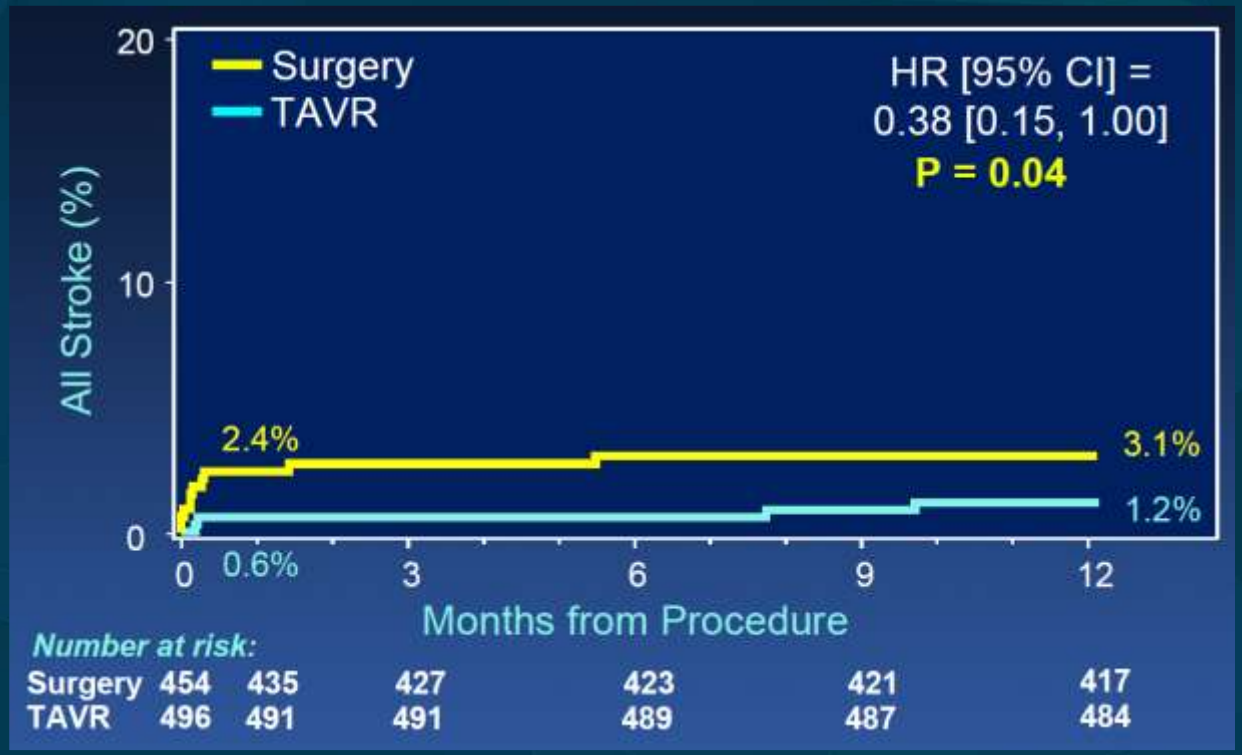
All-Cause Mortality



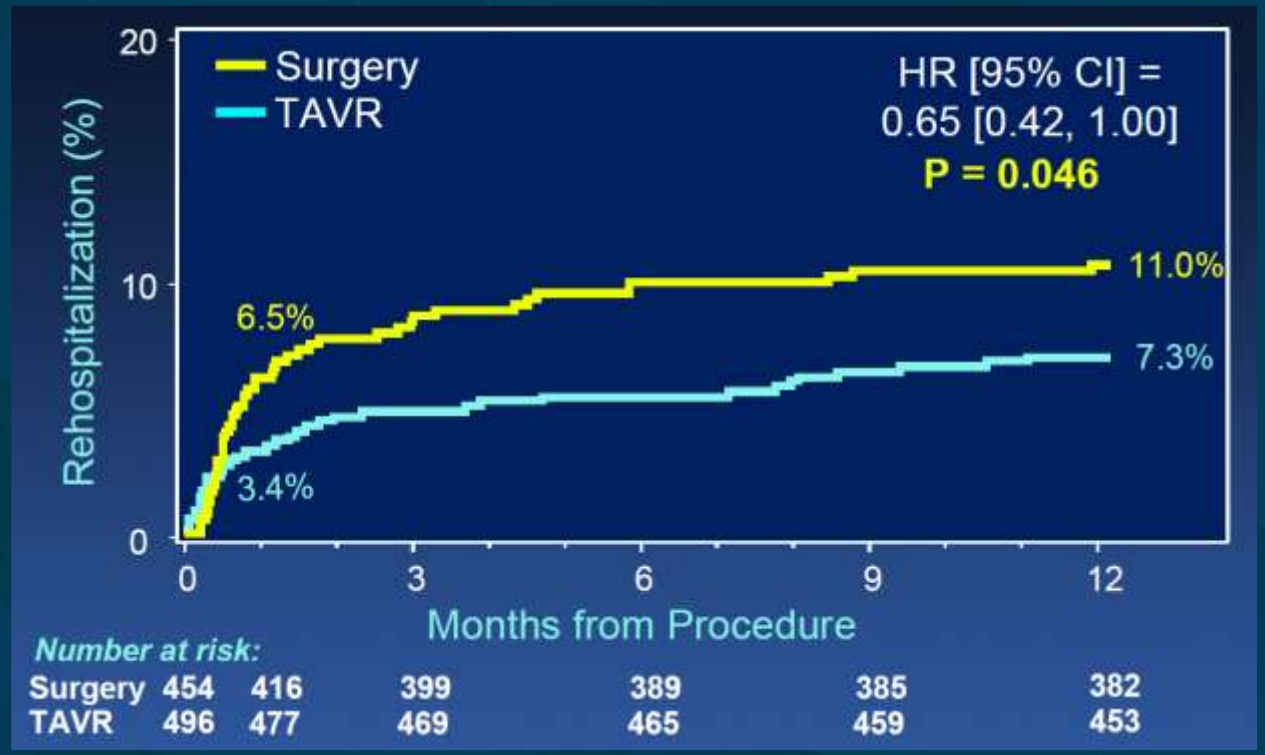
N Engl J Med 2019;380:1695-705.

Clinical Outcomes

All Stroke



Rehospitalization



N Engl J Med 2019;380:1695-705.

Other Secondary Endpoints

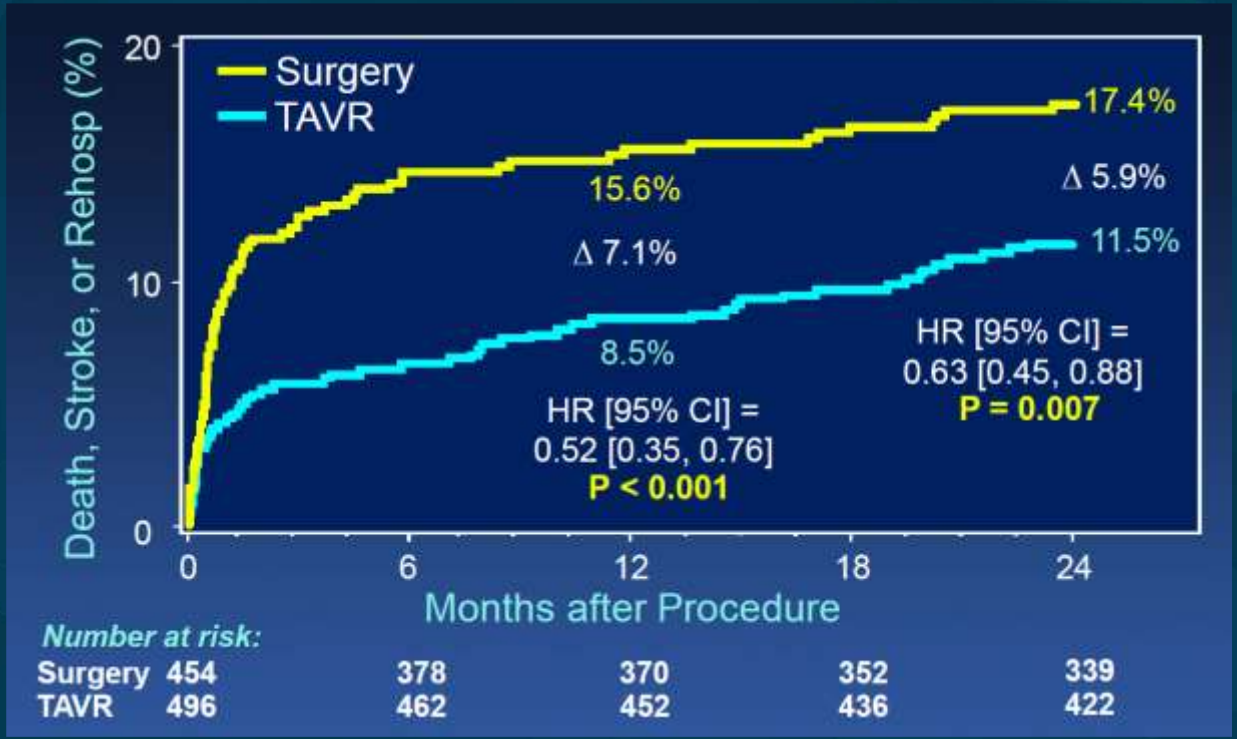
Outcomes	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
Bleeding - Life-threat/Major	3.6% (18)	24.5% (111)	<0.001	7.7% (38)	25.9% (117)	<0.001
Major Vascular Complics	2.2% (11)	1.5% (7)	0.45	2.8% (14)	1.5% (7)	0.19
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21
New LBBB	22.0% (106)	8.0% (35)	<0.001	23.7% (114)	8.0% (35)	<0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0% (0)	0% (0)	NA	0.6% (3)	0.5% (2)	0.76
Endocarditis	0% (0)	0.2% (1)	0.29	0.2% (1)	0.5% (2)	0.49
Asymp Valve Thrombosis	0.2% (1)	0% (0)	0.34	1.0% (5)	0.2% (1)	0.13

Lessons from PARTNER 3

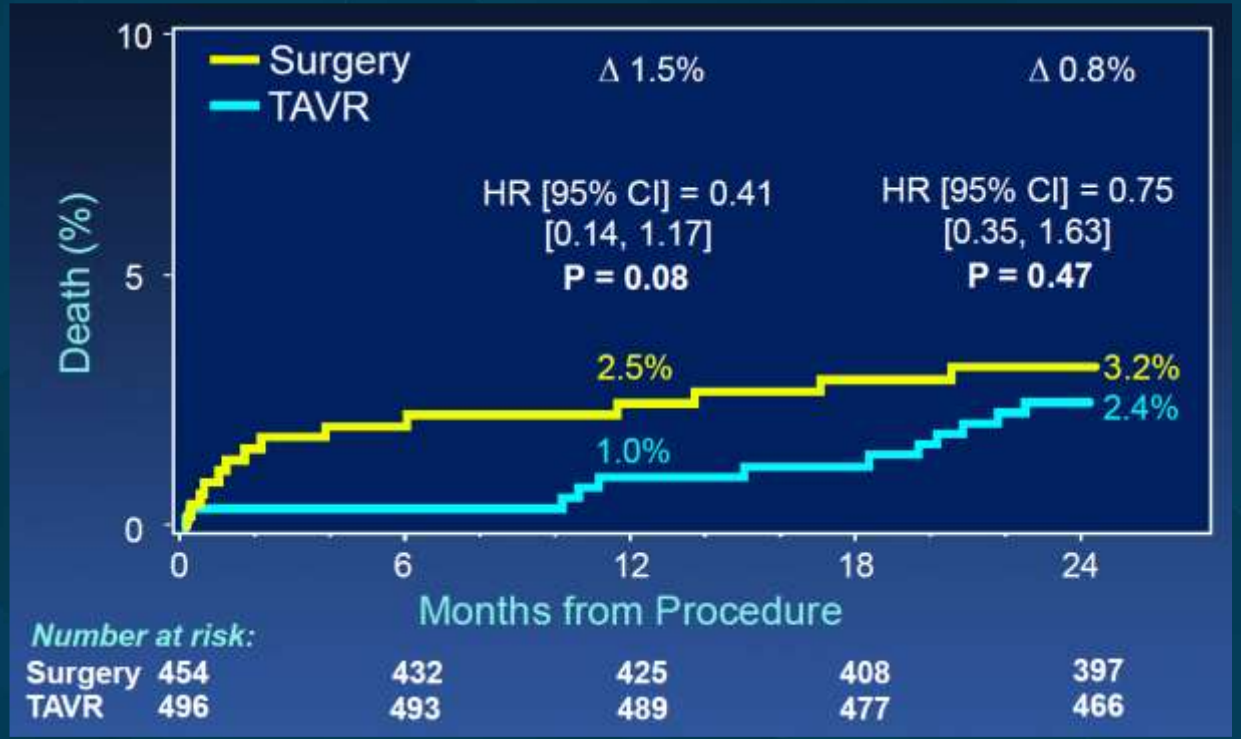
- TAVR (using the SAPIEN 3) significantly reduced the primary endpoint of death, stroke, or rehospitalization by 46% at 1-year.
- Other secondary endpoint analyses also showed reduced bleeding after TAVR and no differences in the need for new permanent pacemakers, major vascular complications, coronary obstruction, and mod-severe PVR.
- Some secondary endpoints favored surgery, including reduced new LBBB, reduced mild PVR, and lower aortic valve gradients.

