The Anatomy And Clinical Trial Results Of Bicuspid Valve

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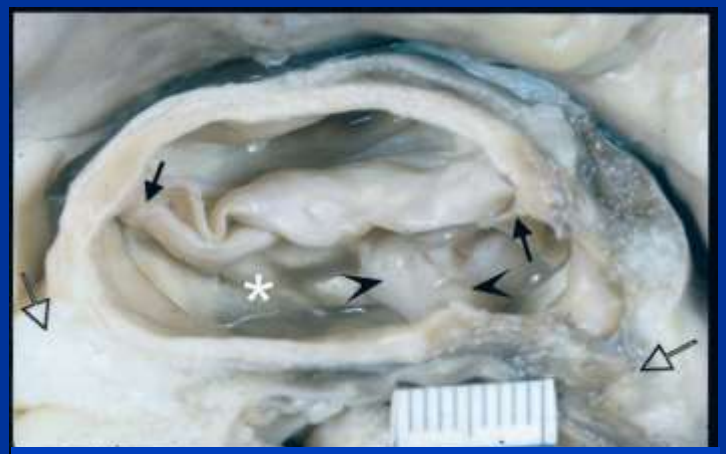
Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
Grant/ Research Support:	
Consulting Fees/Honoraria:	**Edwards Lifesciences** **Medtronic** **St Jude**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit:	

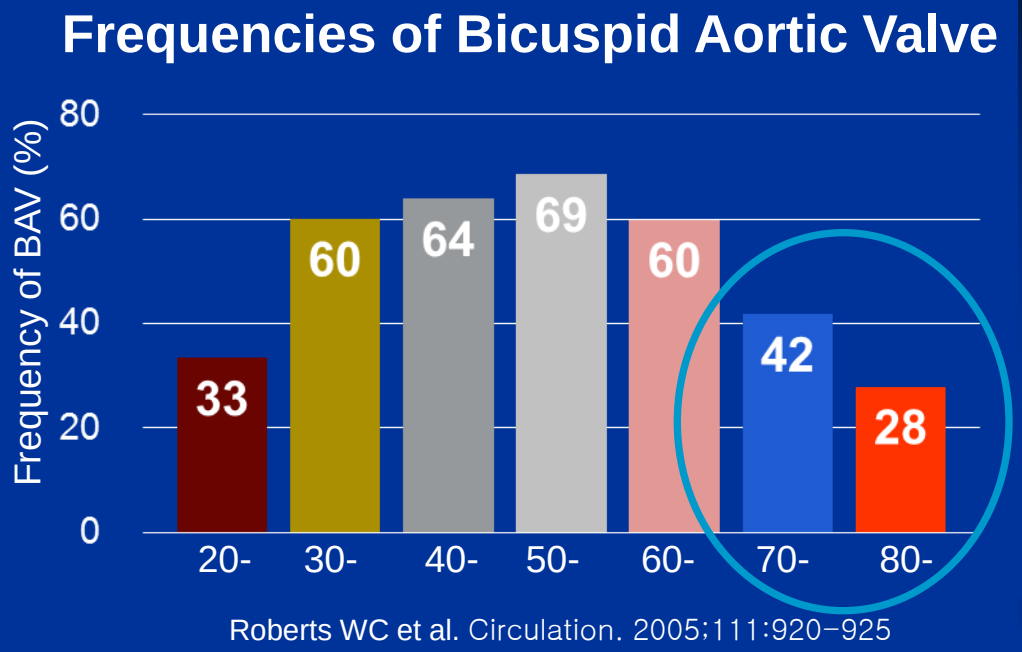
ANATOMY OF BICUSPID AORTIC VALVE

Bicuspid Valve - Anatomy



Bicuspid aortic valve

Fedak P W et al. Circulation. 2002;106:900-904



Roberts WC et al. Circulation. 2005;111:920–925

- The most common congenital cardiac malformation (1-2%)
- Serious complications occurred > 30%
  - **Aortic Stenosis** (the most common)
  - Aortic Regurgitation
  - Aortic dilation and dissection

