

Outcomes After TAVR in Bicuspid Aortic Stenosis: US/EU data

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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

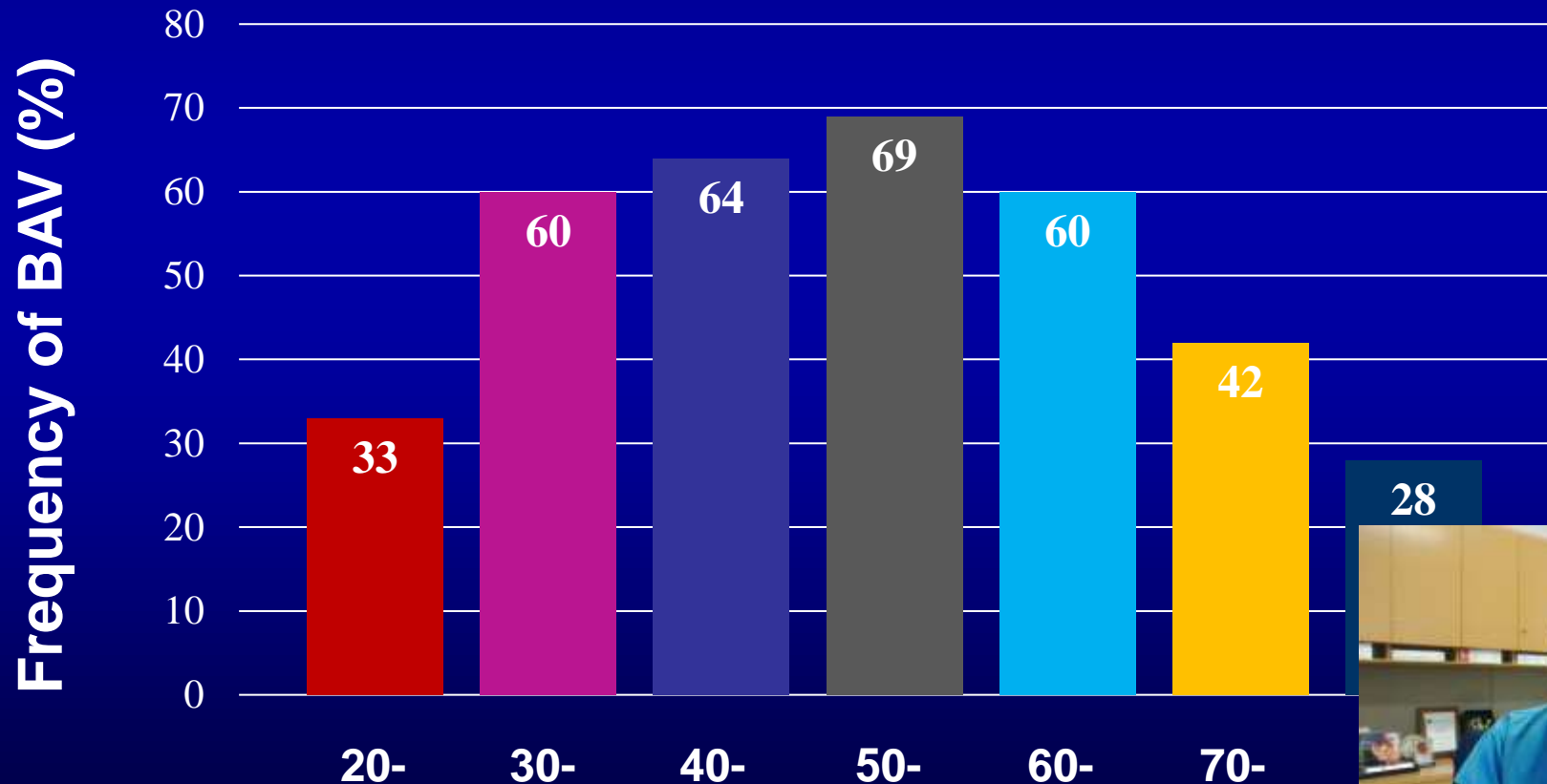
Grant/Research Support

Company

Edwards, Medtronic, Abbott, Boston Scientific



Prevalence of bicuspid valve in patients undergoing isolated AVR-almost 50%!