2-Year Clinical Outcomes

Primary Endpoint: All-cause mortality + all strokes + CV re-hospitalization



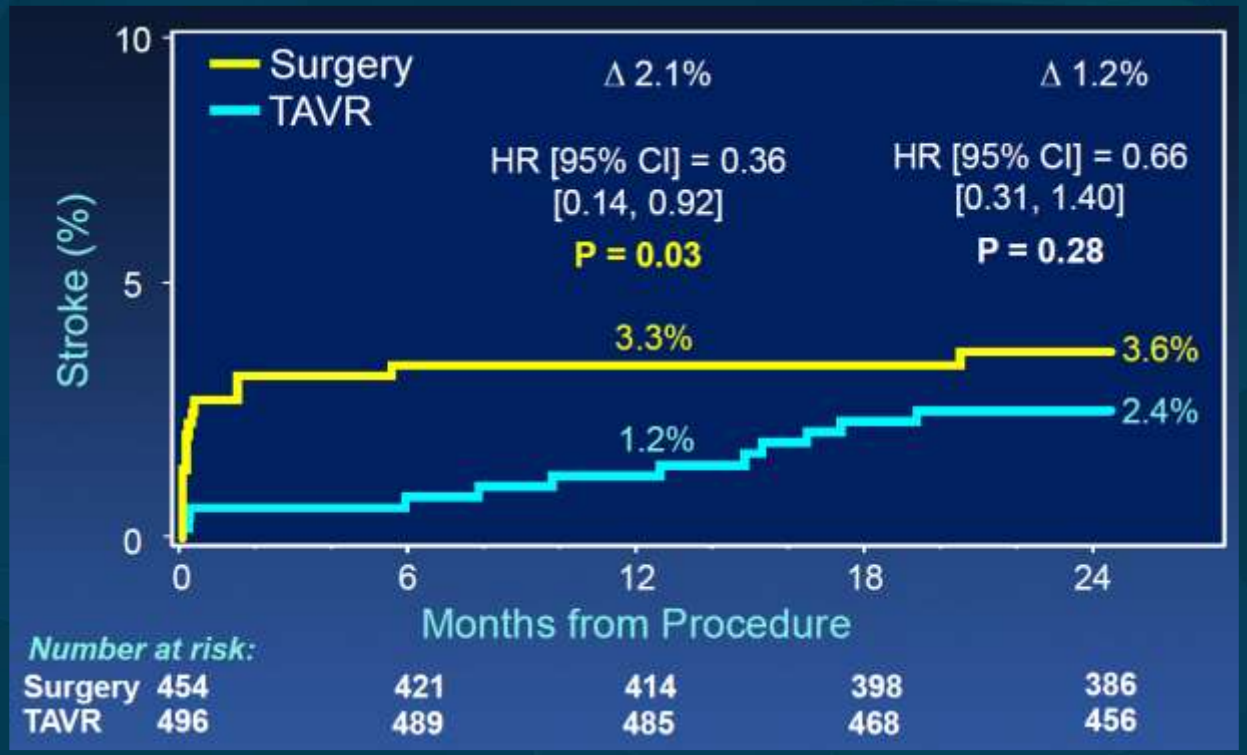
All-Cause Mortality



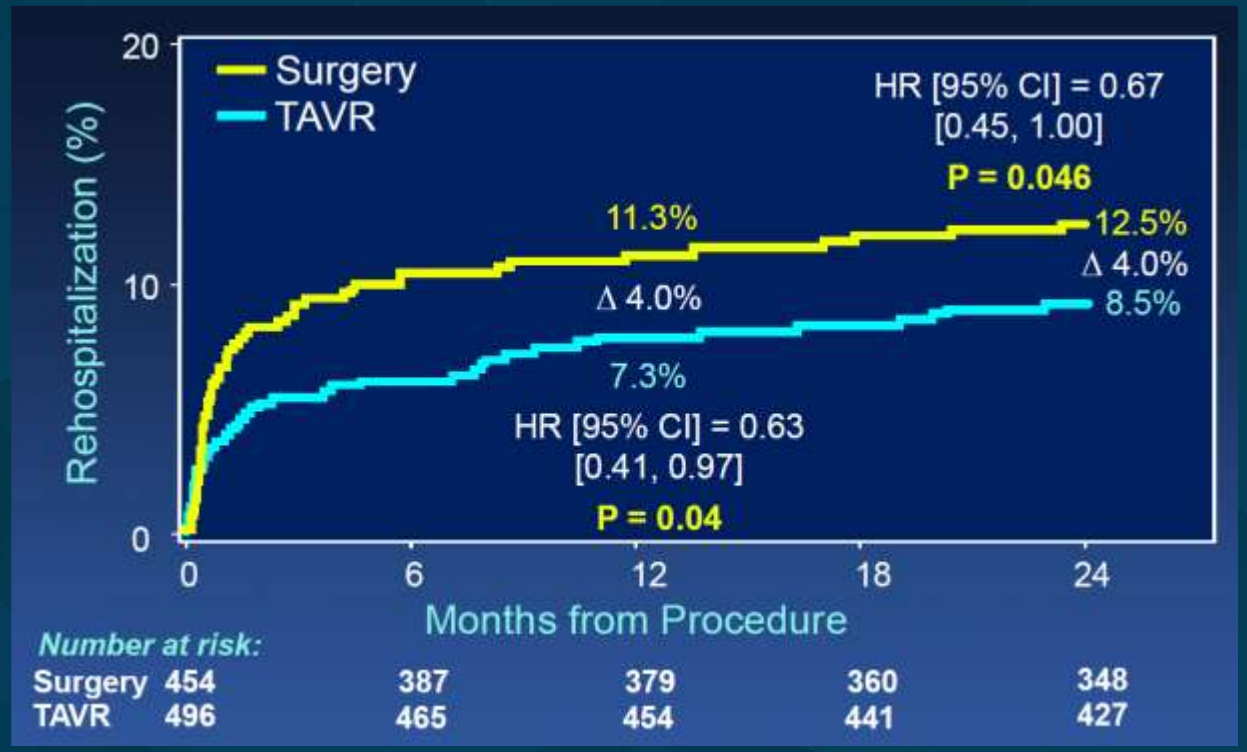
J Am Coll Cardiol 2021;77(9):1149-61.

2-Year Clinical Outcomes

All Stroke



Rehospitalization



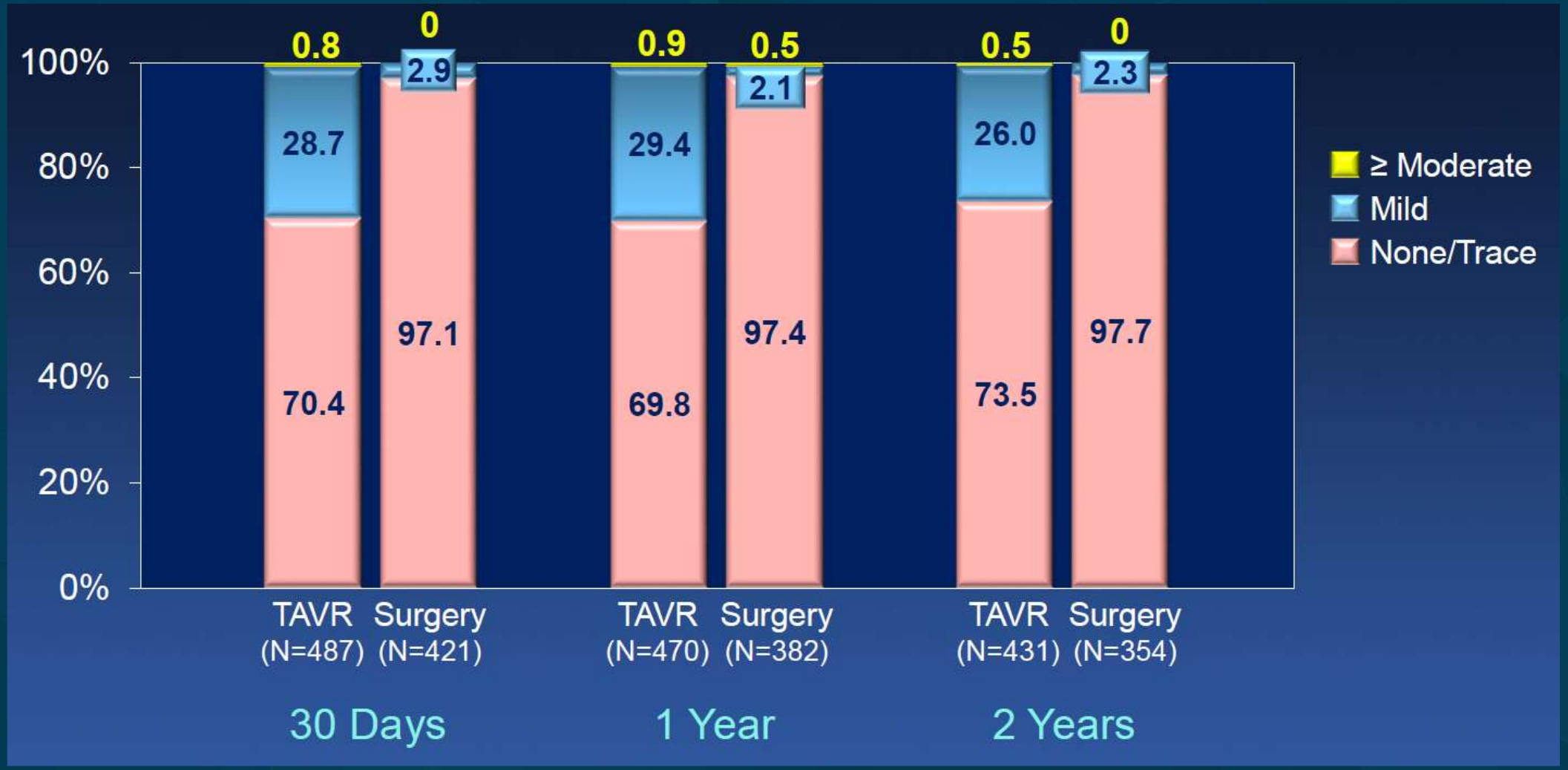
J Am Coll Cardiol 2021;77(9):1149-61.

2-Year Secondary Endpoints

Outcomes	1 Year			2 Years		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
MI	1.2% (6)	2.2% (10)	0.23	1.8% (9)	2.7% (12)	0.36
New onset atrial fibrillation	7.2% (30)	40.9% (150)	< 0.001	7.9% (33)	41.8% (153)	< 0.001
New PPM (incl baseline)	7.3% (36)	5.4% (24)	0.21	8.5% (42)	6.3% (28)	0.19
New LBBB	23.9% (115)	8.0% (35)	< 0.001	24.4% (117)	9.4% (41)	< 0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0.6% (3)	0.5% (2)	0.76	0.8% (4)	0.9% (4)	0.85
Endocarditis	0.2% (1)	0.5% (2)	0.49	0.2% (1)	0.9% (4)	0.13
Valve Thrombosis*	1.0% (5)	0.2% (1)	0.13	2.6% (13)	0.7% (3)	0.02

J Am Coll Cardiol 2021;77(9):1149-61.

Paravalvular Regurgitation



J Am Coll Cardiol 2021;77(9):1149-61.

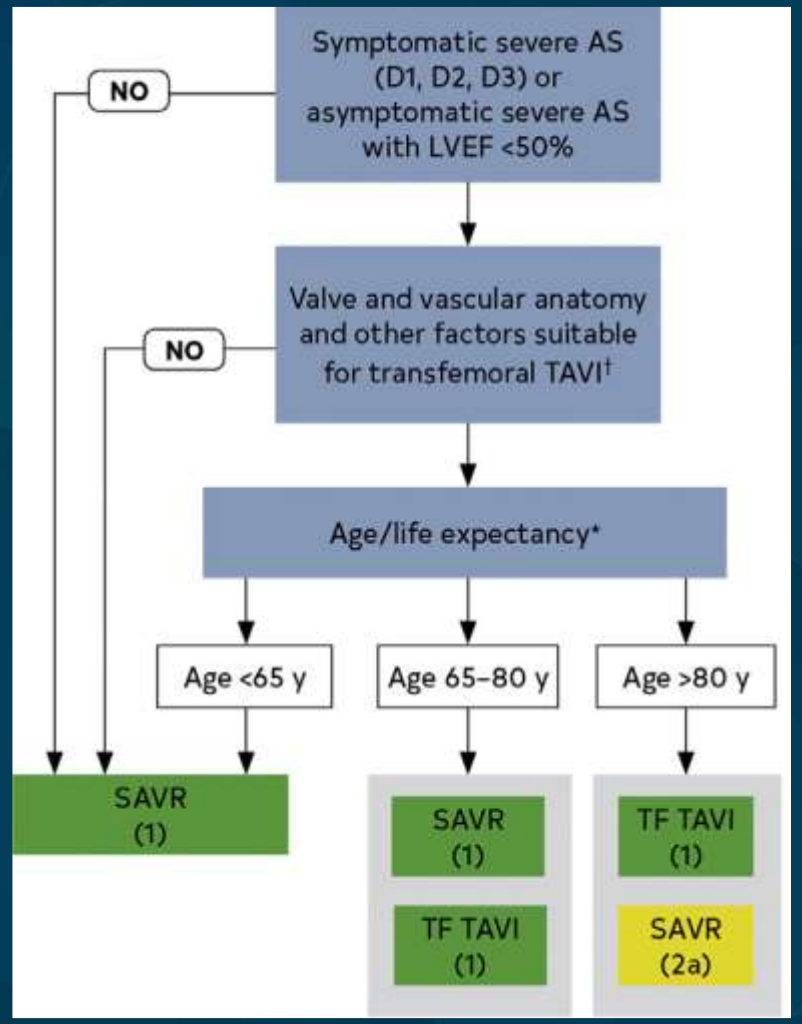
Lessons from 2-year FU data of the PARTNER 3

- At 2 years, the primary endpoint remained significantly lower with TAVR vs. surgery, but initial differences in death and stroke favoring TAVR were diminished.
- Increased valve thrombosis events in TAVR patients, esp. from 1 to 2 years
- Hemodynamic improvements and frequency of moderate or mild paravalvular regurgitation were unchanged between 1 and 2 year in both TAVR and surgery patients

2020 ACC/AHA Valve Disease Guideline

SAVR vs. TAVI

- Decision between SAVR vs. TAVI should include the presence of symptoms, patient age and anticipated life expectancy, the indication for intervention, predicted surgical risk, and anatomy or other factors referable to transfemoral (TF) TAVI feasibility (all Class 1).



J Am Coll Cardiol 2020;Dec 17 [Epub]

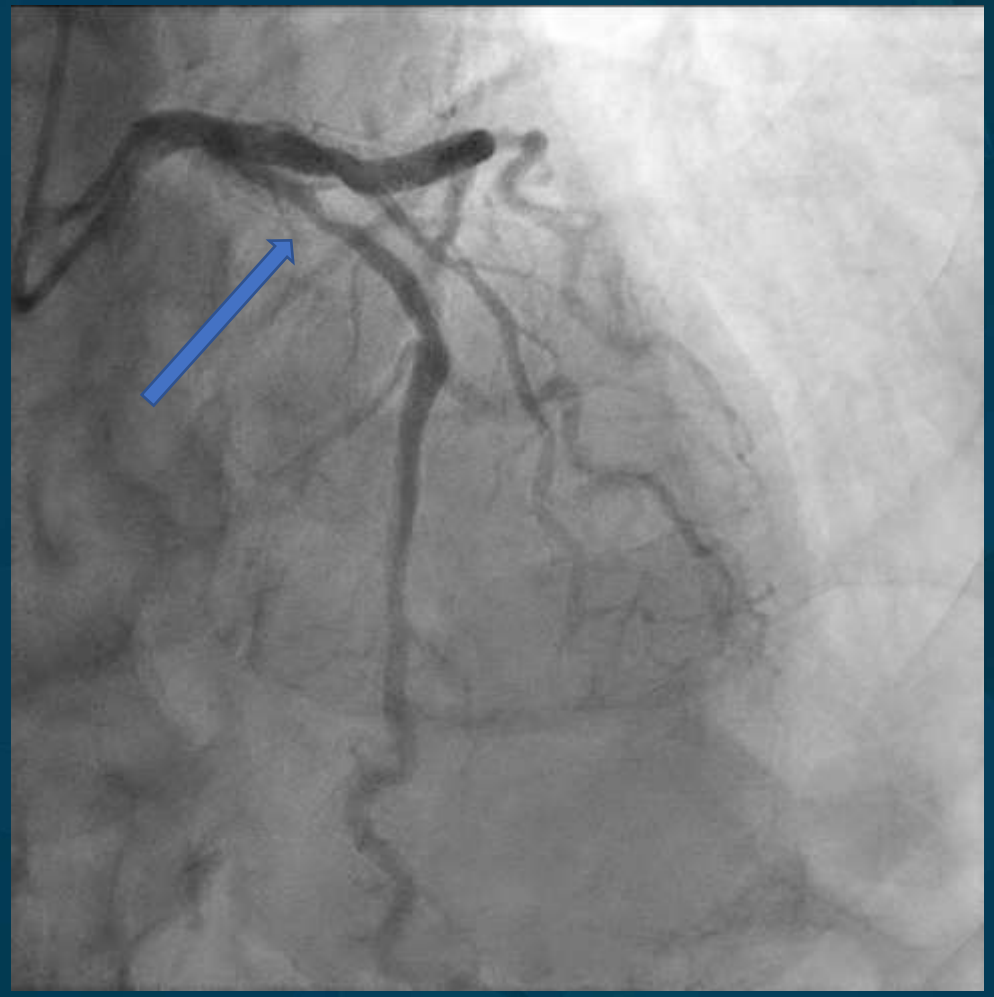
CASE

M/85

- CC
  - Dyspnea
- Comorbidities
  - CSAP, 1 vs disease - pLAD 60%
  - HTN
  - BPH
- STS score : 1.77%