Courtery – Dr Yoon

Siever's Classification

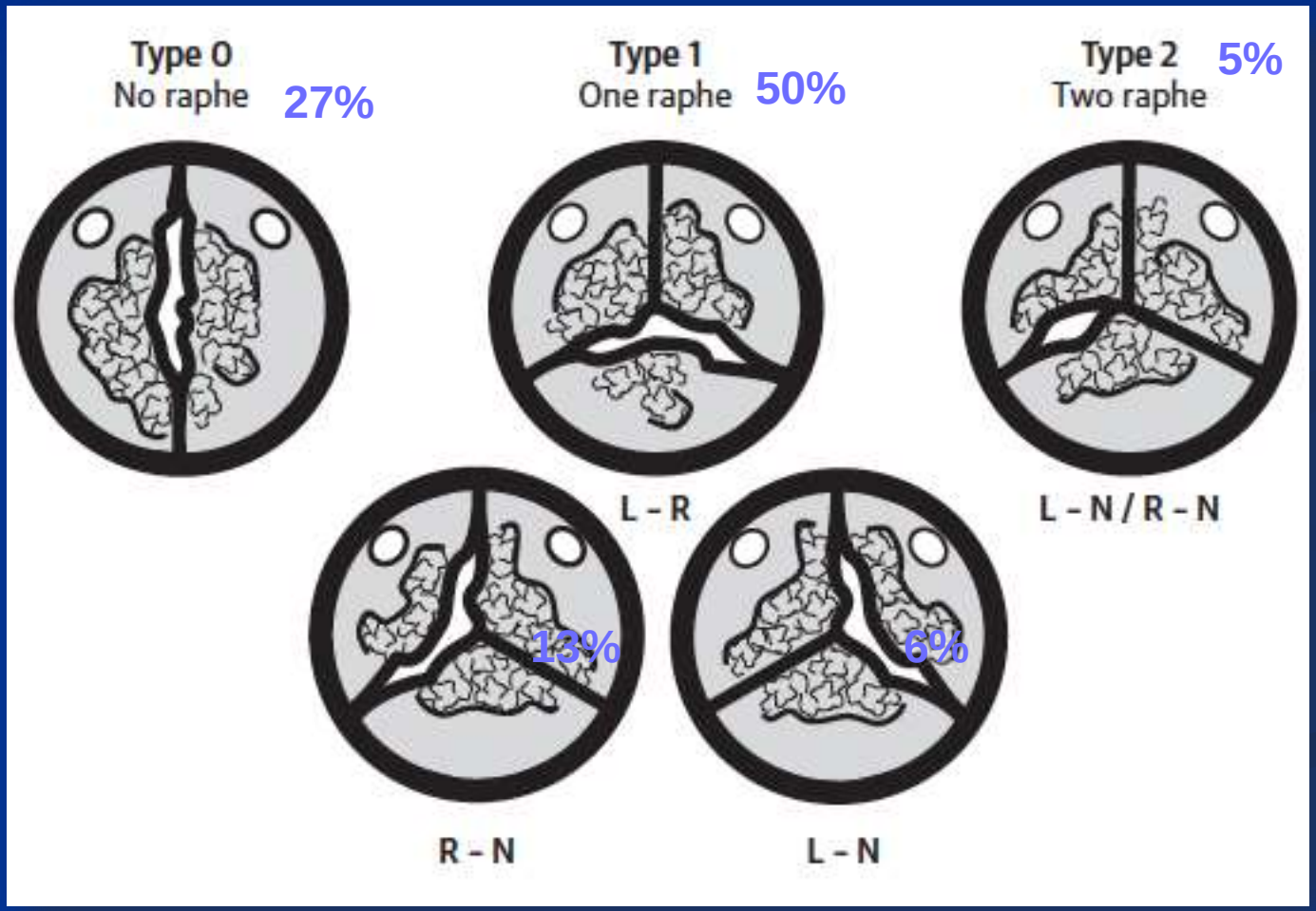


TABLE II. Anatomic Dimensions of the Aortic Root

Characteristics	Tricuspid aortic valve $N=200$	Bicuspid aortic valve $N=200$	P value
Annulus			
Area (mm^2)	463 (106)	521 (102)	<0.00 1
Diameter max	27 (3.4)	28.3 (3.6)	<0.001
Diameter min	21 (2.9)	23 (3.2)	<0.001
Δ Diameter	5.3 (2.8)	4.1 (5.4)	0.22
Ellipticity index	1.29 (0.1)	1.24 (0.1)	0.002
Circularity	21 (4)	78 (39)	<0.001
Eccentric calcification	64 (32)	136 (68)	<0.001
Sinus			
Perimeter	106 (15)	116(18)	<0.001
Diameter, left coronary cusp	30.8 (3.0)		
Diameter, right coronary cusp	28.6 (3.3)		
Diameter, non-coronary cusp	31.2 (3.3)		
Height, left coronary cusp	22 (3.6)	22 (5)	0.8
Height, right coronary cusp	23 (3.3)	22 (5)	0.8
Height, non-coronary cusp	21.3 (3.1)	24 (6)	<0.006
Sino-tubular Junction			
Perimeter	85.5 (12.3)	99.5 (20.3)	<0.001
Diameter	27.2 (3.9)	31.9(5.7)	<0.001
Coronary ostia			
Height, left coronary artery	14.1 ± 3.2	14.9 ± 5.7	0.14
Height, right coronary artery	16.4 ± 4.5	16.3 ± 5.3	0.14
Long axis diameter (mm)	26.9 ± 7	27.4 ± 5	0.76
Ascending aorta			
Area (mm^2)	688 (133)	740 (132)	<0.001
Diameter	29.8 (3.6)	36.9 (8)	<0.001

- CT imaging of 200 tricuspid and 200 bicuspid AS pre-AVR

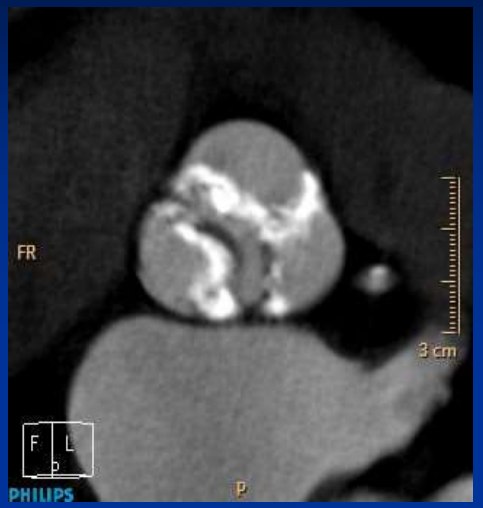
Bisucpid valve assoc with

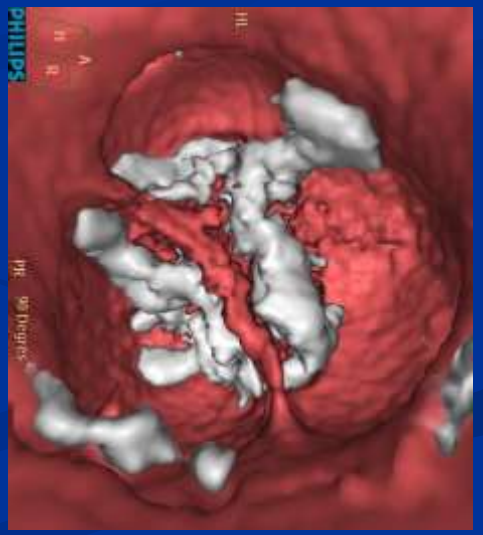
- Larger
  - Annulus
  - Sinus of valsalva
  - STJ
  - Ascending aorta
- More eccentric calcification

Philip - Catheter Cardiovasc Interv. 2015;86:E88-98

Bicuspid Aortic Valve disease and TAVR

- ✓ Bicuspidy is regarded as a relative CI to TAVR due to the risk of uneven expansion of the bioprosthesis.
- ✓ Not indicated in the IFU of approved devices
- ✓ Exclusion criteria in clinical trials
- ✓ Thus, the safety and efficacy of TAVI for this anatomic variation still remains unclear.





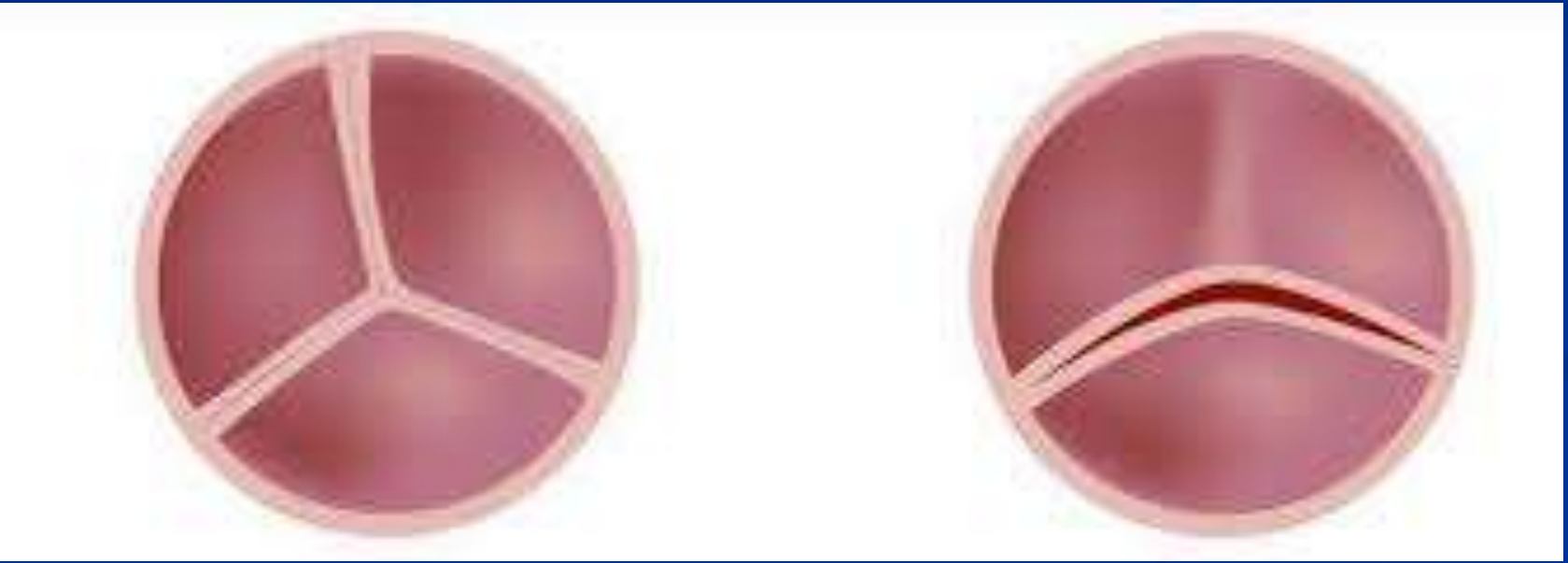
OUTCOMES OF TAVR IN BICUSPID AORTIC STENOSIS

Baseline Characteristics

	Hayashida (N = 21)	Bauer (N=38)	Kochman (N=28)	Costopouls (N=21)	Mylotte (N=143)	Yoon (N=199)
Age	82	81	78	77	78	77
Male	57%	42%	46%	57%	56%	65%
L. EuroSCORE	19.9	18	19	24	14.8	15.0%
Type of device						
CoreValve	48%	68%	82%	62%	65%	56%
SAPIEN	52%	32%	18%	38%	35%	44%
Device success	100%	100%	93%	86%	90%	73%
AR ≥ Grade 2	19%	-	32%	24%	28%	17.6%
Stroke	0	0	0	0	2.1%	2.5%
30-day mortality	4.8%	11%	4%	14%	5.0%	4.5%
1-year mortality	-	13%	18%	32%	18%	

Hayashida. Circulation CI. 2013; 6:284-291
Bauer. Am J Cardiol. 2014; 113:518-21
Costopoulos. Am J Cardiol. 2014 ;113:1390-1393
Kochman. Am J Cardiol. 2014;114:757-62
Mylotte. J Am Coll Cardiol. 2014; 64: 2330-39
Yoon. – J Am Coll Cardiol (in-press)

How does the outcome compare between bicuspid and tricuspid aortic valve?