Roberts WC



In the US TVT registry 3-7% of TAVRs are for Bicuspid AS

TAVR is therefore being used selectively in bicuspid AS and data should be interpreted accordingly...



Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke

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Study population

2726 Bicuspid AS TAVRs, Average age 74, STS 4.9

92236 SAPIEN 3 Cases in TVT Registry

(June 2015 – Nov 2018)

552 Sites

3196 Valve-in-Valve
136 Prior TAVR

7082 N/A, Uncertain,
Unicuspid, Quadricuspid

2726 Bicuspid AS
SAPIEN 3 Patients

79096 Tricuspid AS
SAPIEN 3 Patients

1:1 Propensity Matching

2691 Bicuspid AS
SAPIEN 3 Patients

2691 Tricuspid AS
SAPIEN 3 Patients

25 Covariates used for propensity matching

Age	Chronic Lung Disease
Gender (male)	Prior PCI
NYHA III/IV	Prior CABG
BMI	Porcelain Aorta
Hypertension	Mean Gradient
Diabetes	LVEF
Creatinine ≥ 2	Mitral Regurgitation
Peripheral Arterial Disease	Tricuspid Regurgitation
Carotid Stenosis	
Atrial Fibrillation	
Prior Stroke	
Immunocompromised	
GFR	



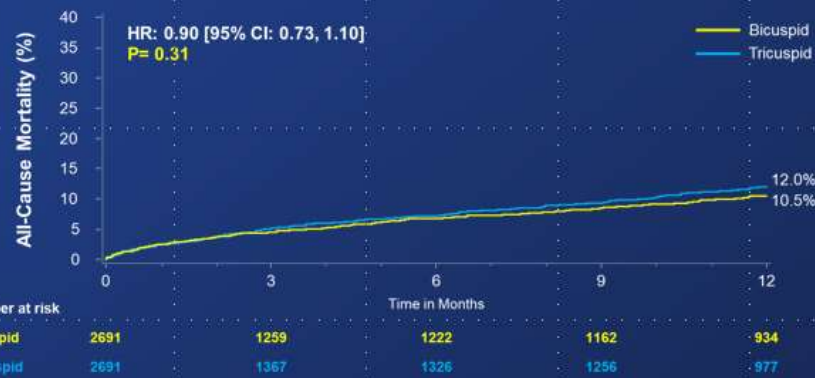
Procedural Outcomes

Characteristic % or mean \pm SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Device success	96.5	96.6	0.87
Procedure Time, min	100.7 \pm 51.80	98.2 \pm 52.09	0.08
Fluoroscopy Time, min	18.5 \pm 10.96	17.1 \pm 10.17	<0.0001
Conversion to open surgery	0.9	0.4	0.03
Annulus Rupture	0.3	0.0	0.02
Cardiopulmonary bypass	1.4	1.0	0.13
Aortic dissection	0.3	0.1	0.34
Coronary Obstruction	0.4	0.3	0.34
Need for a second valve	0.4	0.2	