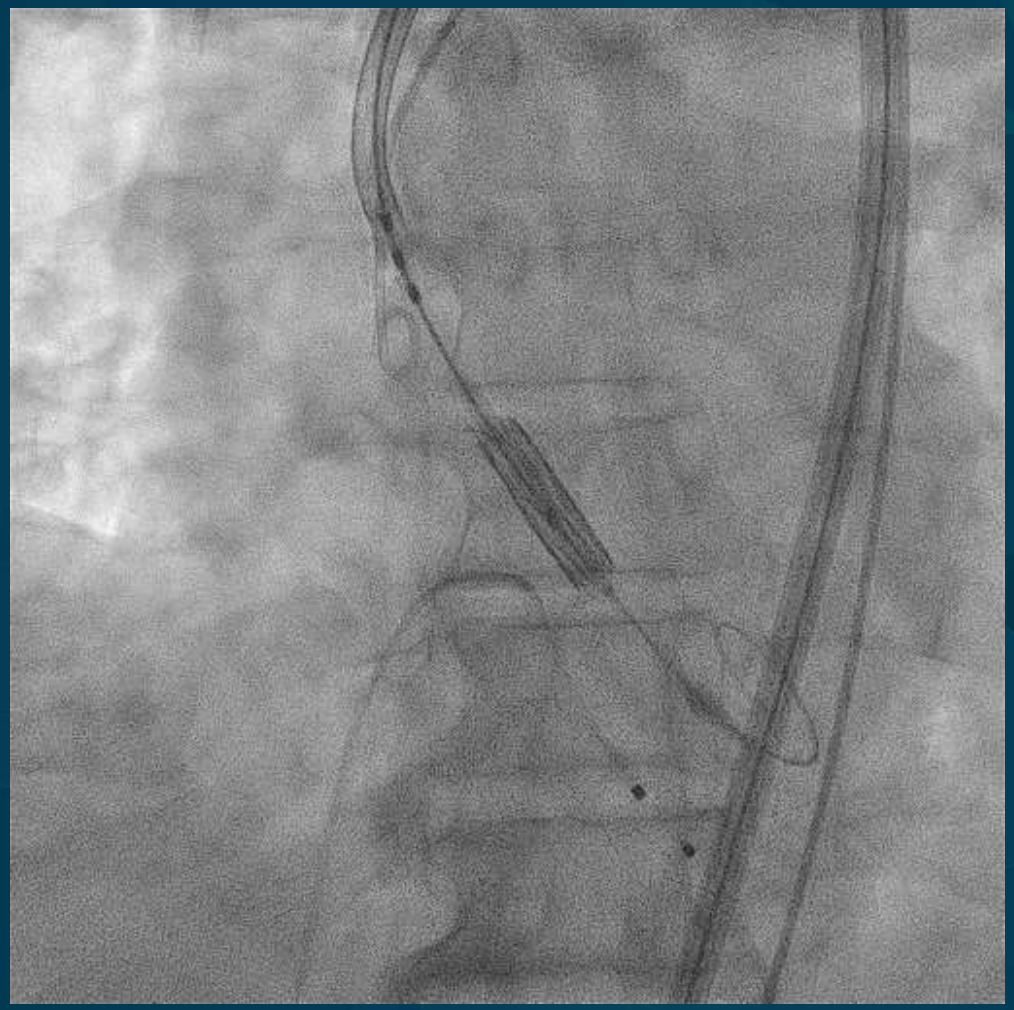
- Echo
  - EF : 65%, No RWMA
  - AV V_{max} 4.2m/s, MSPG 43mmHg
  - AVA 0.91cm^2
- CT
  - Annulus 466.2mm^2
    - Area driven diameter 24.4mm
  - SoV 33.9mm, STJ 28.7mm
  - Coronary Height : Lt 12.3mm, Rt 18.7mm

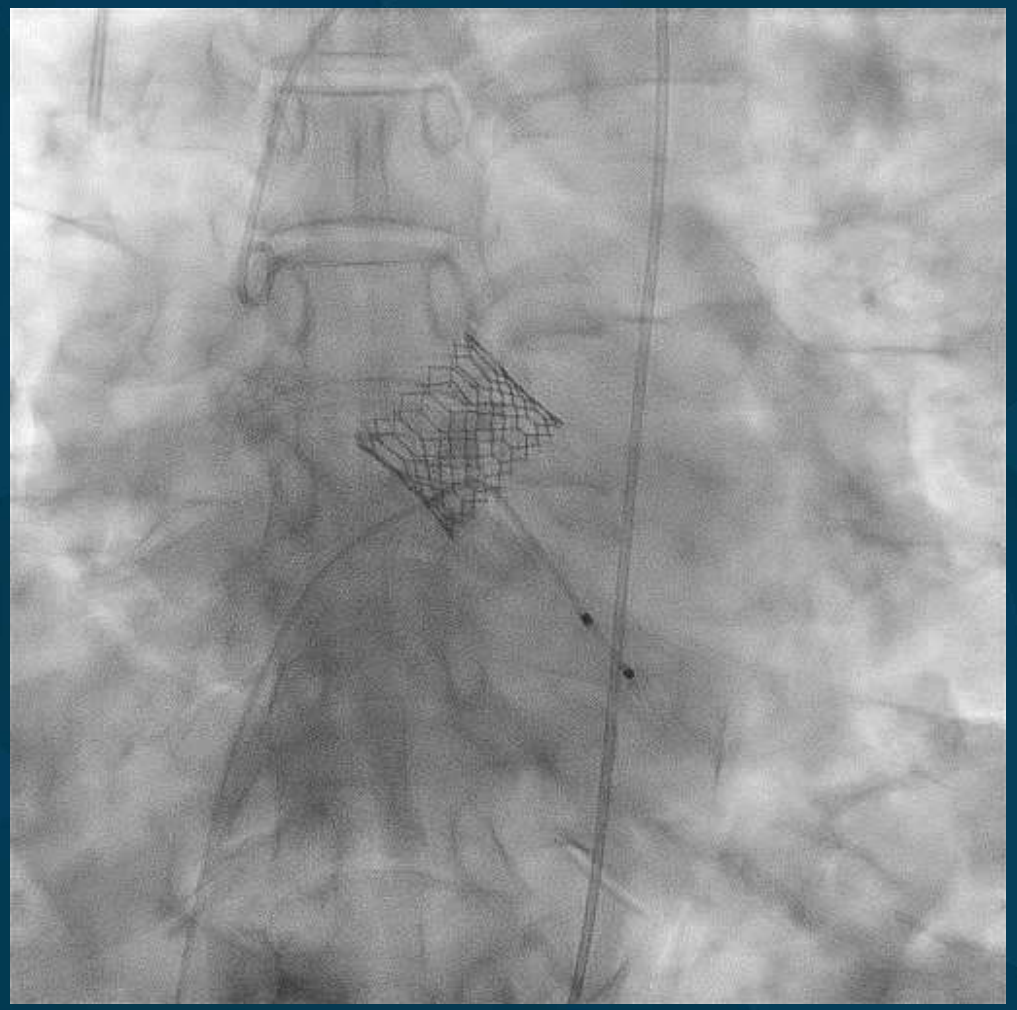
Coronary



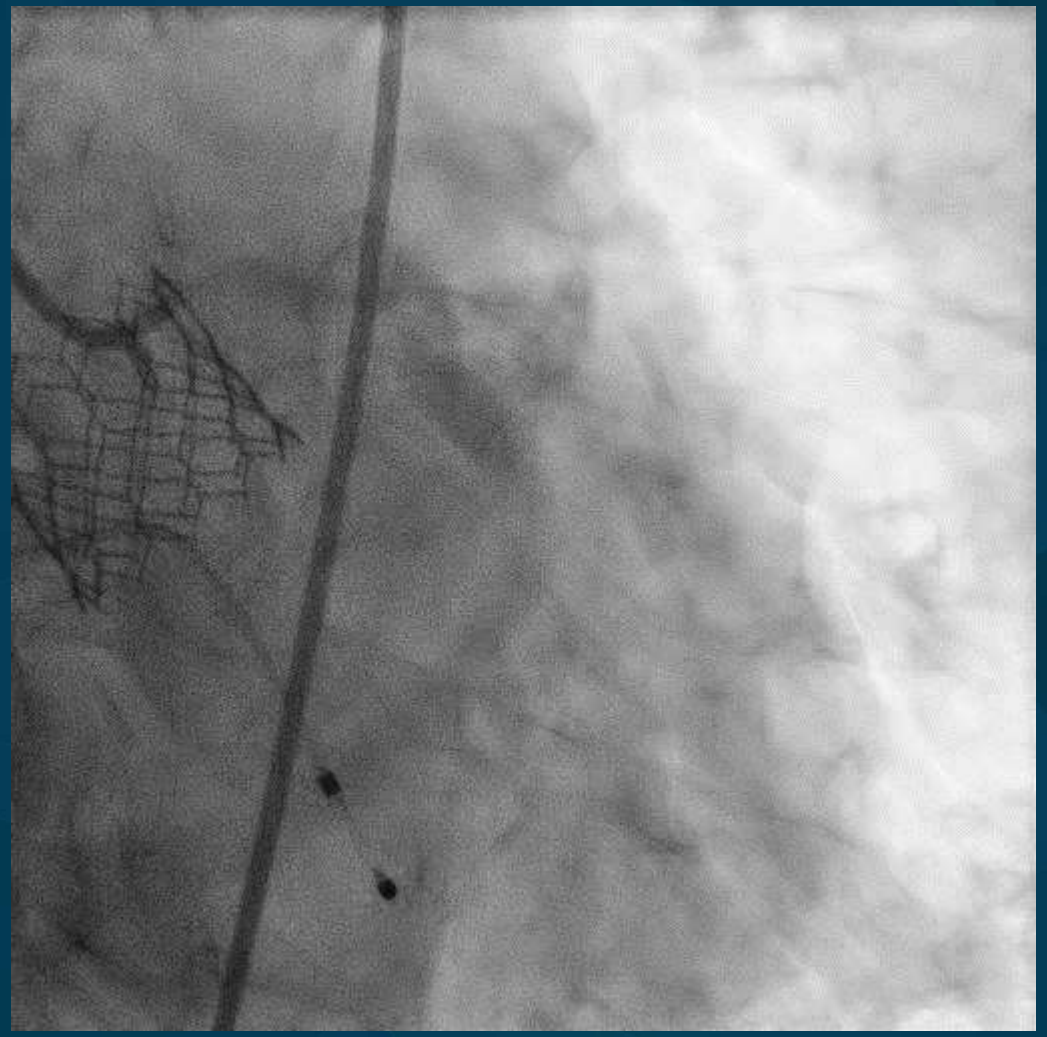

Yeungnam Univ. Medical Center
LAD Prox Pre-PCI
200
150
100
50
0
Pa
92
Pd
75
Time
00:48
1.25
1.00
0.75
0.50
0.25
0.00
FFR
0.81
Pd/Pa: 0.91
FFR: 0.81
01:02

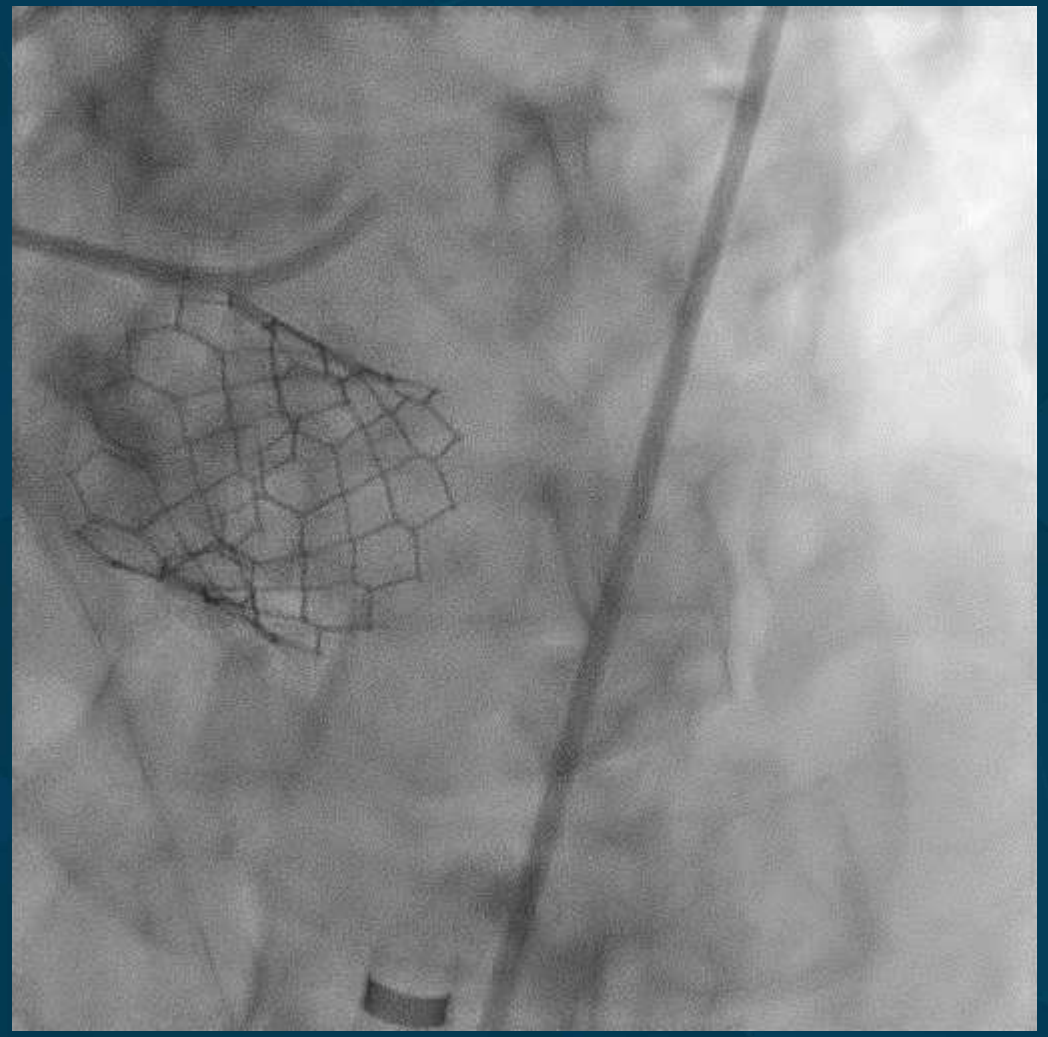
TAVI procedure (SAPIEN 26mm)