Bicuspid TAVR Registry

NCT 02394184

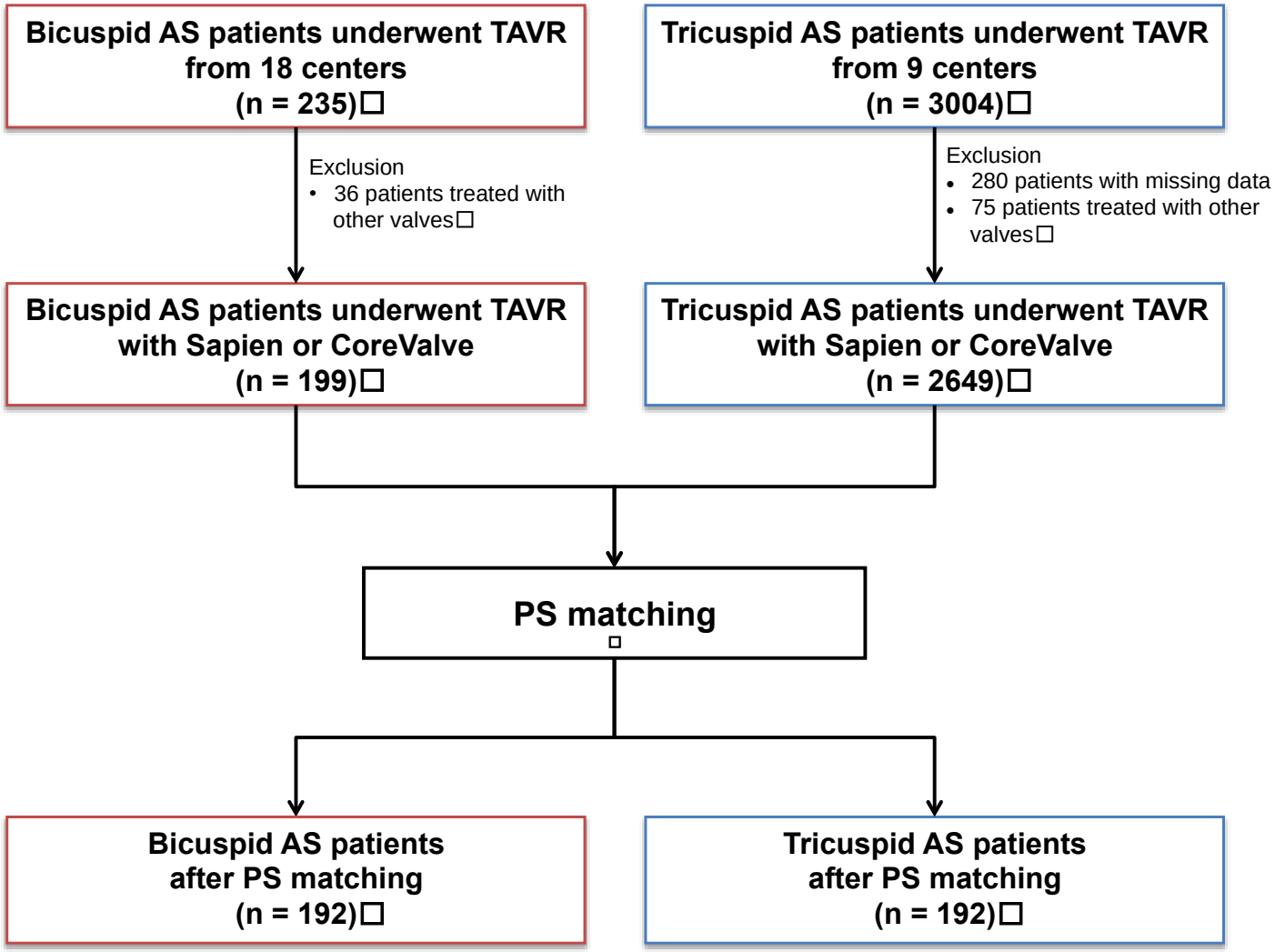
Total (n=301)	Early-generation devices (n=199)		New-generation devices (n=102)	
	SAPIEN XT (n=87)	CoreValve (n=112)	SAPIEN 3 (n=91)	Lotus (n=11)

20 centers from 14 countries
in Europe, North America and Asia-Pacific

Yoon. – J Am Coll Cardiol (in-press)

BICUSPID TAVR REGISTRY

Comparison of Outcomes with Tricuspid AS Early Generation Devices



Baseline Characteristics

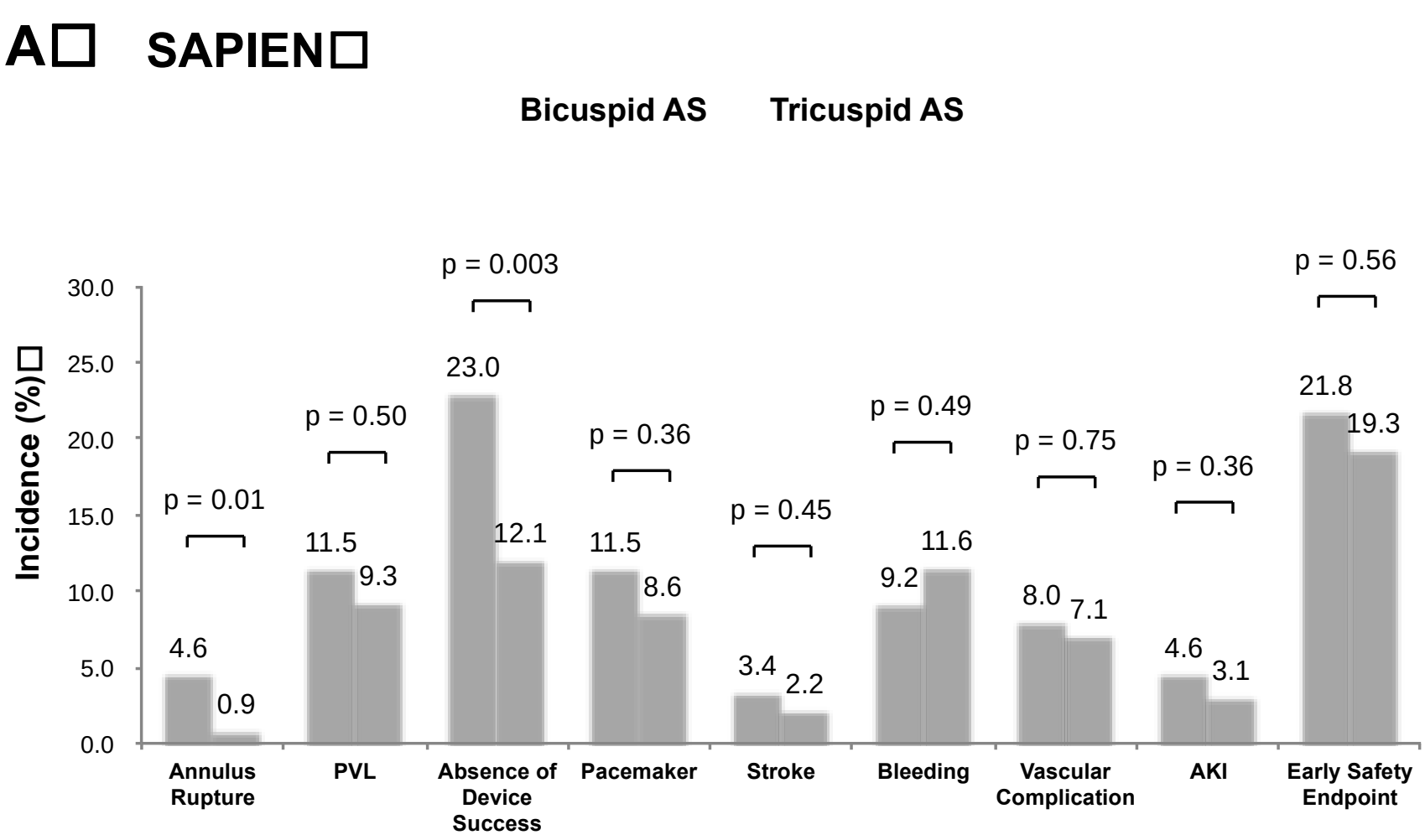
	Bisucpid Aortic Stenosis (n=192)	Trisucpid Aortic Stenosis (n=192)
Age	77.7	78.4
	36%	42%
Logistic EuroSCORE	15.3	15.6
	4.7	4.4
Previous stroke	14.1%	18.1%
	11.5%	7.8%
LVEF, %	53.4%	51.6%