1 year Mortality and Stroke-Bicuspid vs Tricuspid AS

1-Year Mortality – Matched



1-Year Stroke – Matched

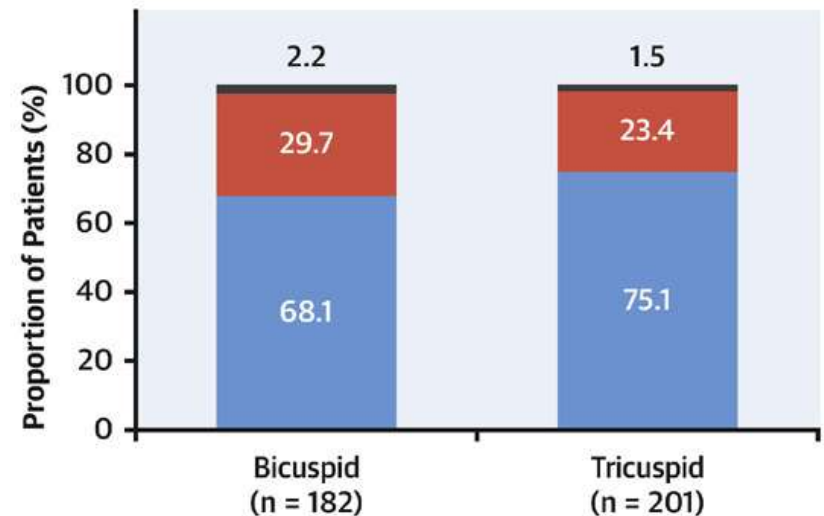
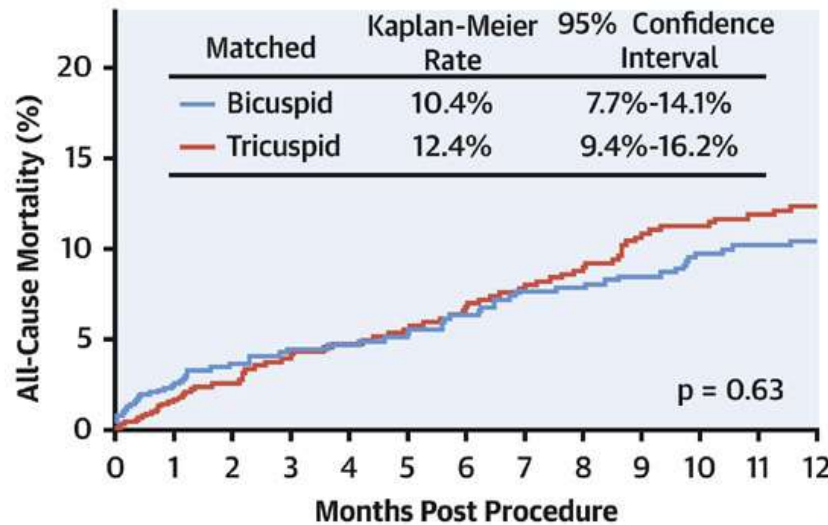