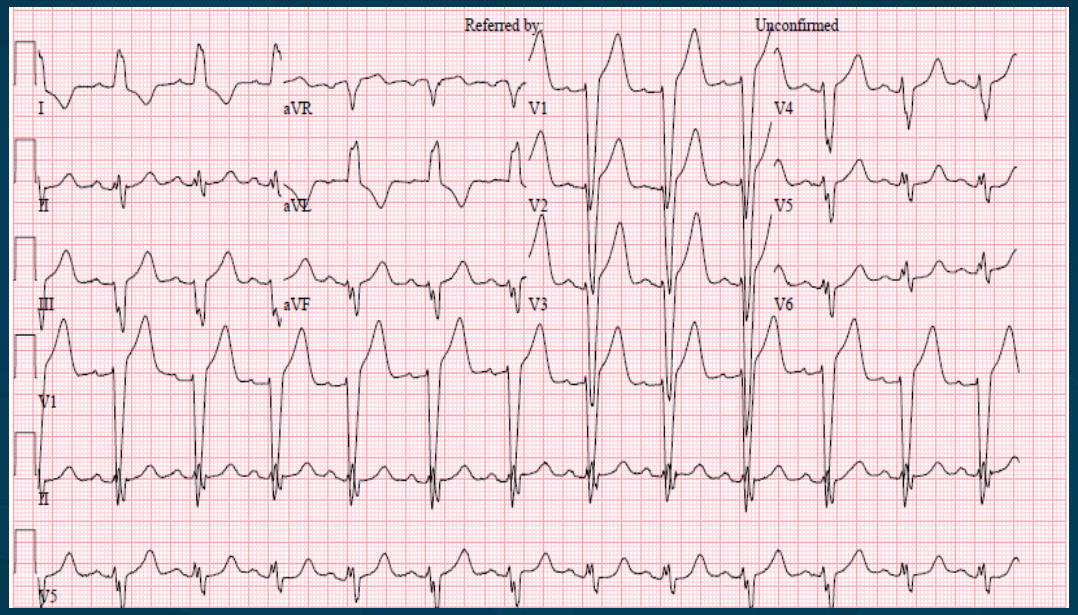
TAVI procedure

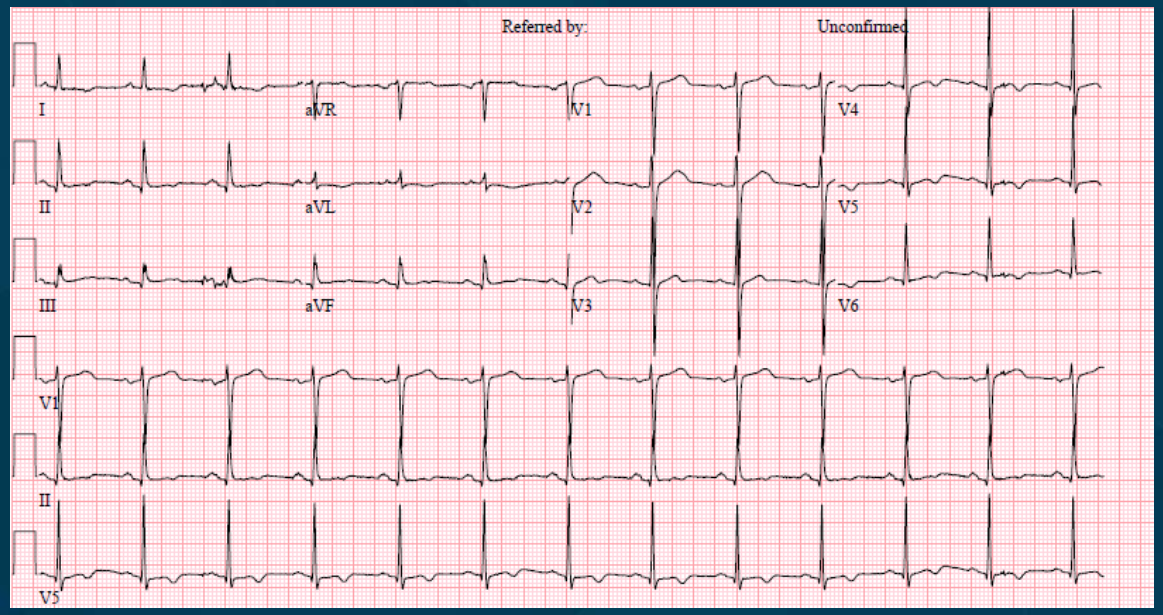




Post-procedure ECG

- LBBB → normal

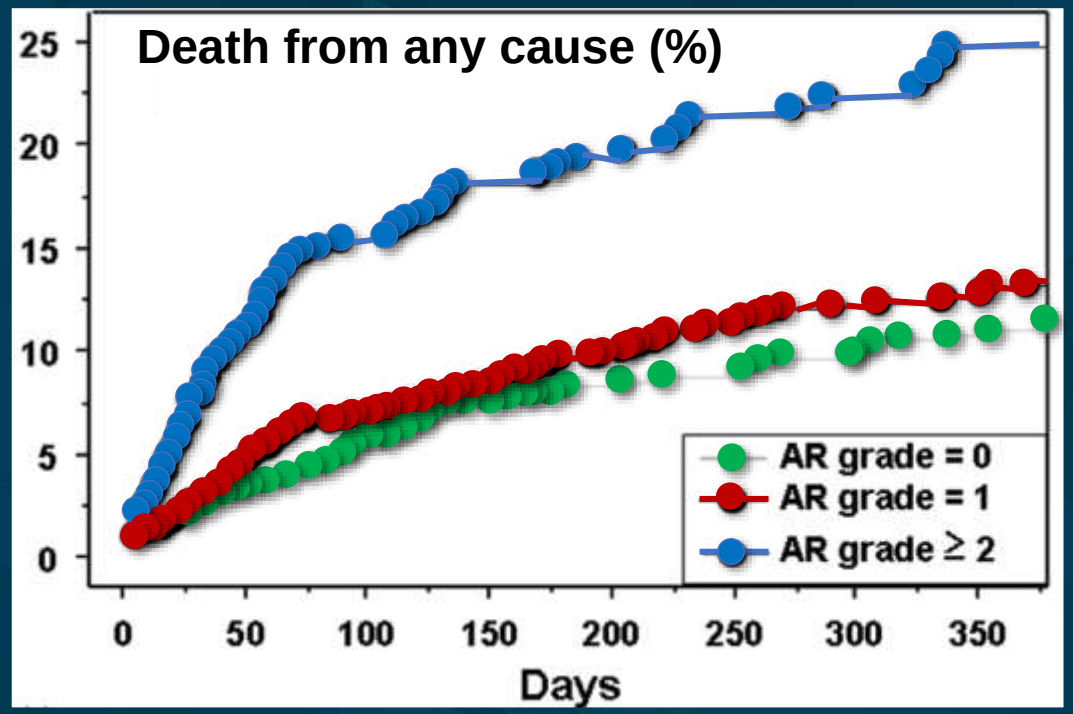




SAPIEN & Paravalvular Leakage (PVL)

Importance of PVL

Patient:	**3195 TAVI patients from FRANCE2 Registry**
Comparison:	**AR after TAVI grade 0 vs. grade 1 vs. grade 2**
Outcomes:	**All-cause mortality**



PVL ≥ grade 2 after TAVI was associated with higher mortality.

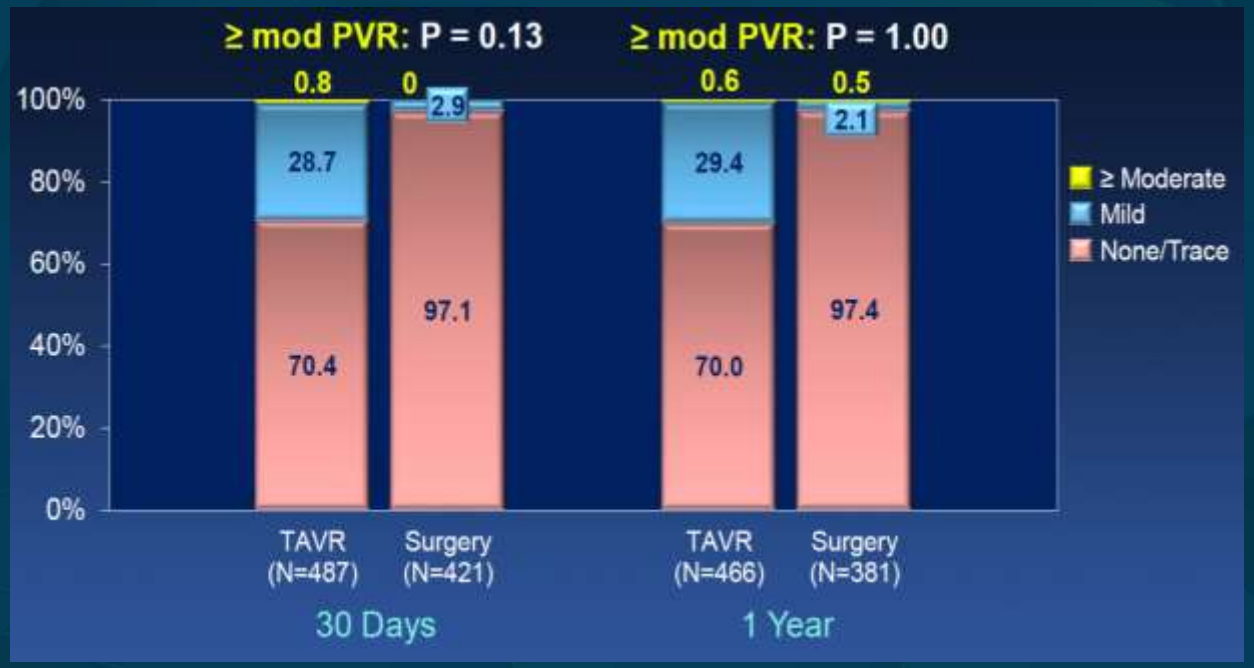
HR 2.33 , 95% CI [1.82 – 2.99], P<0.001

Van Belle E et al. Circulation. 2014;129:1415-27

Balloon-expandable vs. Self-expandable

Regarding PVL

PARTNER 3 trial



≥ mod PVL : **0.8%** (1 month) → **0.6%** (1 year)

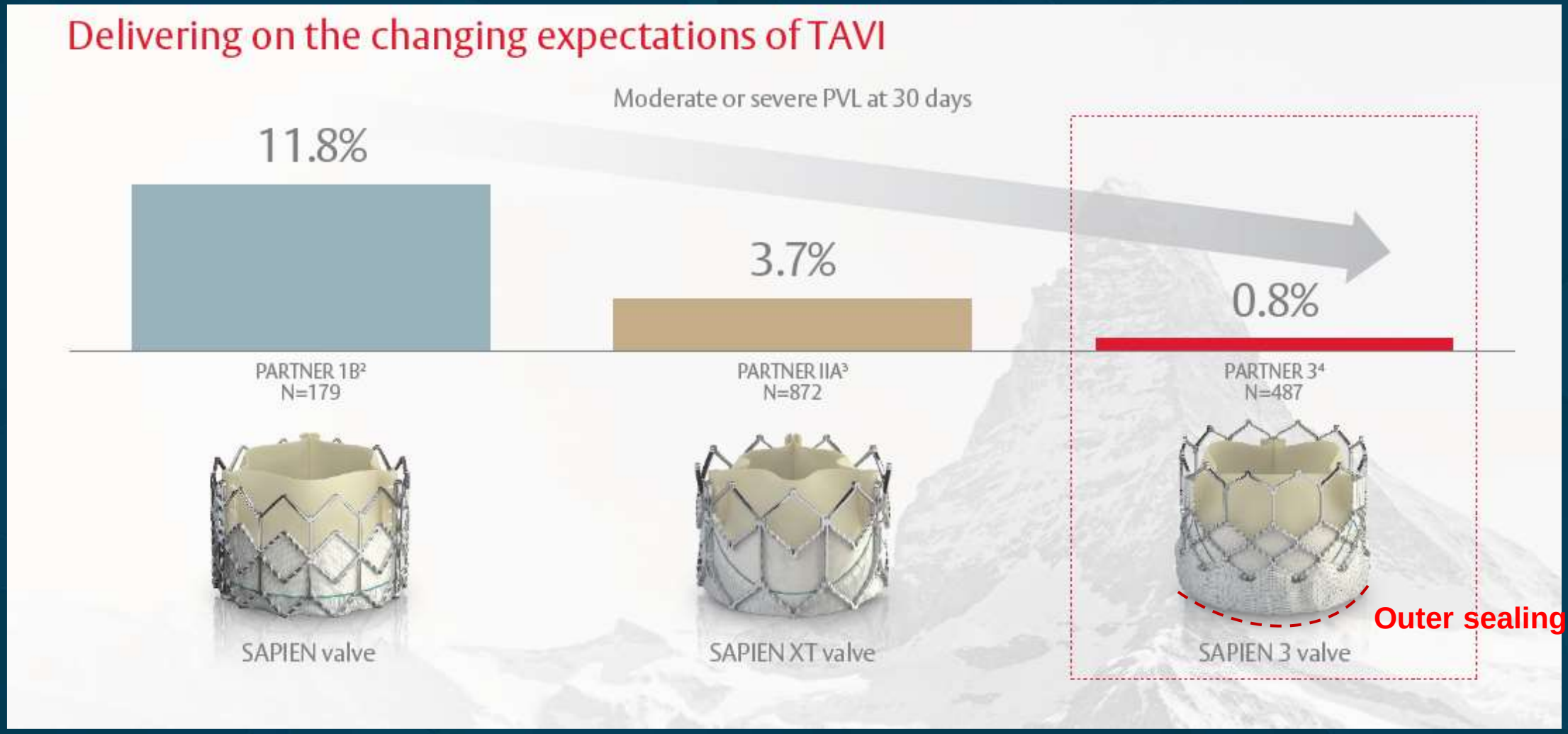
N Engl J Med 2019;380:1695-705.

EVOLUT Low Risk trial

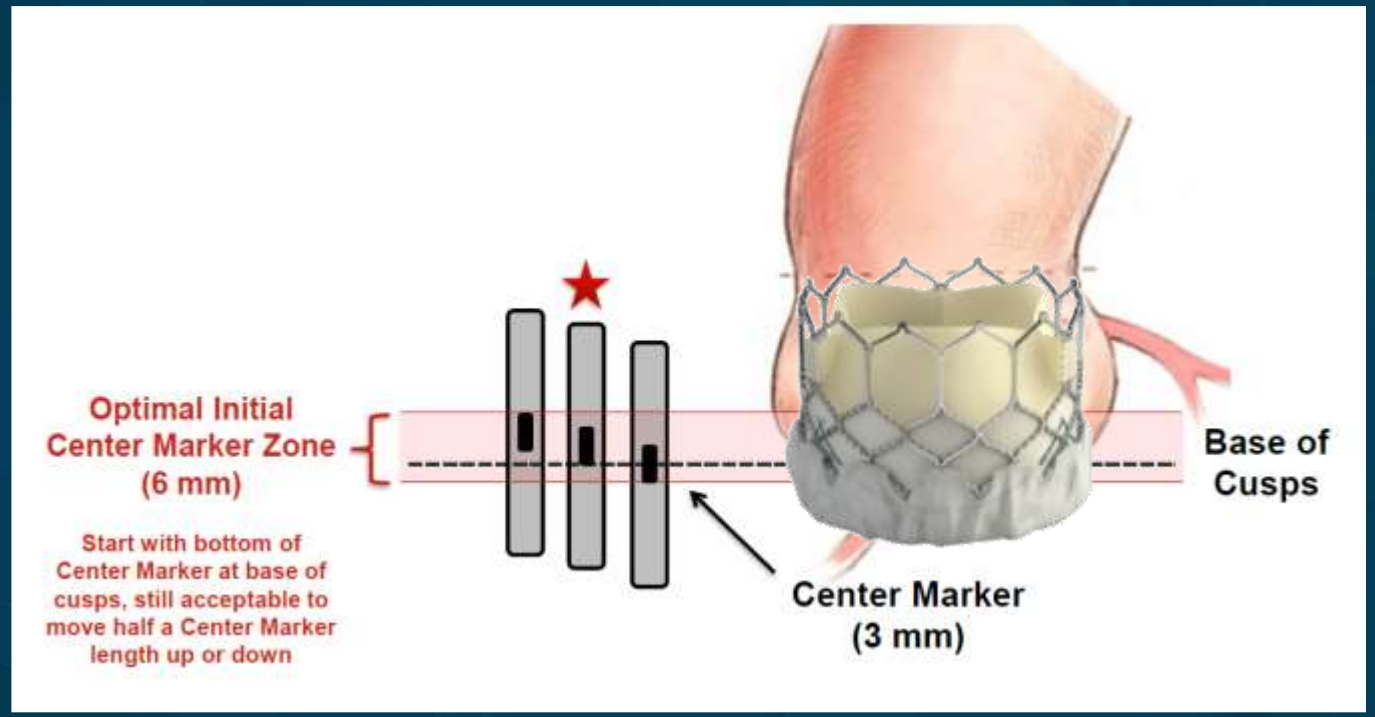
≥ mod PVL : **3.5%** (1 month) → **4.3%** (1 year)

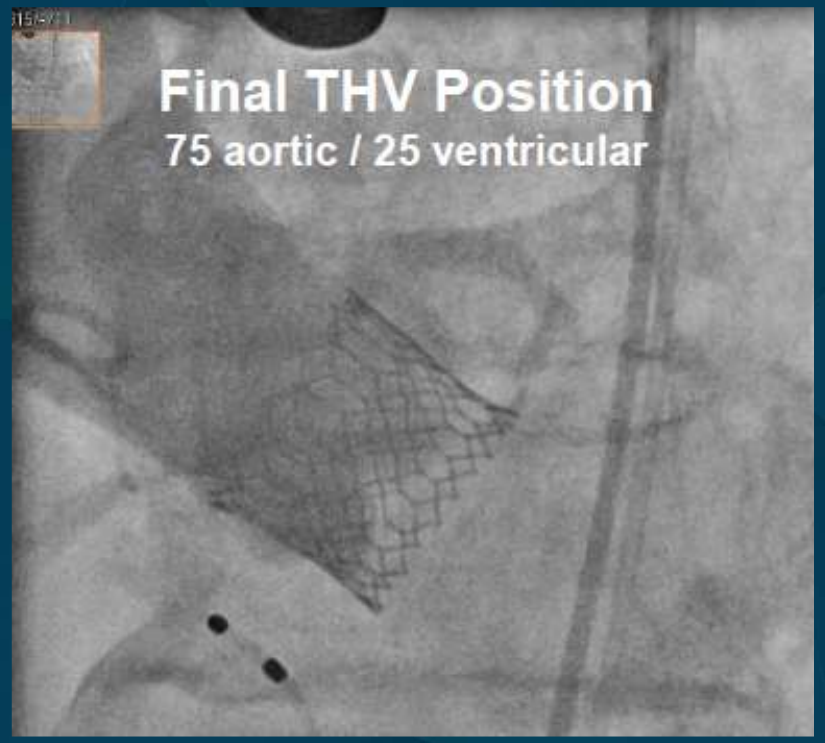
N Engl J Med 2019;380:1706-1715.