Procedural Data

	Bisucpid Aortic Stenosis (n=192)	Trisucpid Aortic Stenosis (n=192)
Transfemoral access	78.6%	76.6%
Device type		
Sapien XT	43.8%	42.8%
CoreValve	56.3%	56.8%
Type of bicuspid		
Type 0	13.4%	
Type 1	84.1%	
Type 2	2.5%	

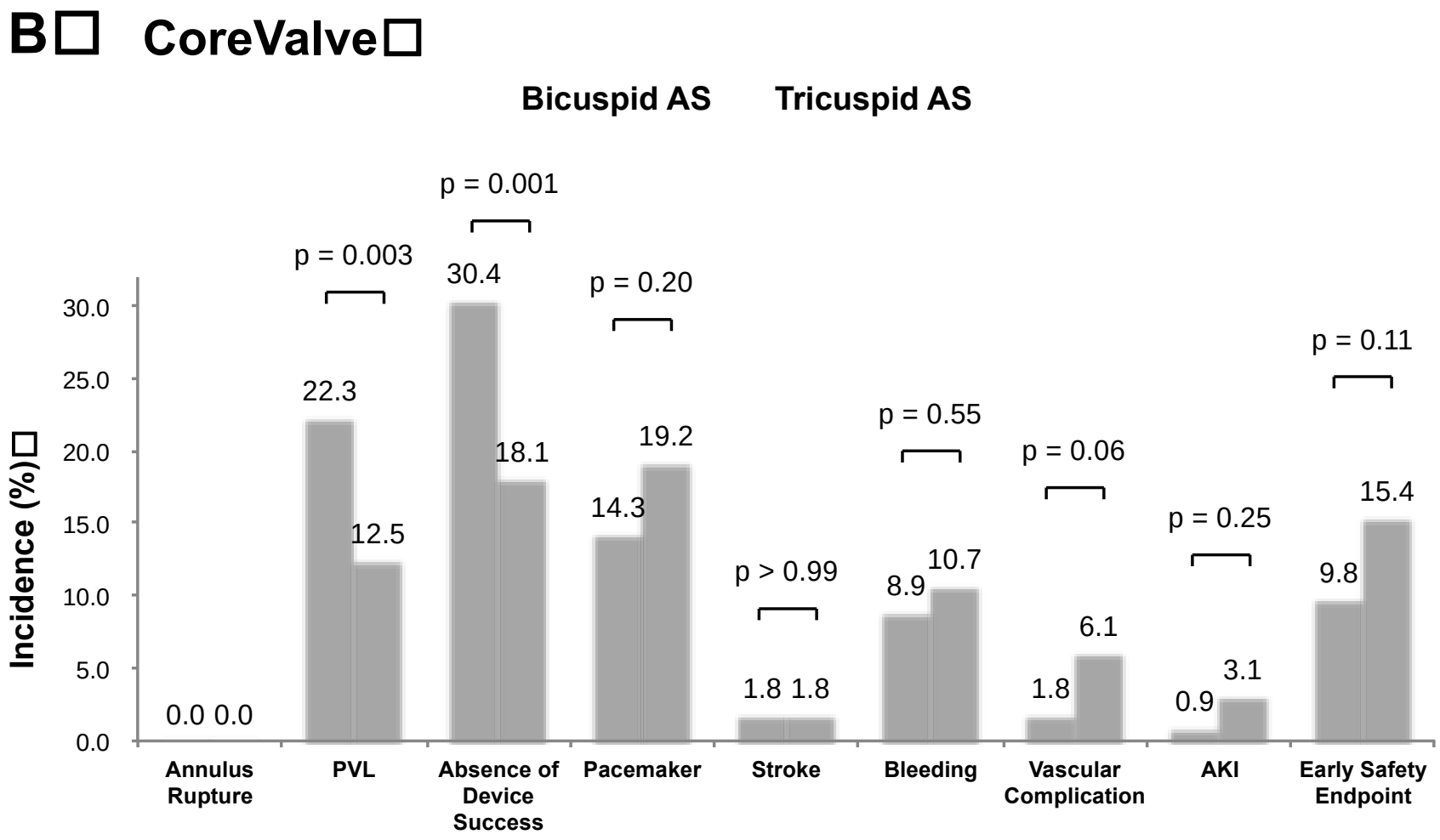
Outcomes – SAPIEN / XT valve

Higher risk of annular rupture

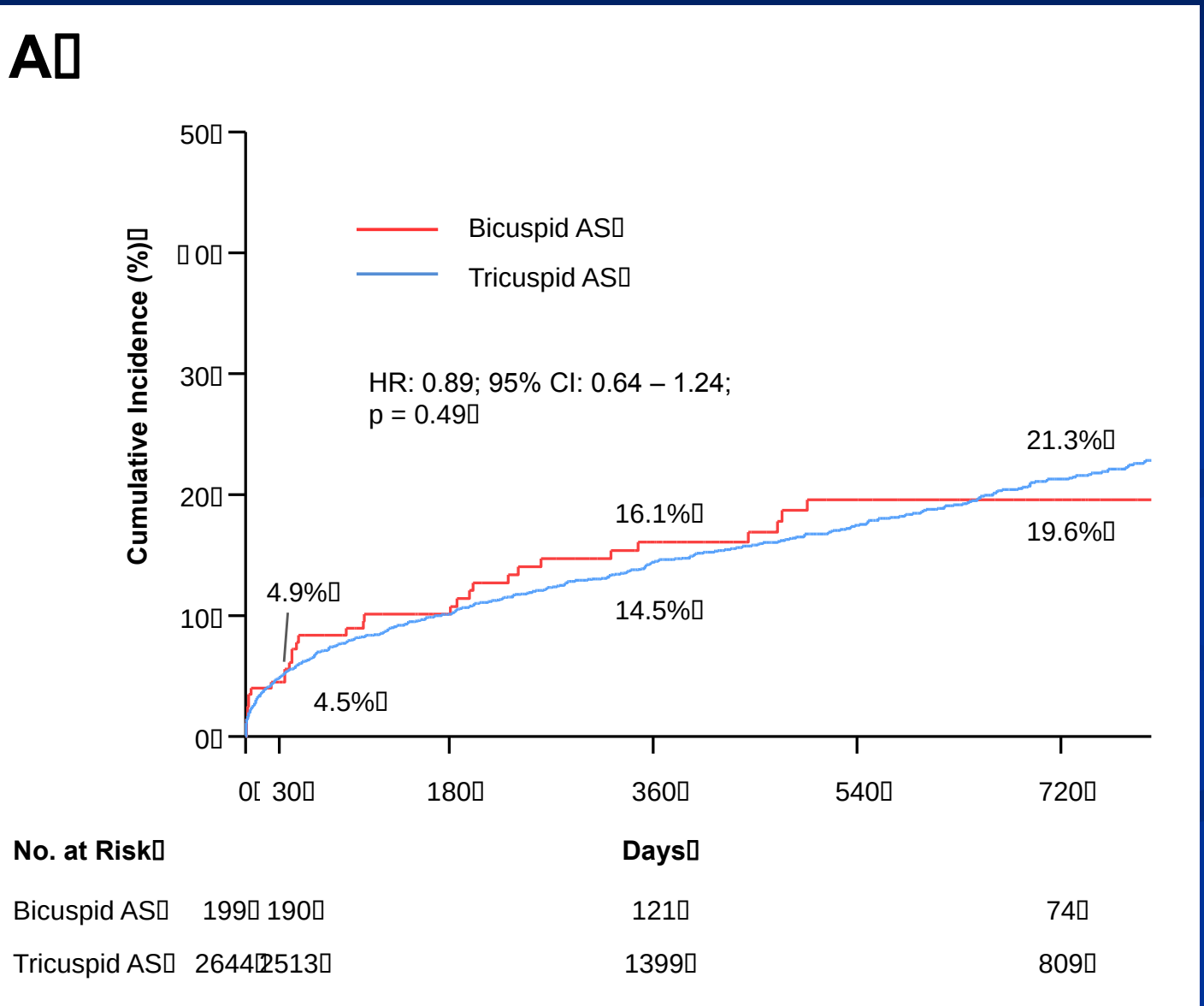


Outcomes – CoreValve

Higher Risk of significant PVL



Similar short and medium term survival



How does the newer transcatheter valve perform?

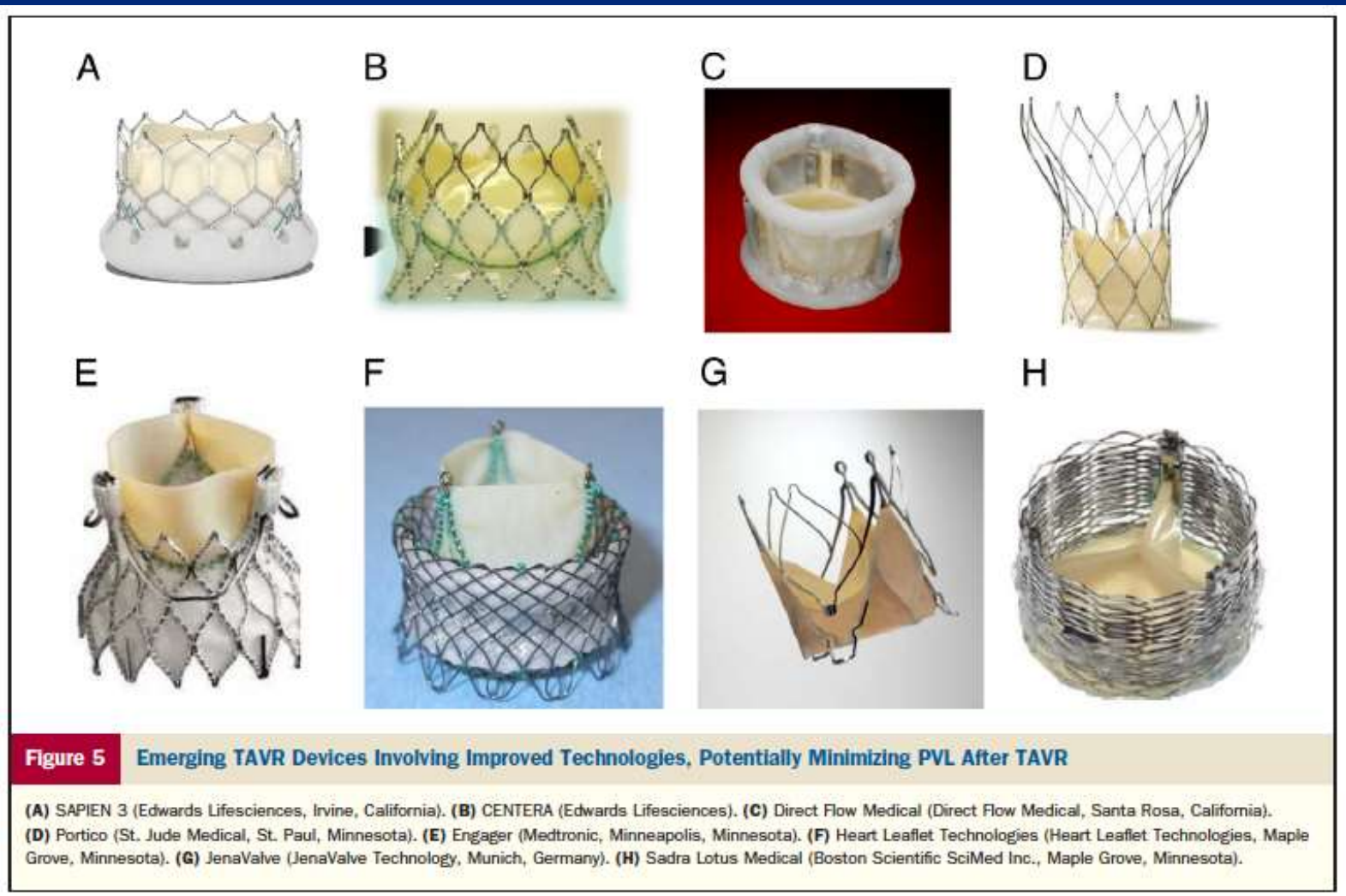


Figure 5 Emerging TAVR Devices Involving Improved Technologies, Potentially Minimizing PVL After TAVR

(A) SAPIEN 3 (Edwards Lifesciences, Irvine, California). **(B)** CENTERA (Edwards Lifesciences). **(C)** Direct Flow Medical (Direct Flow Medical, Santa Rosa, California). **(D)** Portico (St. Jude Medical, St. Paul, Minnesota). **(E)** Engager (Medtronic, Minneapolis, Minnesota). **(F)** Heart Leaflet Technologies (Heart Leaflet Technologies, Maple Grove, Minnesota). **(G)** JenaValve (JenaValve Technology, Munich, Germany). **(H)** Sadra Lotus Medical (Boston Scientific SciMed Inc., Maple Grove, Minnesota).