Bicuspid AS treated with Evolut R/Pro in US TVT Registry

Average age 73 y, STS 5.3, 929 pairs of Bicuspid vs Tricuspid AS patients

30 day Death 2.6% vs 1.7% 30 day Stroke 3.4 vs 2.7%, p=ns

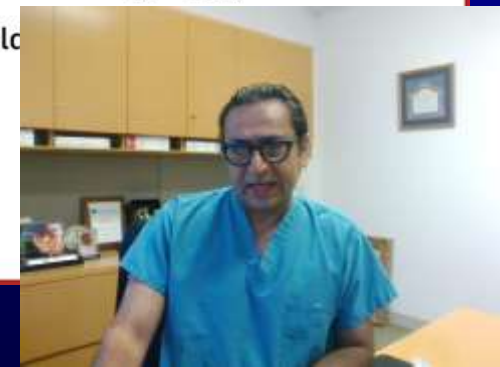
CENTRAL ILLUSTRATION: Key Outcomes



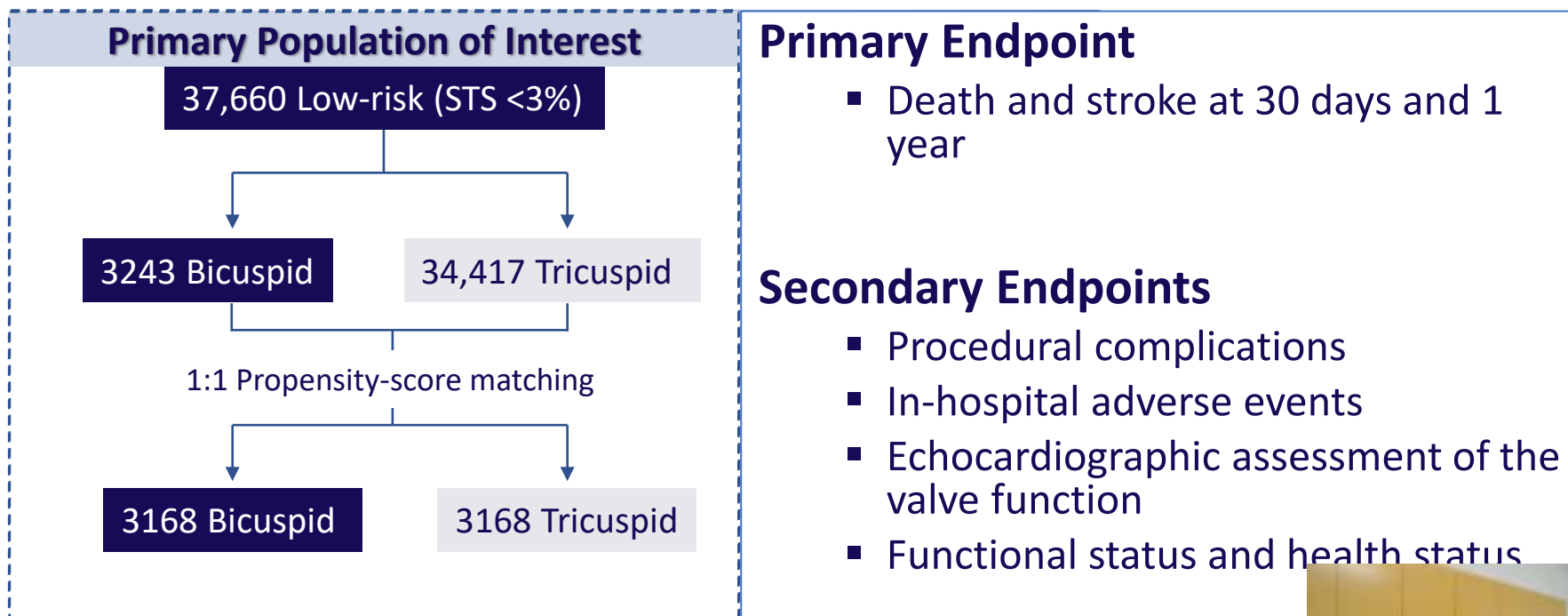
No. at Risk:

	0	1	2	3	4	5	6	7	8	9	10	11	12
Bicuspid	929	791	496	456	445	437	425	425	321				
Tricuspid	929	796	508	474	463	449	432	314					

Forrest, J.K. et al. J Am Coll Cardiol Interv. 2020;13(15):1749-59.



159,661 SAPIEN 3/SAPIEN 3 Ultra TAVRs for Bicuspid or Tricuspid Aortic Stenosis STS/ACC TVT Registry June 2015 – October 2020



Primary Endpoint

- Death and stroke at 30 days and 1 year

Secondary Endpoints

- Procedural complications
- In-hospital adverse events
- Echocardiographic assessment of the valve function
- Functional status and health status

29 Covariates used for Propensity Matching

Age	Prior stroke	Immunocompromise	Aortic mean valve gradient	STS risk score
Sex (male)	Carotid stenosis	Porcelain aorta	Left ventricular ejection fraction	Shock w/in 24
Body mass index	PAD	Atrial fibrillation/flutter	Mitral regurgitation	Hemodialysis
Access site	Hypertension	Creatinine	Tricuspid regurgitation	Hostile chest
Prior PCI	Diabetes	Hemoglobin	NYHA functional class	KCCQ-OS score
Prior CABG	Chronic lung disease	Estimated GFR	5-m walk test	



Baseline Characteristics - Adjusted Cohort Low Surgical-Risk (STS<3%)