Evolution of SAPIEN



Outer sealing skirt can reduce PVL





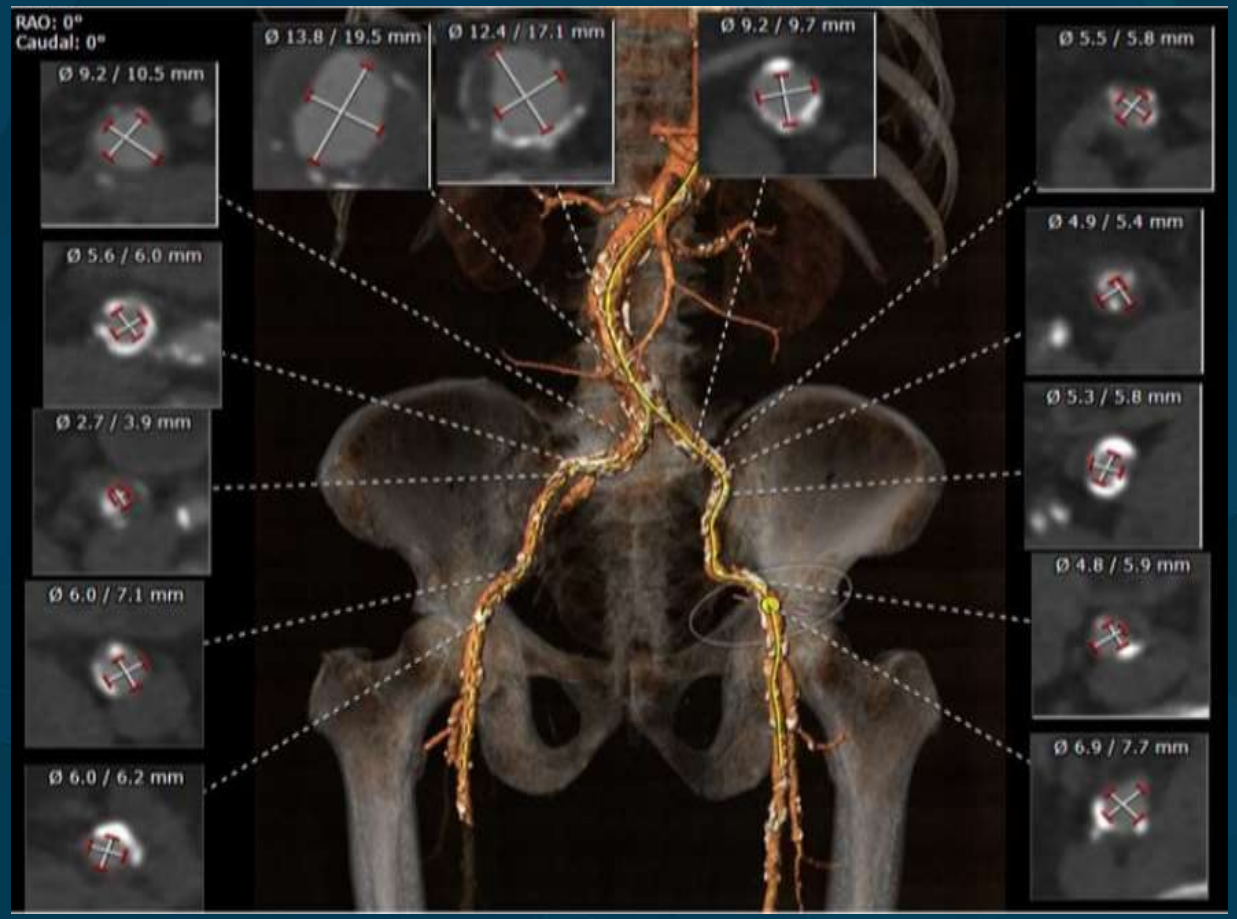
CASE

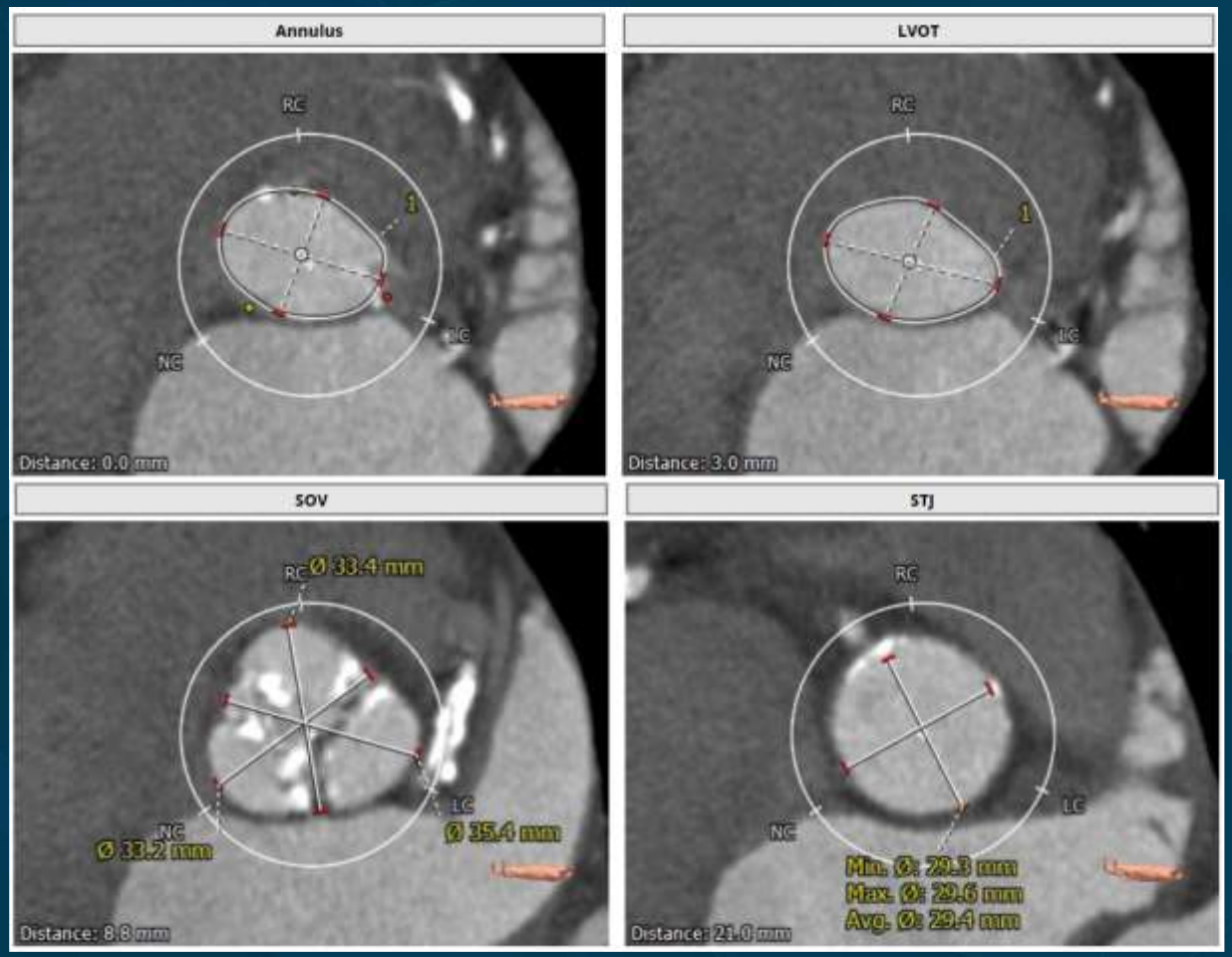
M/87

- CC
  - Dyspnea
- Comorbidities
  - PAD
  - OMI (pLAD, mRCA, mLCX PTCA)
  - Dyslipidemia
  - Hypothyroidism
- STS score : 10.528%

- Echo
  - EF : 53%, No RWMA
  - AV V_{max} 4.95m/s, MSPG 66.4mmHg
  - AVA 0.69cm^2
- CT
  - Annulus 521.3mm^2
    - Area driven diameter 25.8mm
  - SoV 33.4mm, STJ 29.4mm
  - Coronary Height : Lt 12.5mm, Rt 16.7mm