Bicuspid TAVR Registry

Early-generation devices (n=199)		New-generation devices (n=102)	
SAPIEN XT (n=87)	CoreValve (n=112)	SAPIEN 3 (n=91)	Lotus (n=11)

Baseline Characteristics

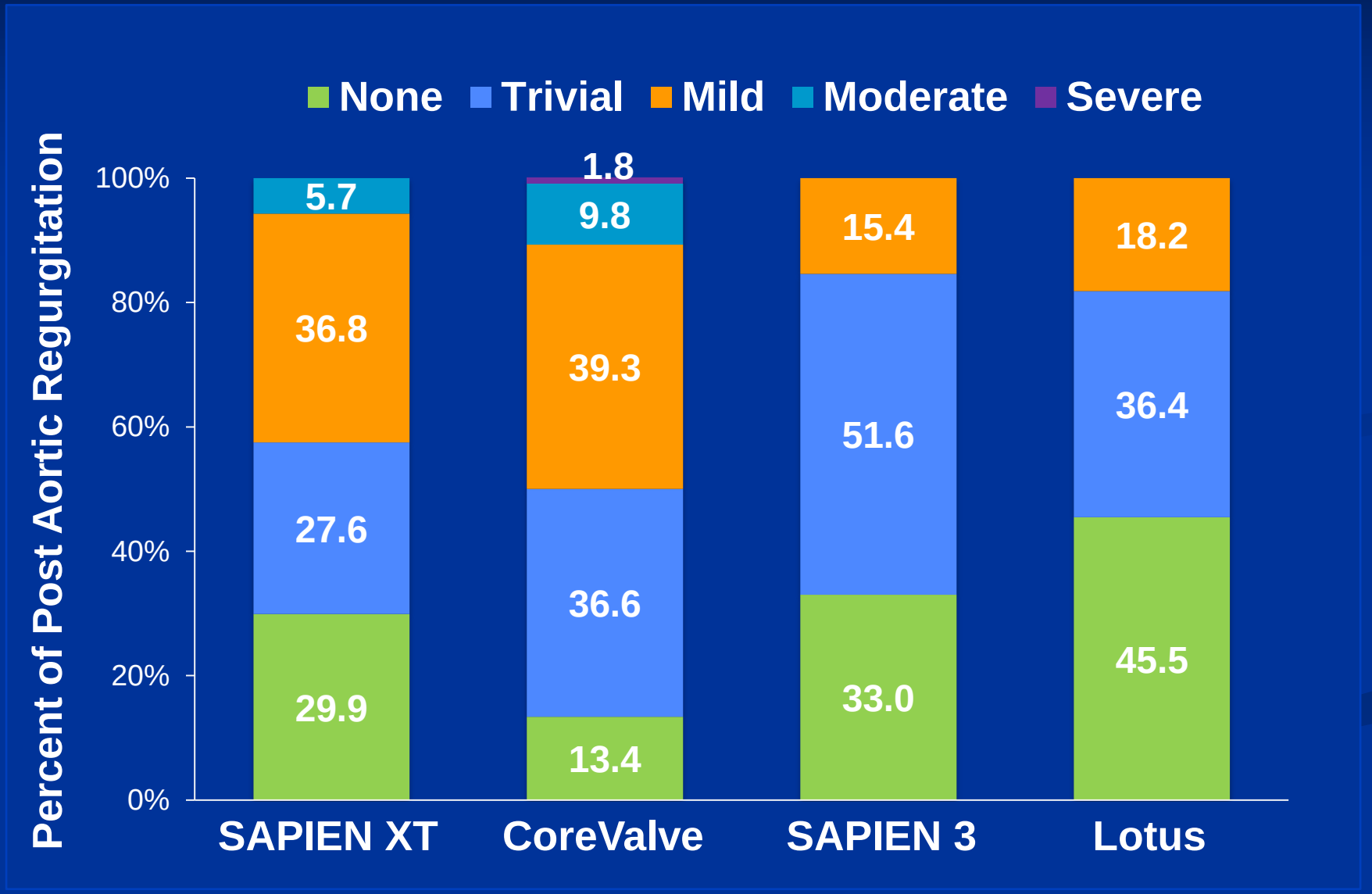
	Overall (N = 301)	Old devices (N = 199)	New devices (N = 102)	p value
	57.5%	64.8%	43.1%	
	74.1%	74.4%	73.5%	
	16.3%	15.7%	18.6%	
	12.6%	11.1%	15.7%	
	17.3%	18.1%	15.7%	
LVEF, %	51±15	53±15	48±16	0.004

Procedural Data

	Overall (N = 301)	Old devices (N = 199)	New devices (N = 102)	p value
Transfemoral access	84.1%	78.4%	95.1%	< 0.001
Device type				
Sapien XT	–	87 (43.7%)	–	< 0.001
CoreValve	–	112 (56.3%)	–	
Sapien 3	–	–	91 (89.2%)	
Lotus	–	–	11 (10.8)	
Type of bicuspid				
Type 0	11.9%	13.0%	10.1%	
Type 1	86.2%	84.5%	88.9%	
Type 2	1.9%	2.5%	1.0%	