<i>Characteristics % or mean ± SD</i>	BICUSPID n = 3168	TRICUSPID n = 3168	p value
Age (years)	68.8 ± 8.7	68.7 ± 9.0	0.59
Male	69.2	70.4	0.28
BMI (kg/m ²)	30.1 ± 7.3	30.1 ± 6.5	0.99
STS Risk Score (%)	1.7 ± 0.6	1.7 ± 0.7	0.55
NYHA III/IV	55.1	55.5	0.71
Prior coronary stenting	19.2	19.1	0.95
Prior CABG	6.4	7	0.32
Hypertension	79.3	80	0.45
Diabetes	27.4	26.8	0.63
Peripheral vascular disease	16.6	16.9	0.79
Carotid stenosis	10.8	10.5	0.69
Atrial fibrillation/flutter	16.5	17.5	0.29
Prior stroke	7.6	8.1	
Chronic lung disease	27.8	29.1	
Porcelain aorta	1.9	2	
Estimated GFR (mL/min/1.73 m ²)	74.5 ± 22.6	73.9 ± 22.6	
5MWT (seconds)	6.4 ± 2.9	6.4 ± 3.0	



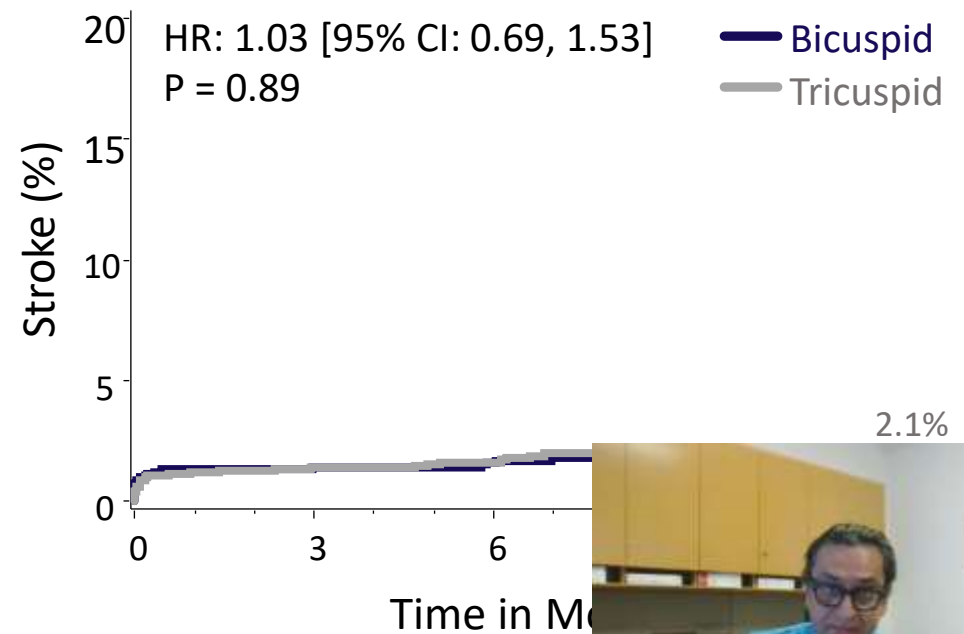
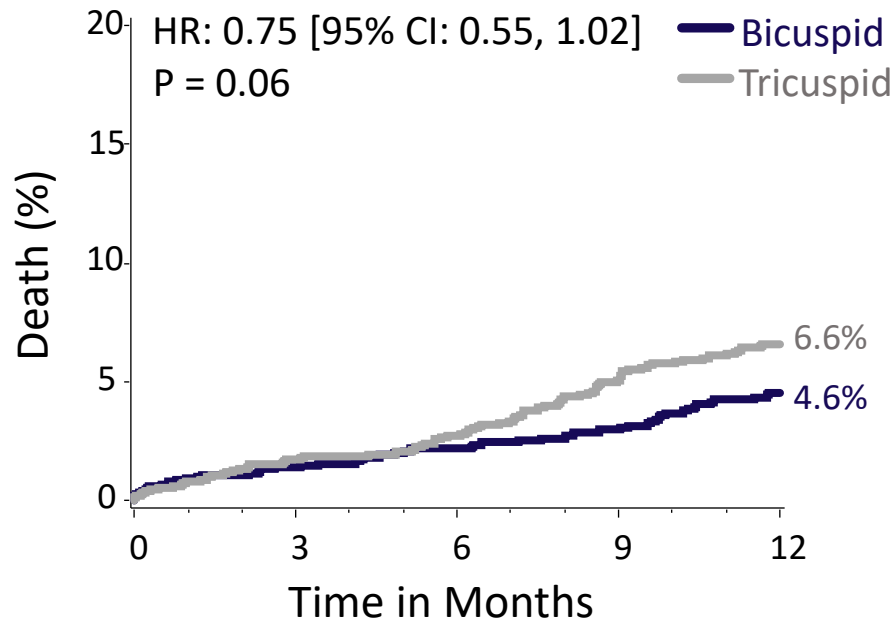
<i>Complication (%)</i>	BICUSPID n = 3168	TRICUSPID n = 3168	p value
Conversion to open heart surgery	0.4	0.4	0.85
Annulus rupture	0.2	0.1	1.00
Cardiopulmonary bypass	0.5	0.4	0.71
Aortic dissection	0.1	0	0.5
Coronary obstruction	0.03	0.1	
Need for second valve	0.3	0.1	