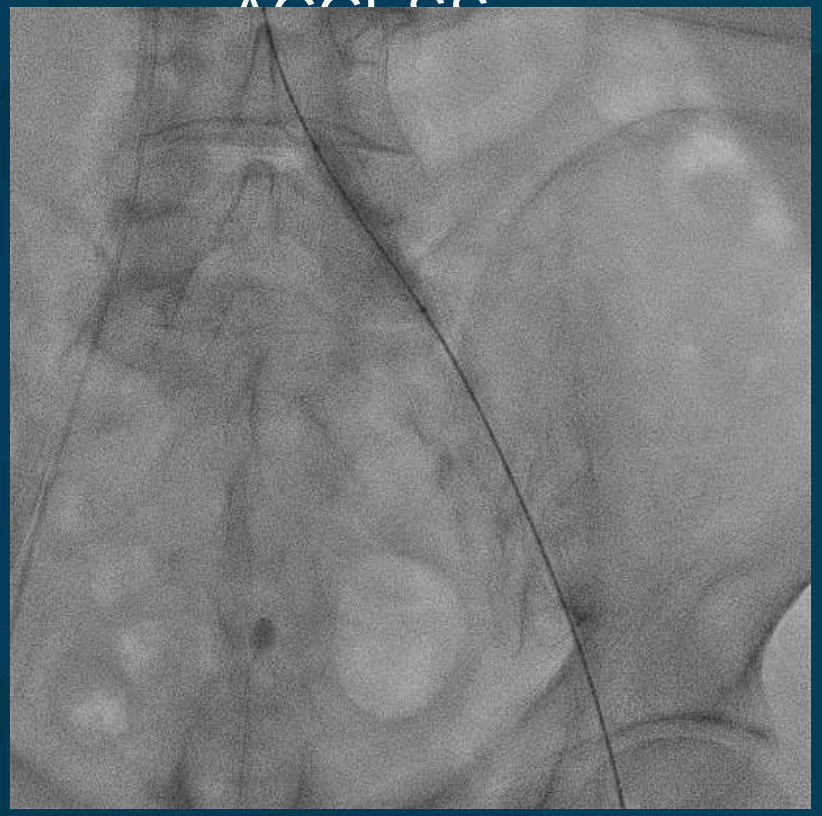
Pre-procedure CT

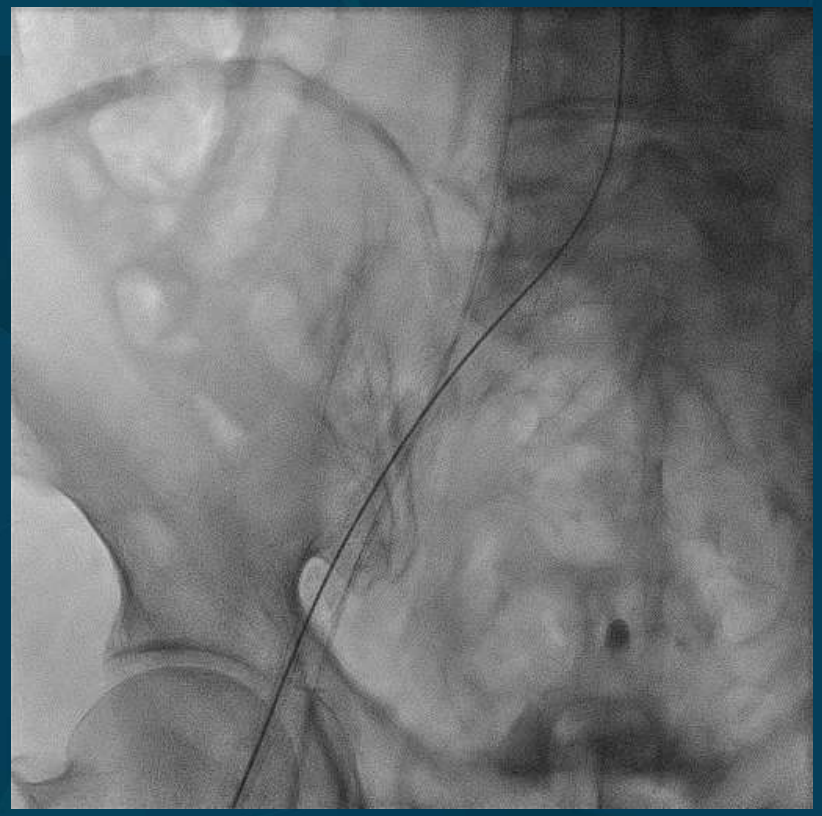


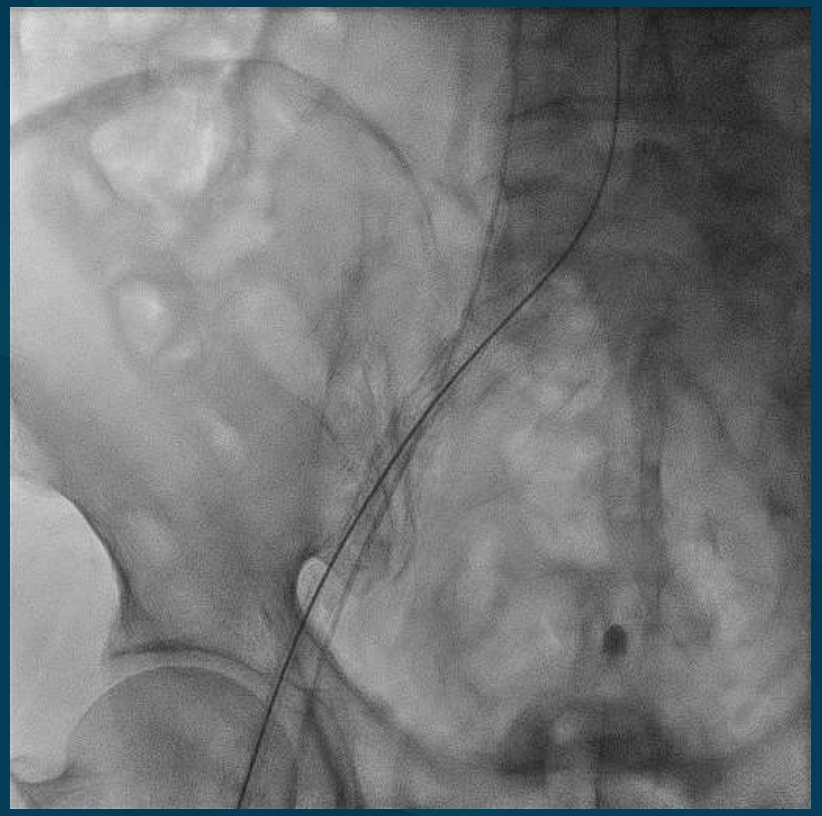


Procedure

ACCESS

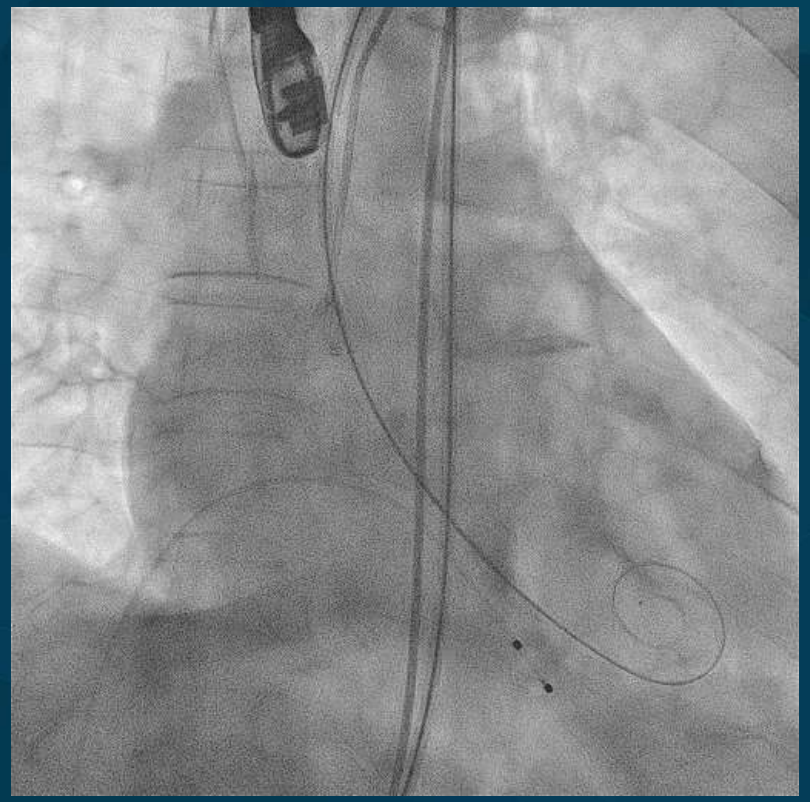




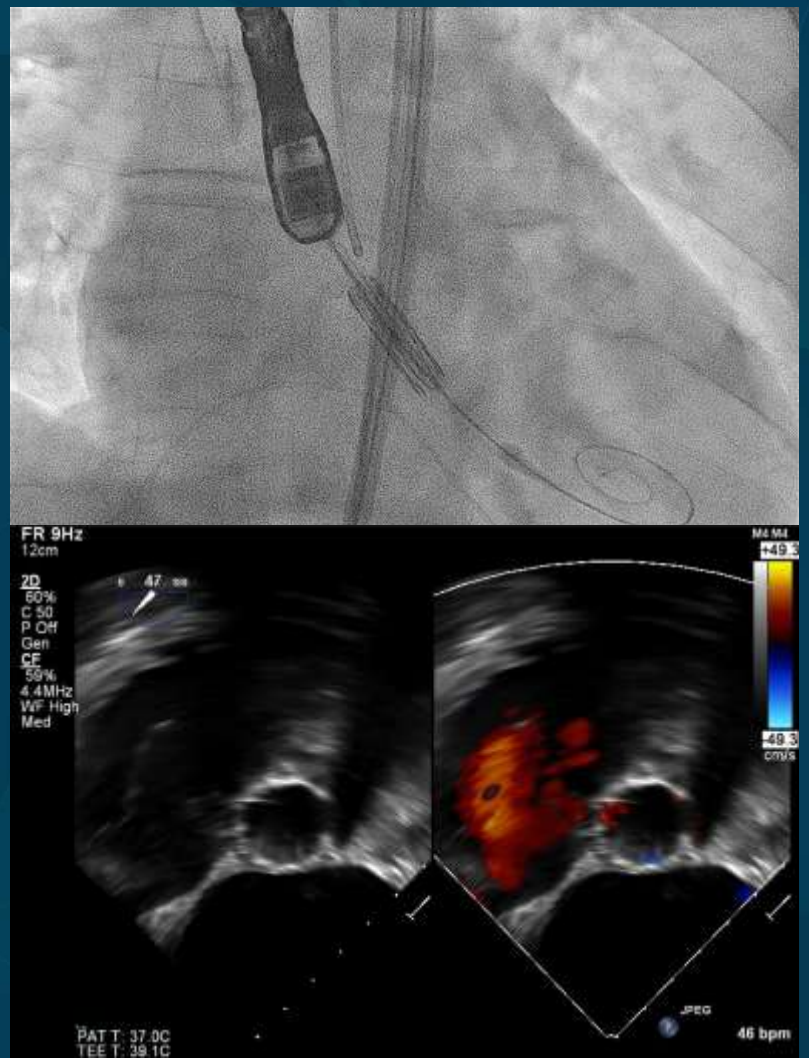


Procedure

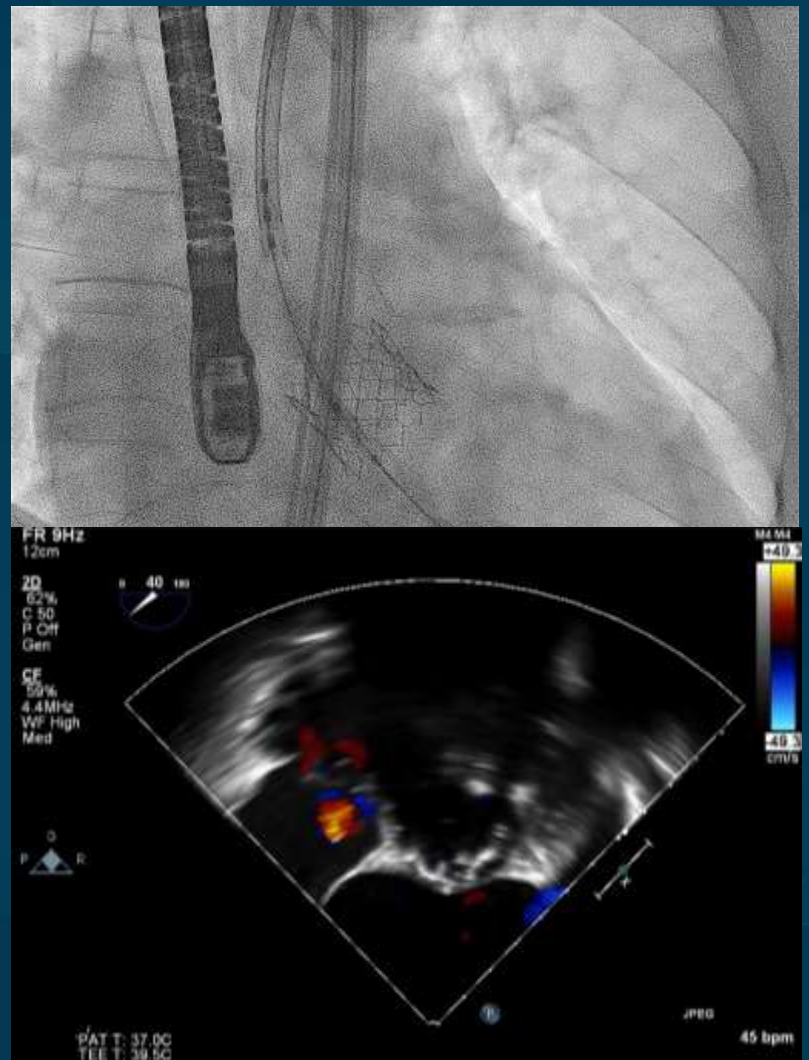
Pre-balloon



Implantation (SAPIEN 26mm)



Post-balloon



Post-procedure Echo

Immediate after TAVI

6 month after TAVI

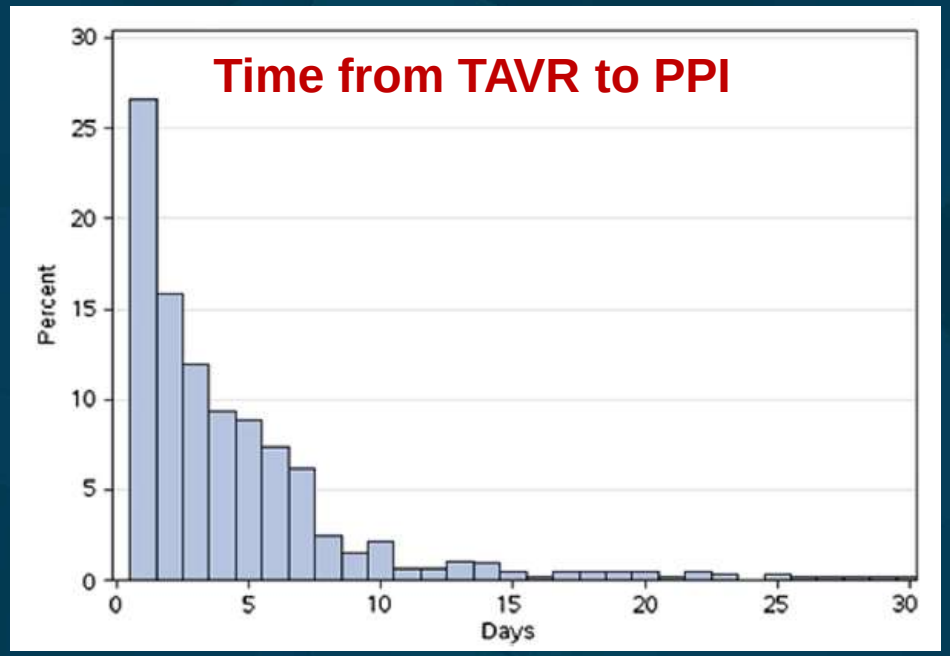
12 month after TAVI

No interval change of mild PVL (<10%)

SAPIEN & Permanent Pacemaker Implantation (PPI)

Incidence of PPI from the *U.S. STS/ACC TVT Registry*

- Incidence
  - 651 / 9785 patients : 6.7%
  - Self-expanding valves (25.1%) vs. Balloon-expanding valves (4.3%)



- The median time from TAVR to PPI : **3 days**

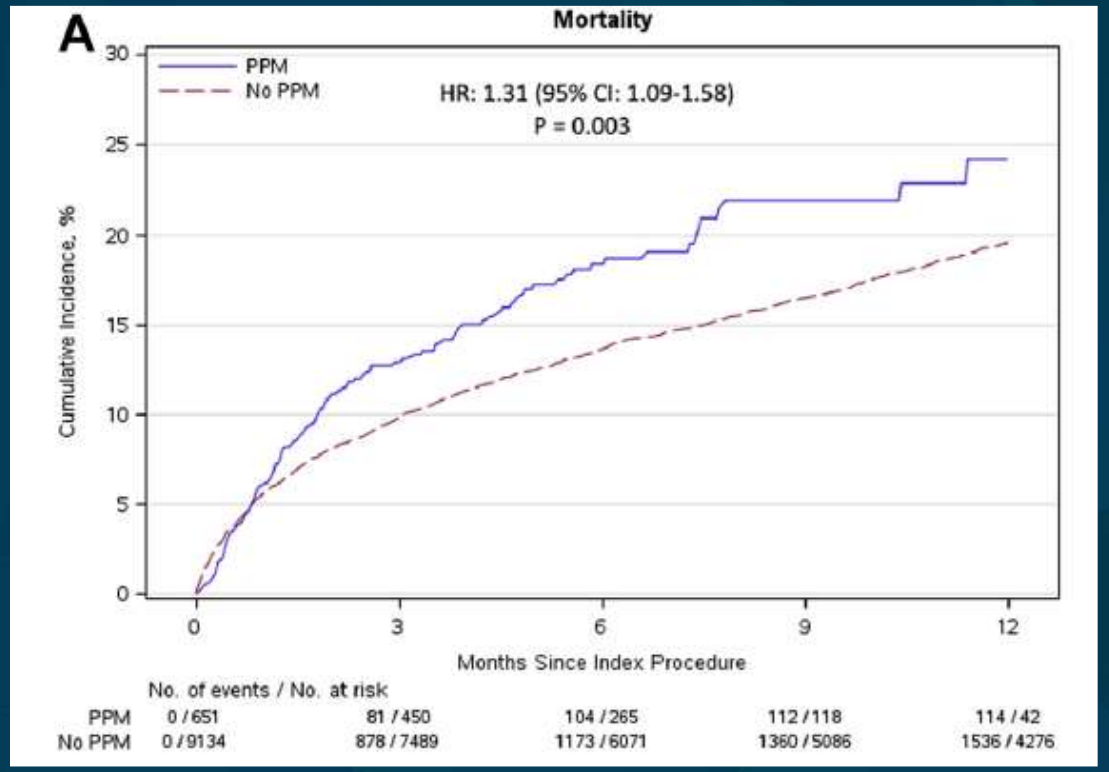
JACC Cardiovasc Interv 2016;9:2189-99

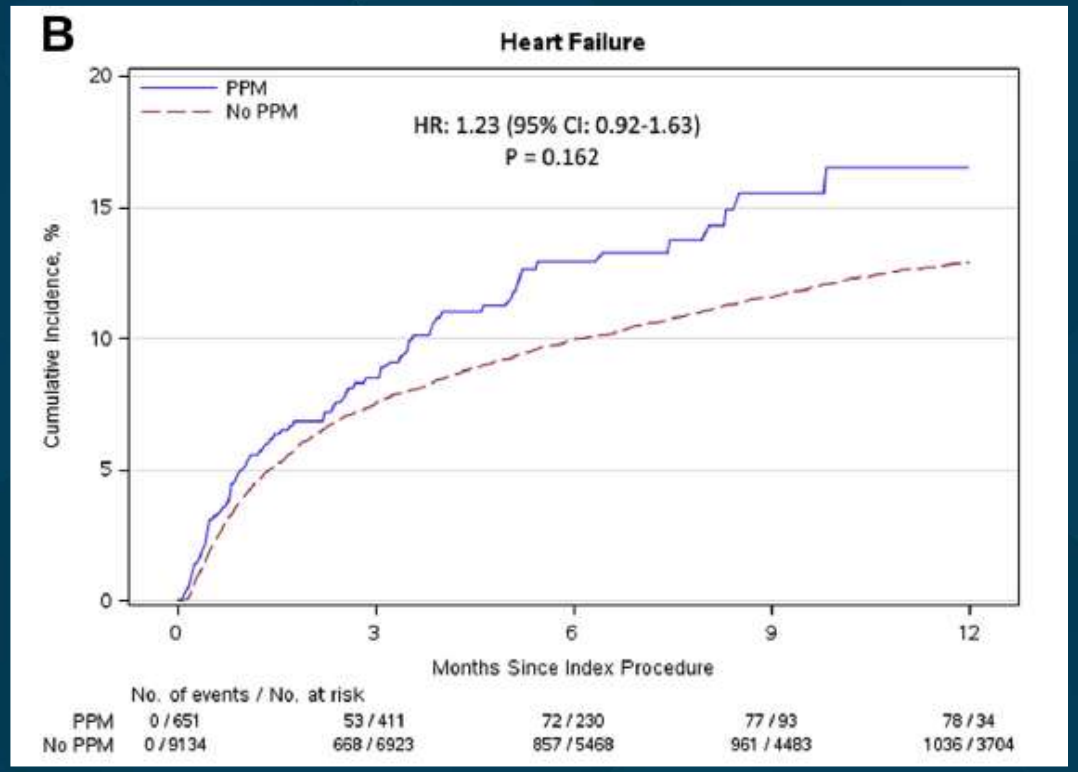
Predictors of 30-Day PPI from the *U.S. STS/ACC TVT Registry*

Predictors	Odds Ratio (95% CI)	p-value
Age (per 5yrs)	1.07 (1.01–1.15)	0.033
Prior aortic valve procedure	0.74 (0.57–0.95)	0.020
Prior conduction defect	1.93 (1.63–2.29)	<0.001
Aortic valve area ≤0.75 cm^2 (per 0.25 cm^2)	1.21 (1.00–1.45)	0.045
Self-expanding valve (vs. balloon-expanding valve)	7.56 (5.98–9.56)	<0.001
Procedure risk classification		
Intermediate risk vs. inoperable / extreme risk	1.78 (1.04–3.04)	0.035
Valve Sheath access site		
Transapical vs. femoral	1.36 (1.10–1.68)	0.004
Transaortic vs. femoral	1.52 (1.09–2.11)	0.013

JACC Cardiovasc Interv 2016;9:2189-99

Clinical Outcomes of PPI



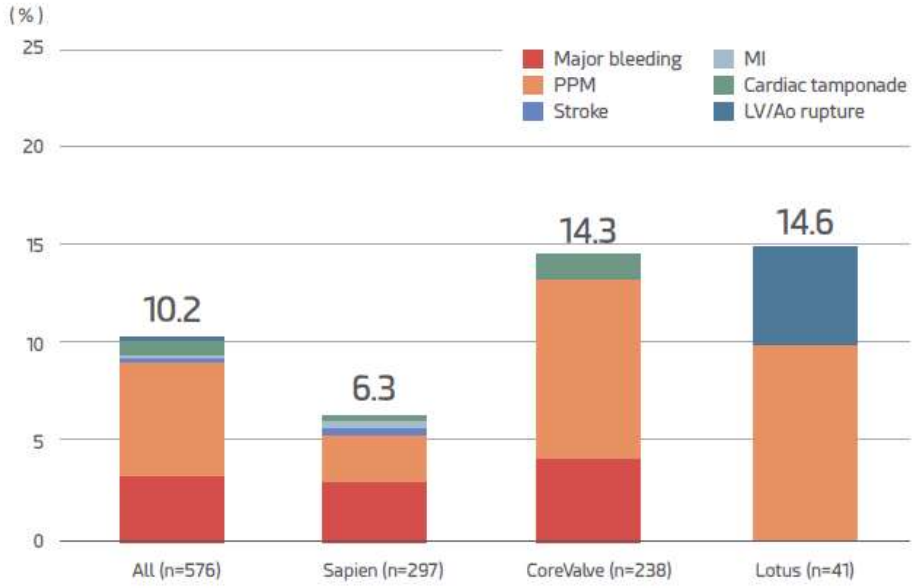


- Early PPI is associated with higher mortality and a composite of mortality or heart failure admission at 1 year