Paravauvular Regurgitation

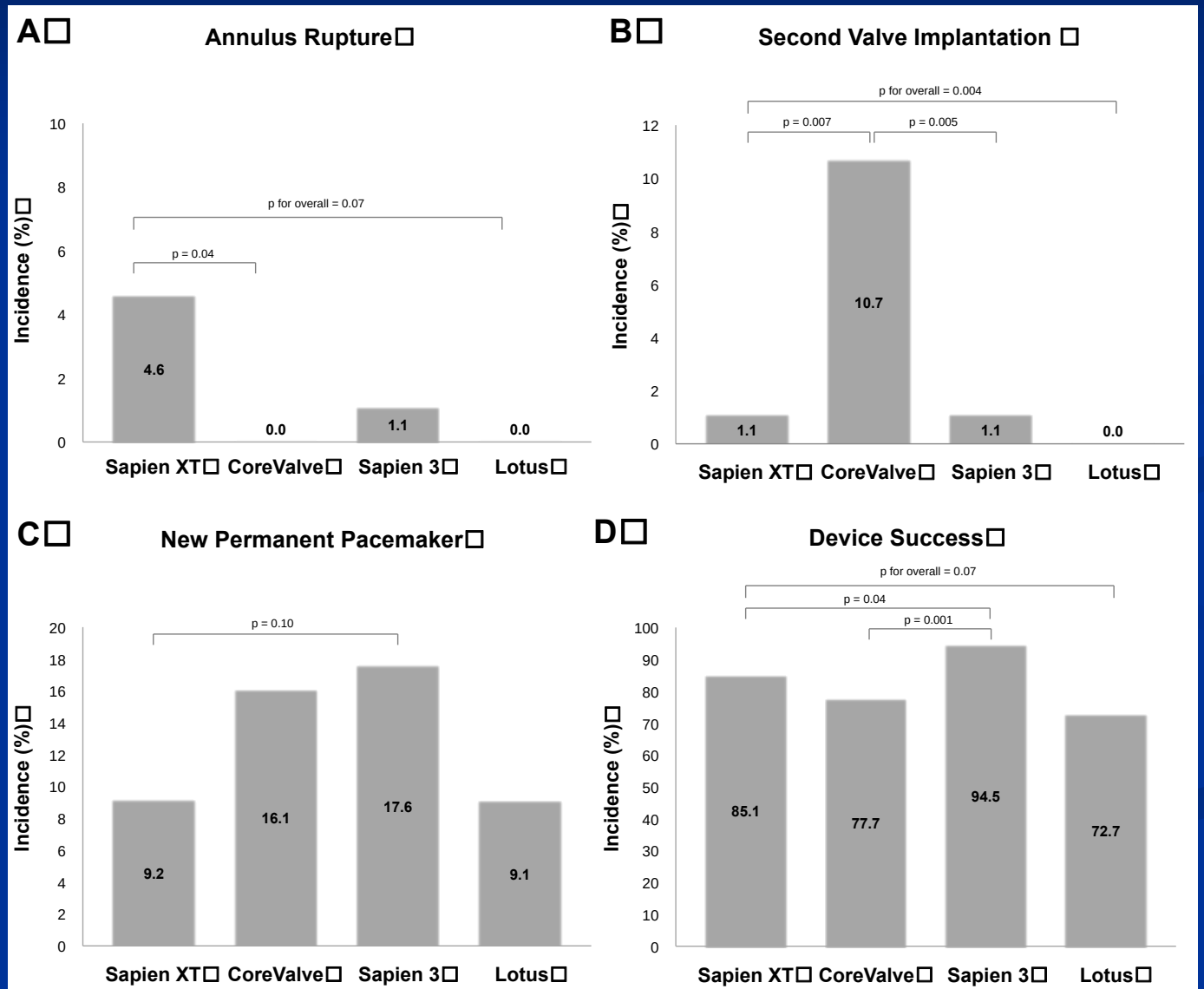
Lower ≥moderate PVL with newer devices



J Am Coll Cardiol. 2016. In Press

Safety Outcomes

Lower annulus rupture with newer generation devices



Bicuspid Aortic Valve Stenosis

Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study

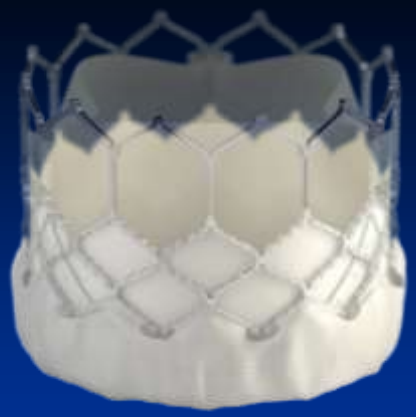


TABLE 4 30-Day Clinical Events (N = 51)*	
Mortality	2 (3.9)
Myocardial infarction	0 (0)
Stroke, total events	1 (1.9)
Disabling stroke	0 (0)
Nondisabling stroke	1 (1.9)
Bleeding, total events	14 (27.5)
Life-threatening	2 (3.9)
Major	3 (5.9)
Minor	9 (17.6)
Vascular complications, total events	7 (13.7)
Major	2 (3.9)
Minor	5 (9.8)
Acute kidney injury ≥2	1 (1.9)
New permanent pacemaker†	12 (23.5)
Device 30-day safety endpoint	6 (11.7)

Values are n (%). *All clinical events were defined according to VARC-2 criteria. †The rate of patients requiring a new pacemaker, excluding 4 patients who had a pacemaker before transcatheter aortic valve replacement, was 25.5%.

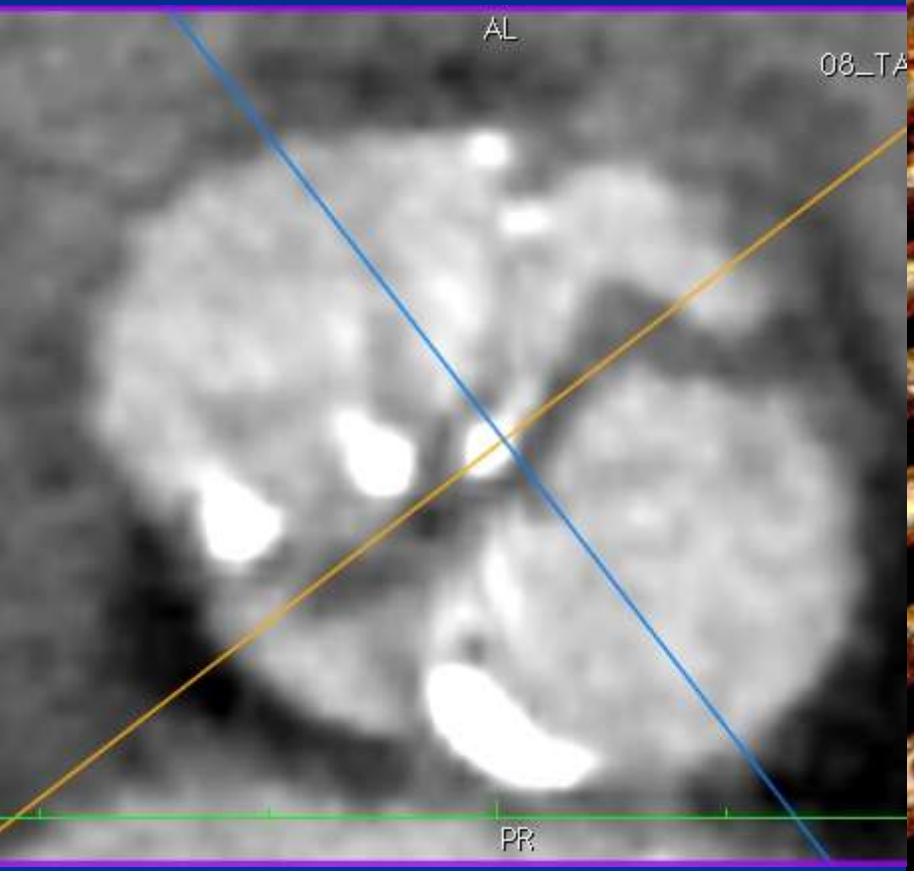
Multicenter registry of SAPIEN 3 Valve in 51 patients with bicuspid aortic stenosis

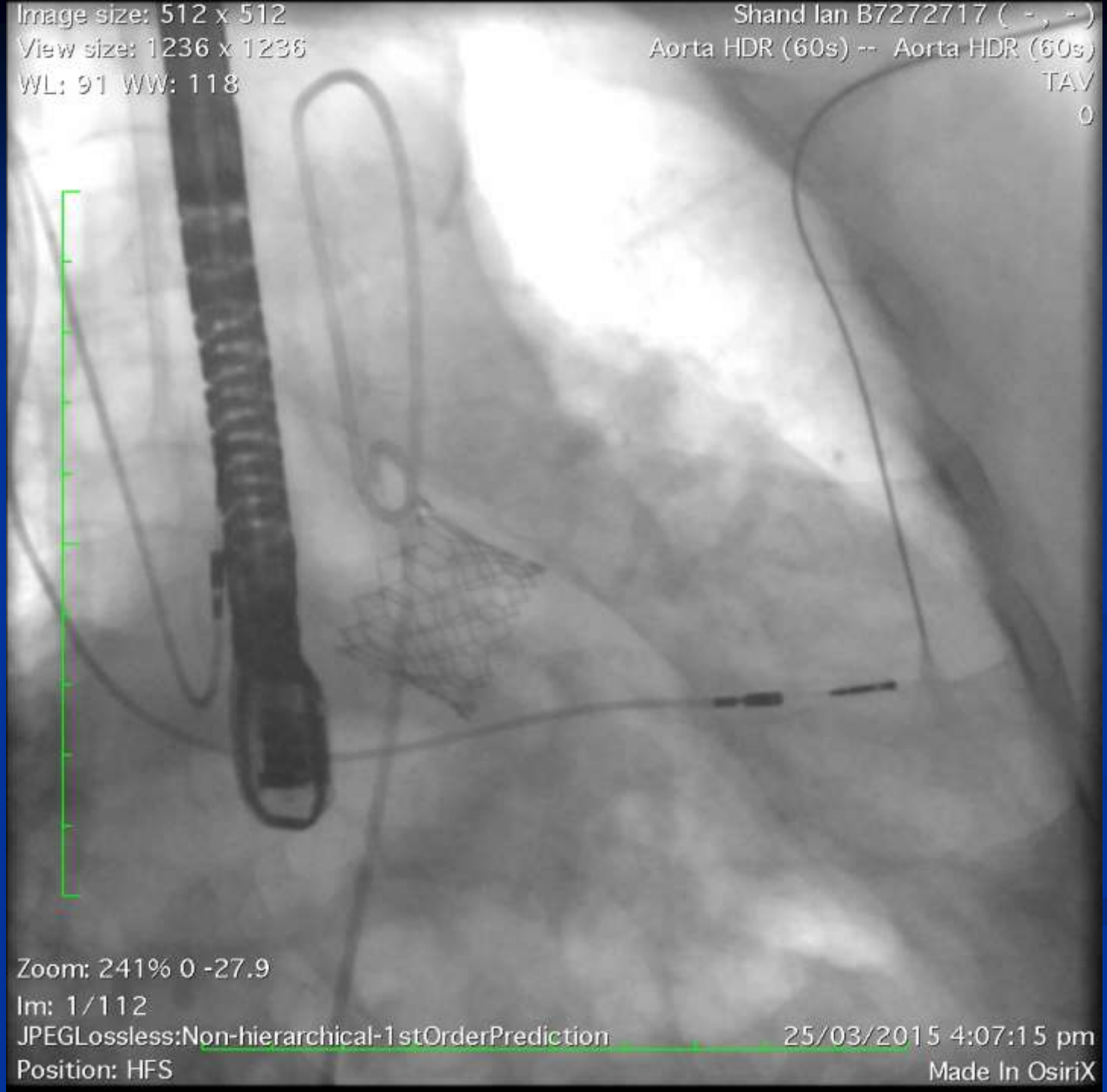
30-day mortality – 3.9%
30-day stroke – 1.9%
Pacemaker – 23.5%