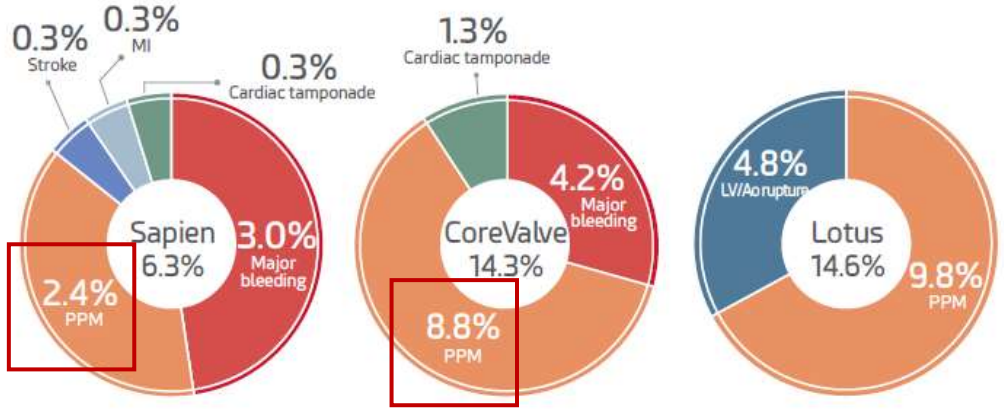
JACC Cardiovasc Interv 2016;9:2189-99

K-TAVI Registry

Complications by device

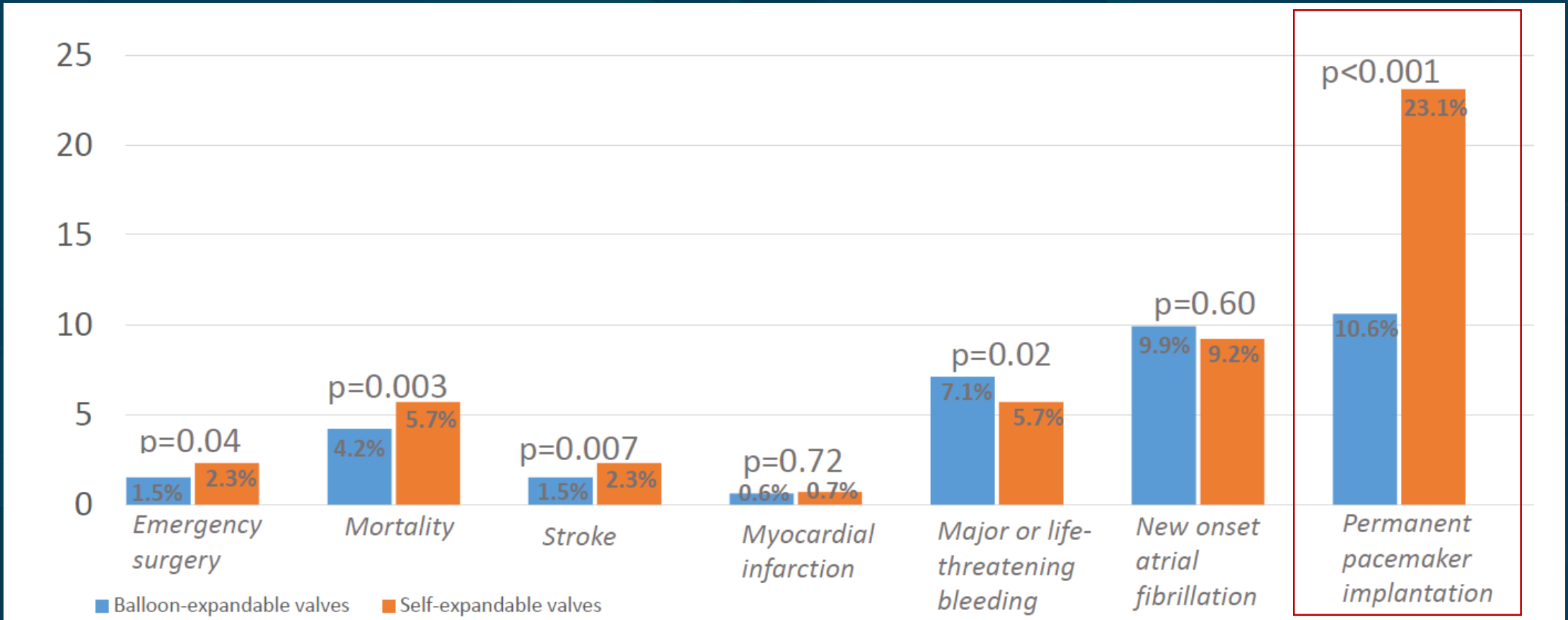


Complications by device



Retrospective multi-center registry from CENTER-Collaboration

N = 12,381 → PS-matched : BE-valve (n=4096) vs. SE-valve (4096)



TCT 2018 presented

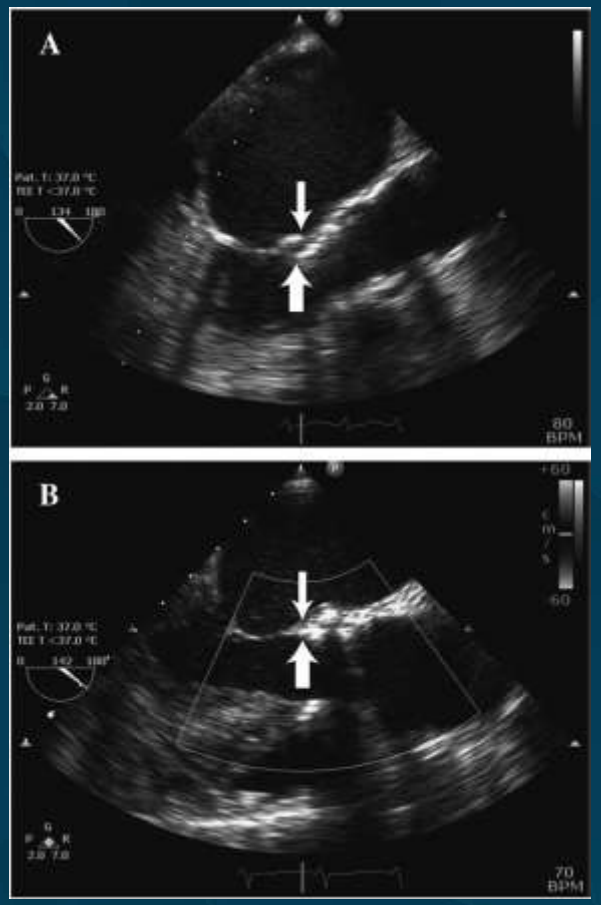
Implant Depth and Conduction Disturbance

- A lower (ventricular) position of the valve relative to the hinge point of the anterior mitral leaflet was associated with a higher incidence of new LBBB (35% vs. 0%, P = .029).

Implanted Above → 0% of patients developed LBBB

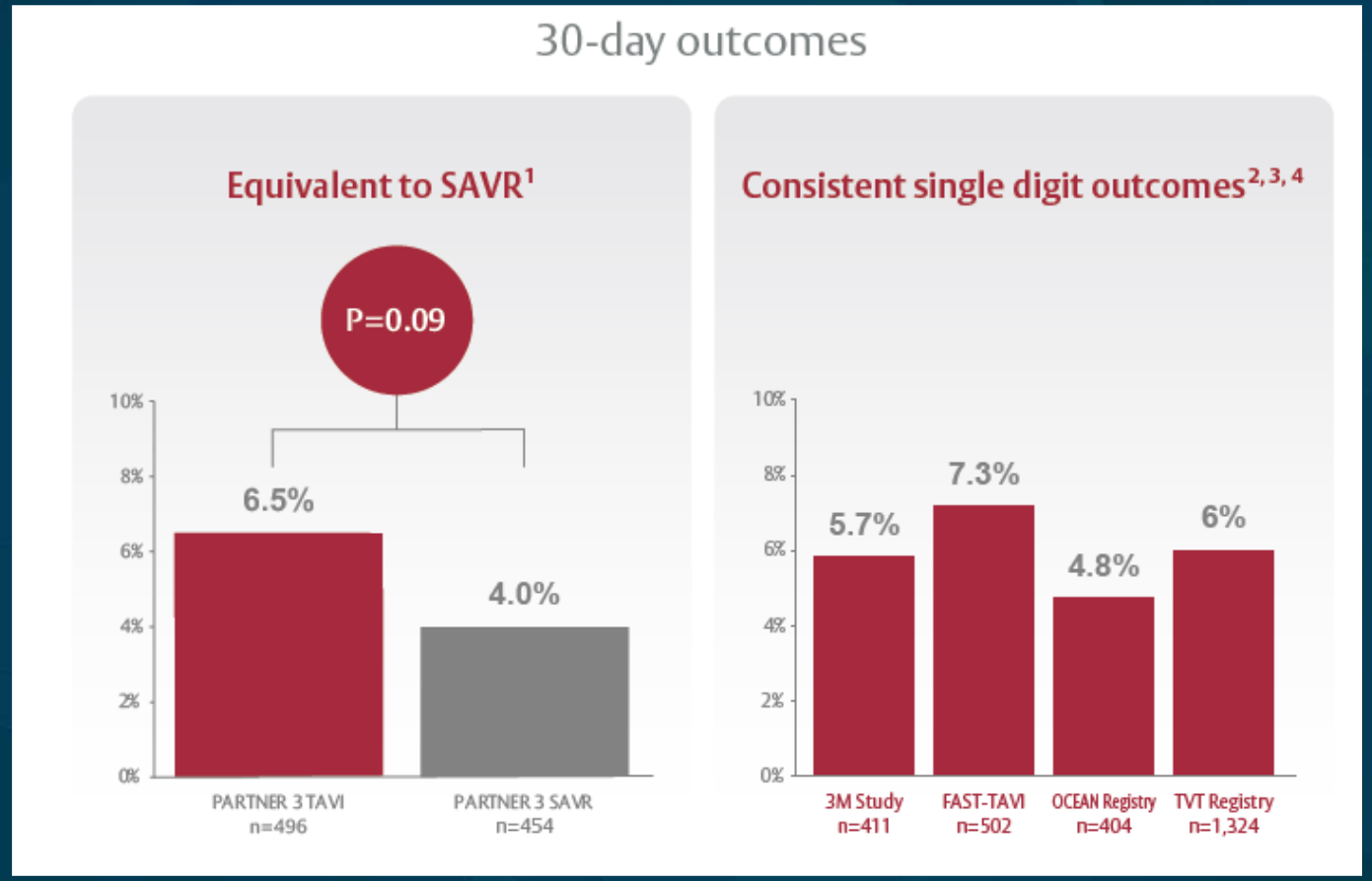
Hinge Point of the Anterior Mitral Valve

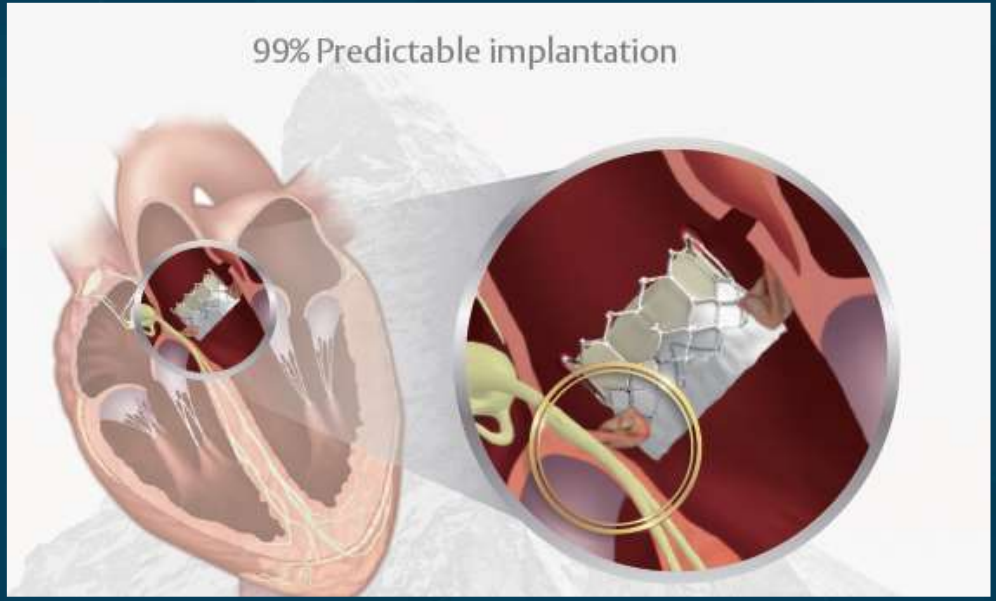
Implanted Below → 35% of patients developed LBBB



Gutierrez et al. Am Heart J 2009, (N=33)

SAPIEN vs. SAVR





N Engl J Med 2019;380:1695-705.

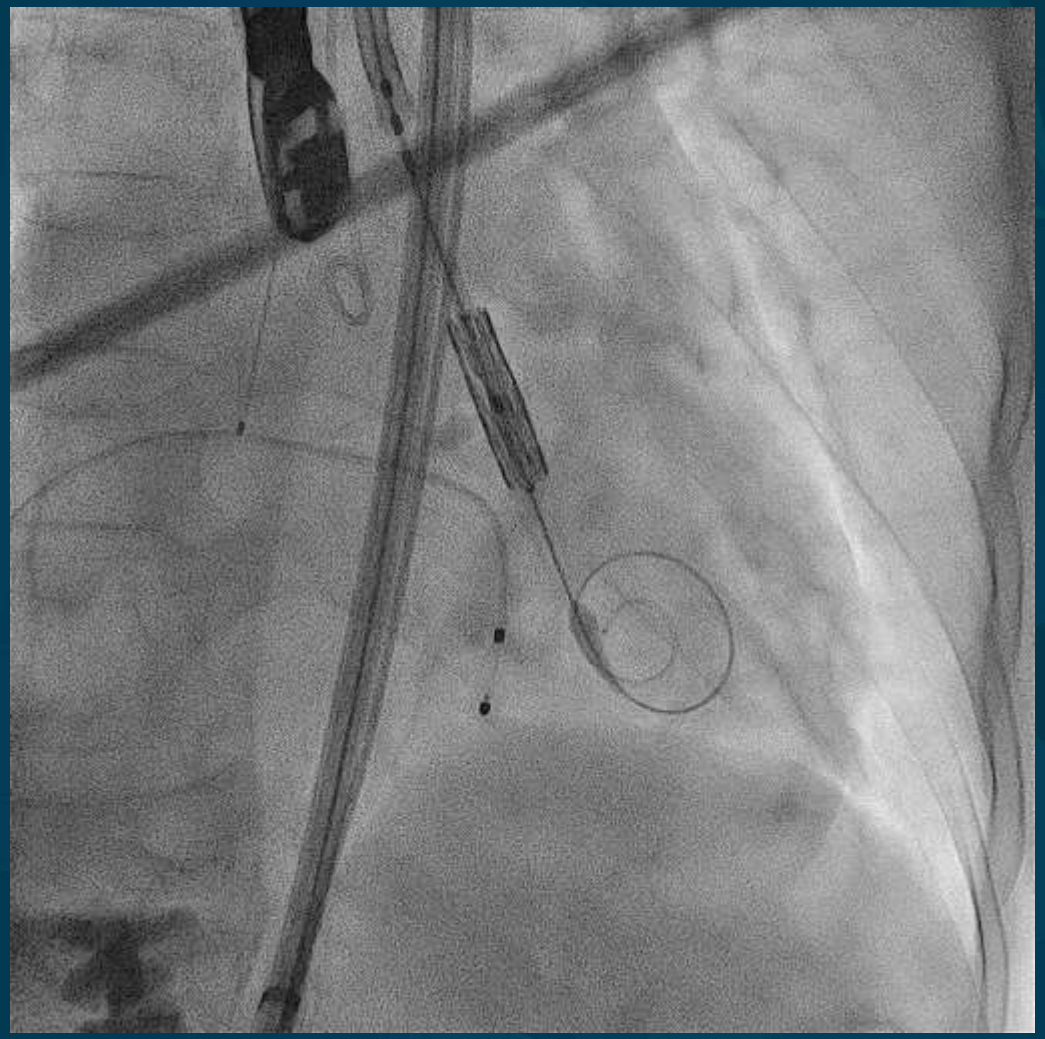
CASE

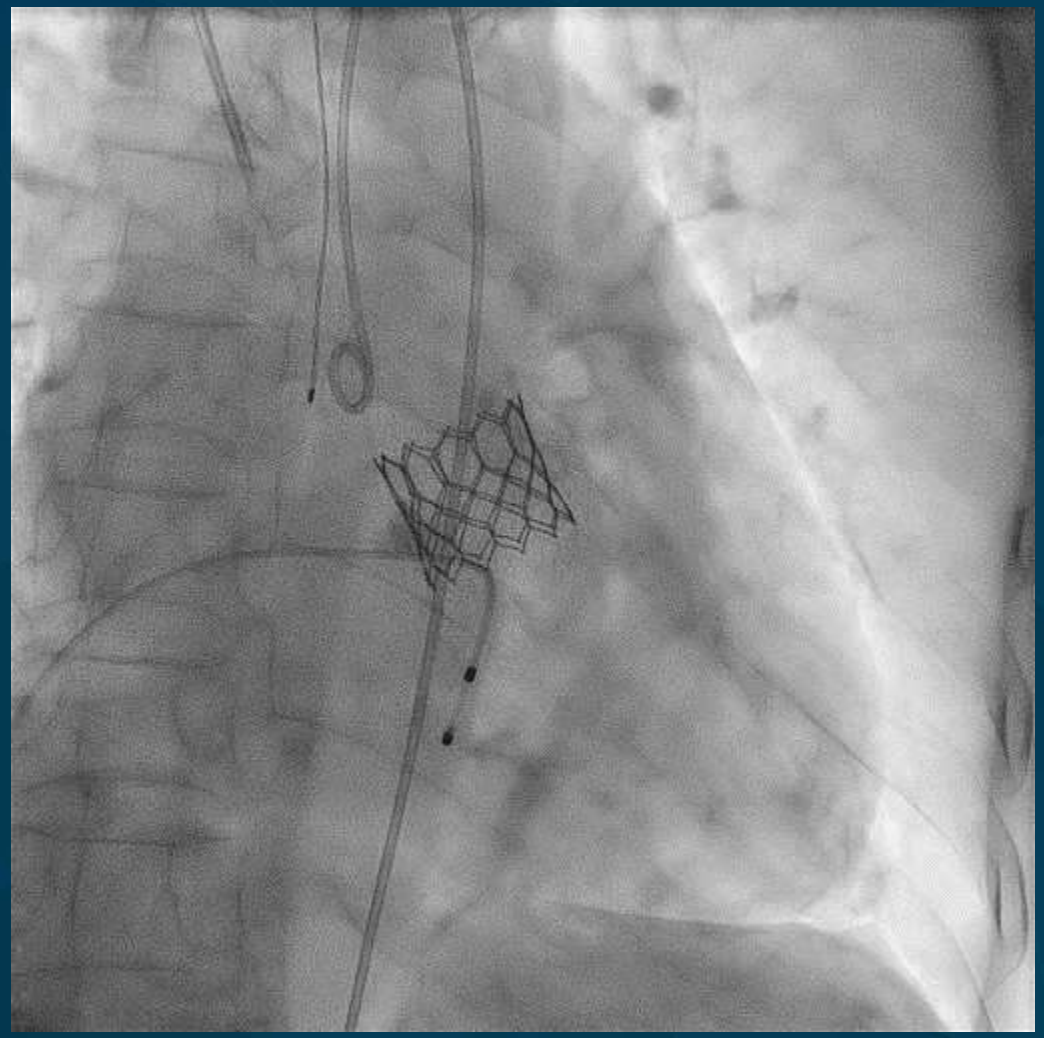
F/84

- CC
  - Dyspnea
- Comorbidities
  - Paroxysmal AF
  - RBBB
  - HTN
  - Dyslipidemia
- STS score : 4.21%

- Echo
  - EF : 62%, No RWMA
  - AV V_{max} 4.69m/s, MSPG 54.0mmHg
  - AVA 0.94cm^2
- CT
  - Annulus 433.3mm^2
    - Area driven diameter 23.5mm
  - SoV 29.5mm, STJ 25.2mm
  - Coronary Height : Lt 10.9mm, Rt 17.2mm

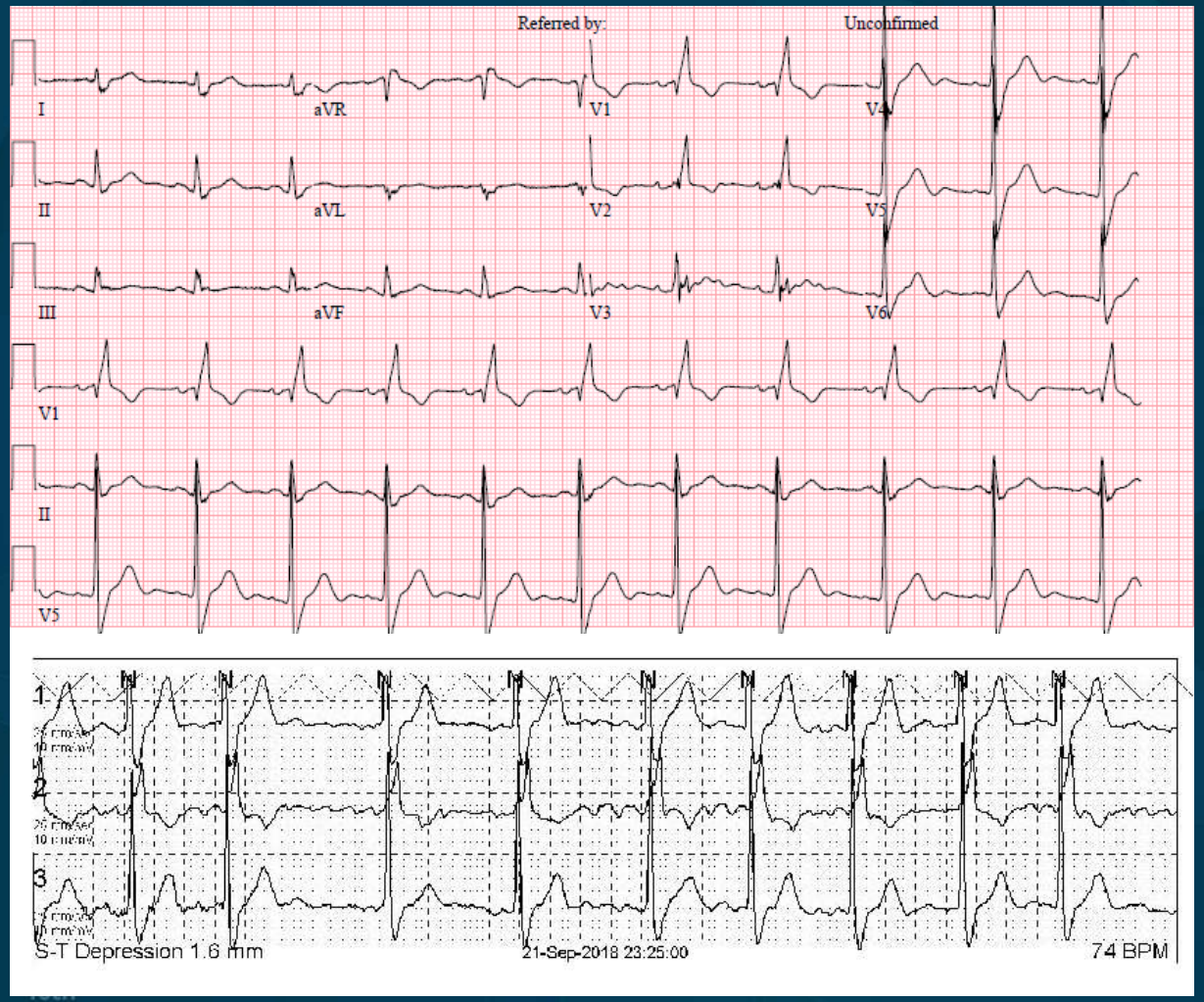
TAVI



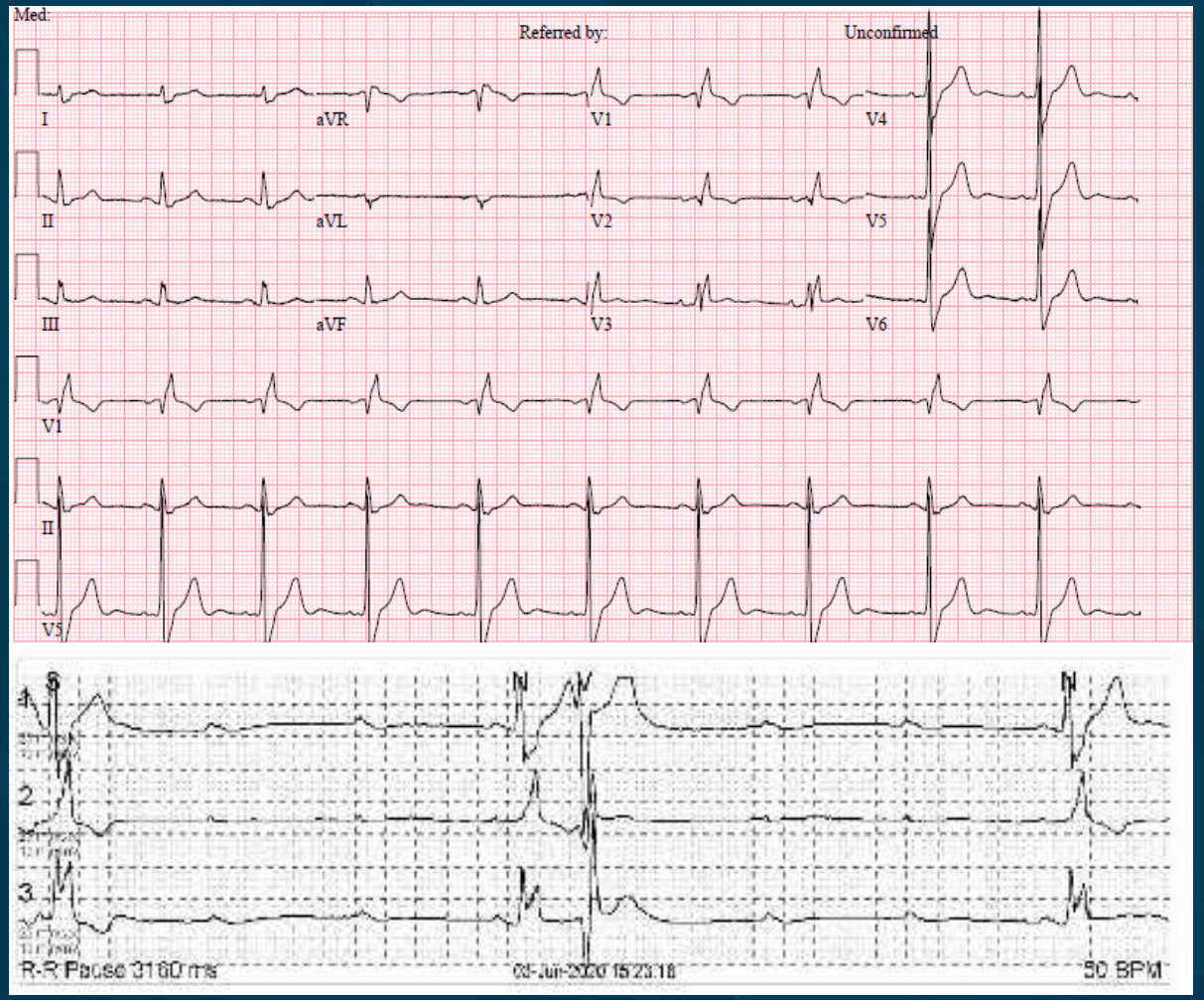


Pre-/Post-ECG & Holter

Pre- **RBBB, Paroxysmal AF**

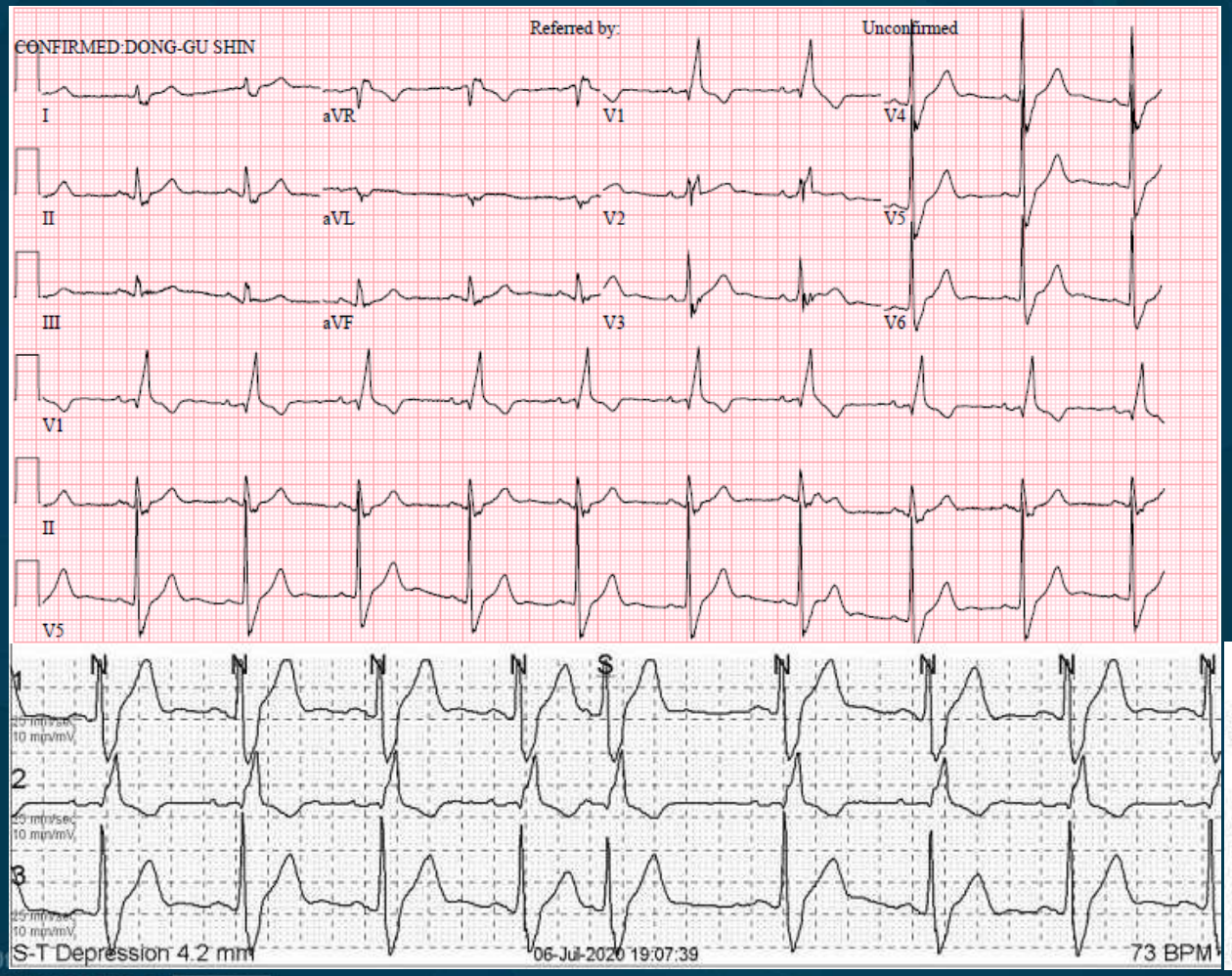


Immediate Post- **RBBB, High degree AV block**



Post-ECG & Holter

1 month after TAVI



RBBB, No evidence of AV block (ECG & holter)

Interpretation

Basal : Normal sinus rhythm
with Right bundle branch block
Isolated & couplet PAC was noted
Non-sustained atrial tachycardia was noted
No pause
Sx unrelated

Conclusion

- PARTNER 3 trial showed the safety and effectiveness of the **SAPIEN 3 TAVR** vs. **conventional surgery** in patients with severe AS at low-risk at 2 years.

- After PARTNER 3 trial, current guideline suggested age-based decision between TAVI vs. surgery for patients with severe AS

- Due to advances in SAPIEN valve system, more than moderate PVL has been dramatically reduced.

- The incidence of PPI, which was related with adverse clinical outcomes, was less frequently observed in SAPIEN compared to self-expandable valve.