Annulus Rupture – 0
≥ Moderate AR - 0

Perlman, G. Y.,JACC Cardiovasc Interv. 2016;9:817-24

Case 1 – Bicuspid valve; Horizontal Aorta

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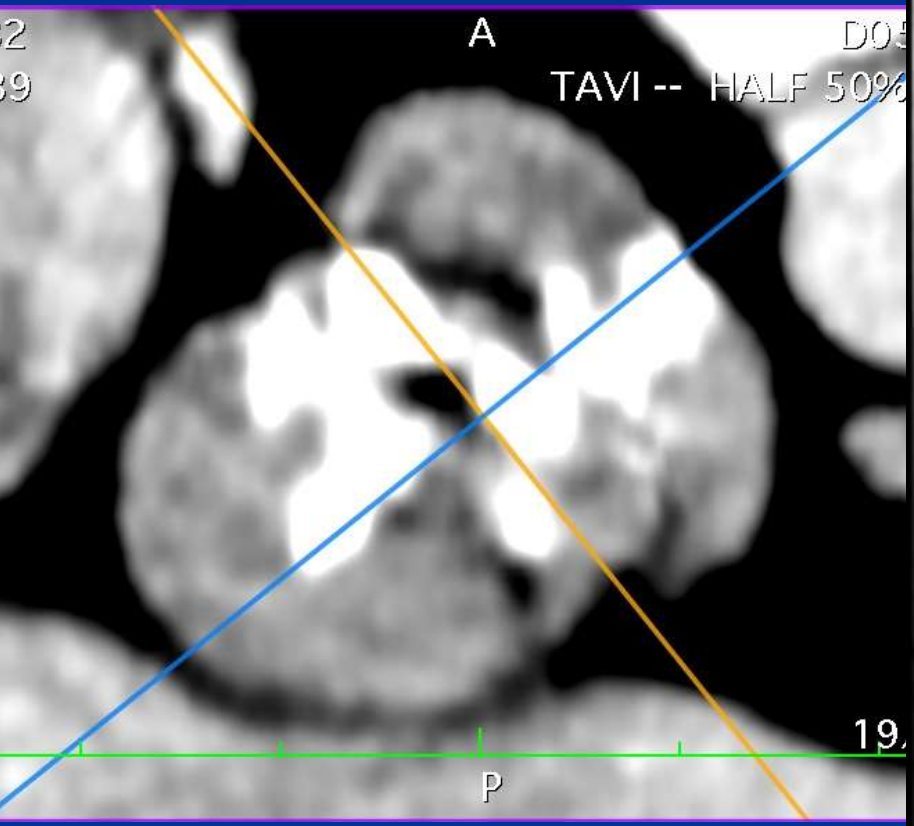
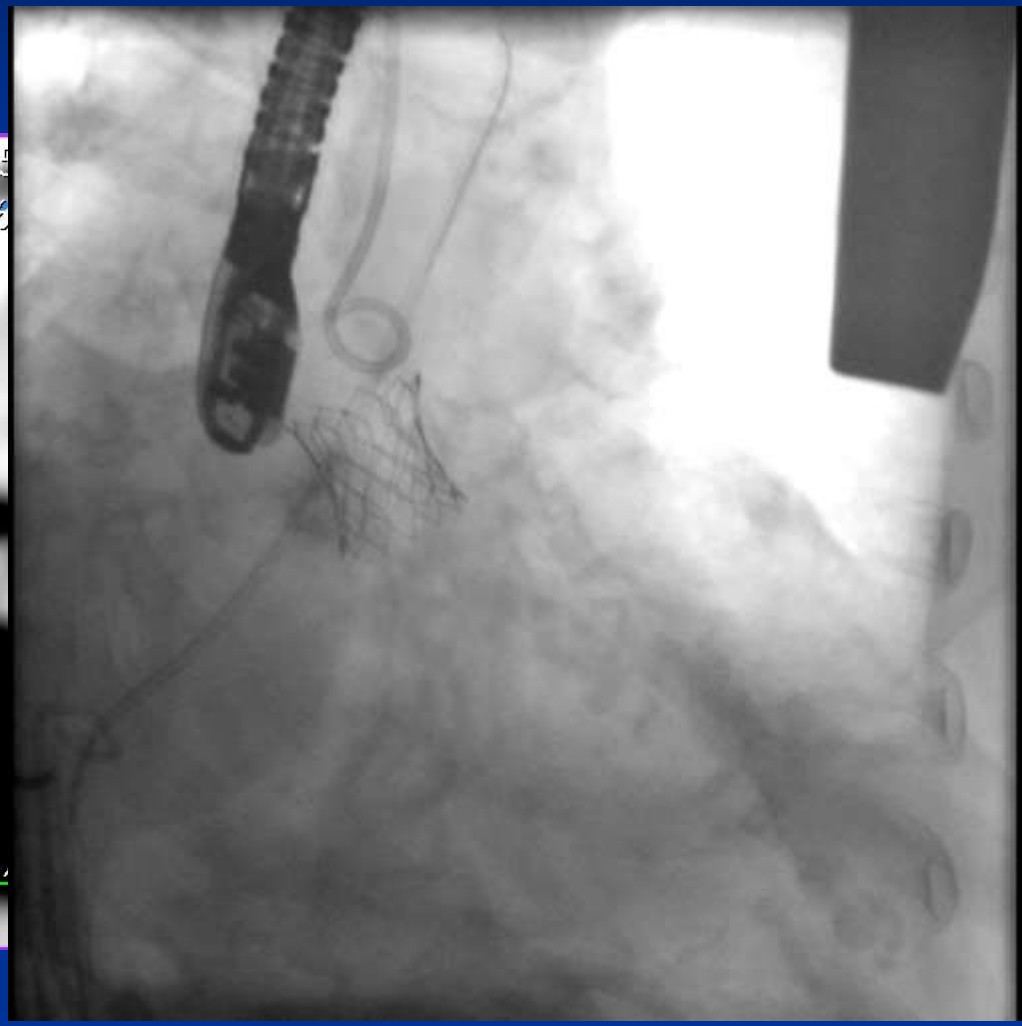
Case 2 – Severe calcified bicuspid aortic stenosis; Small annulus





Conclusion

- Bicuspid aortic valve poses challenges to TAVR
  - Sizing, positioning, calcification
- Clinical outcomes challenging compared to tricuspid aortic valve
  - Annulus rupture risk with balloon expandable valve
  - Paravalvular regurigtation with self-expanding valve
- Newer generation TAVR valves offer significant improvement and trend to abolishment of risks