Primary Endpoints – Death and stroke Adjusted Cohort

30-day outcomes	BICUSPID n = 3168	TRICUSPID n = 3168	p value
All-cause mortality (%)	0.9	0.8	0.55
All stroke (%)	1.4	1.2	0.55

In-hospital mortality			
All-cause mortality (%)	0.6	0.4	NS



Pts at risk 3168	1158	1111	1097	779
Pts at risk 3168	1295	1253	1220	888

Pts at risk 3168	1145	1097
Pts at risk 3168	1274	1232



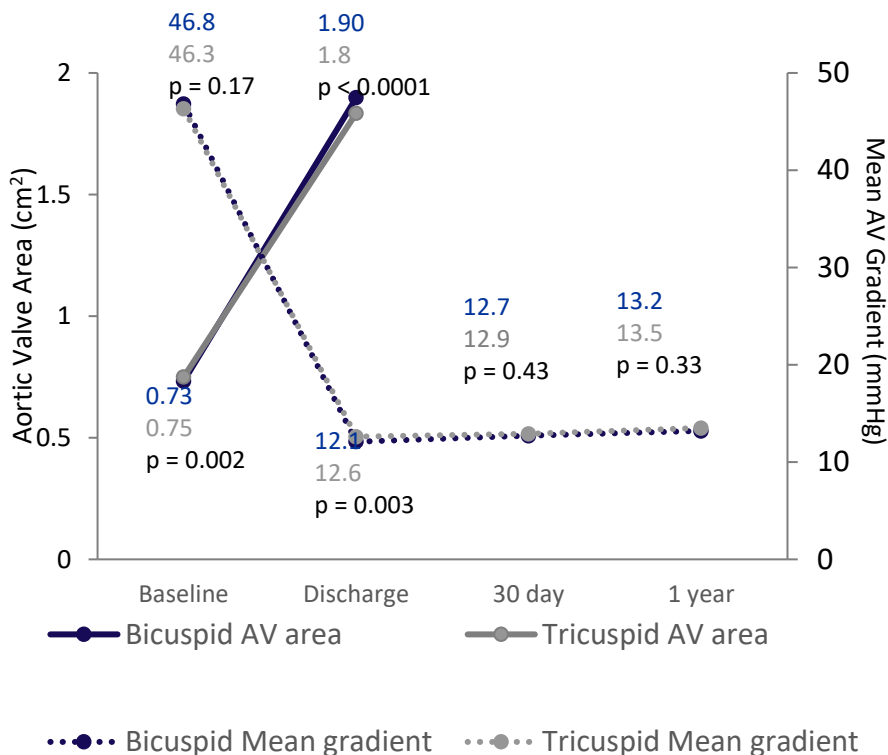
Secondary Endpoints at 30 days and 1 year

Adjusted Cohort

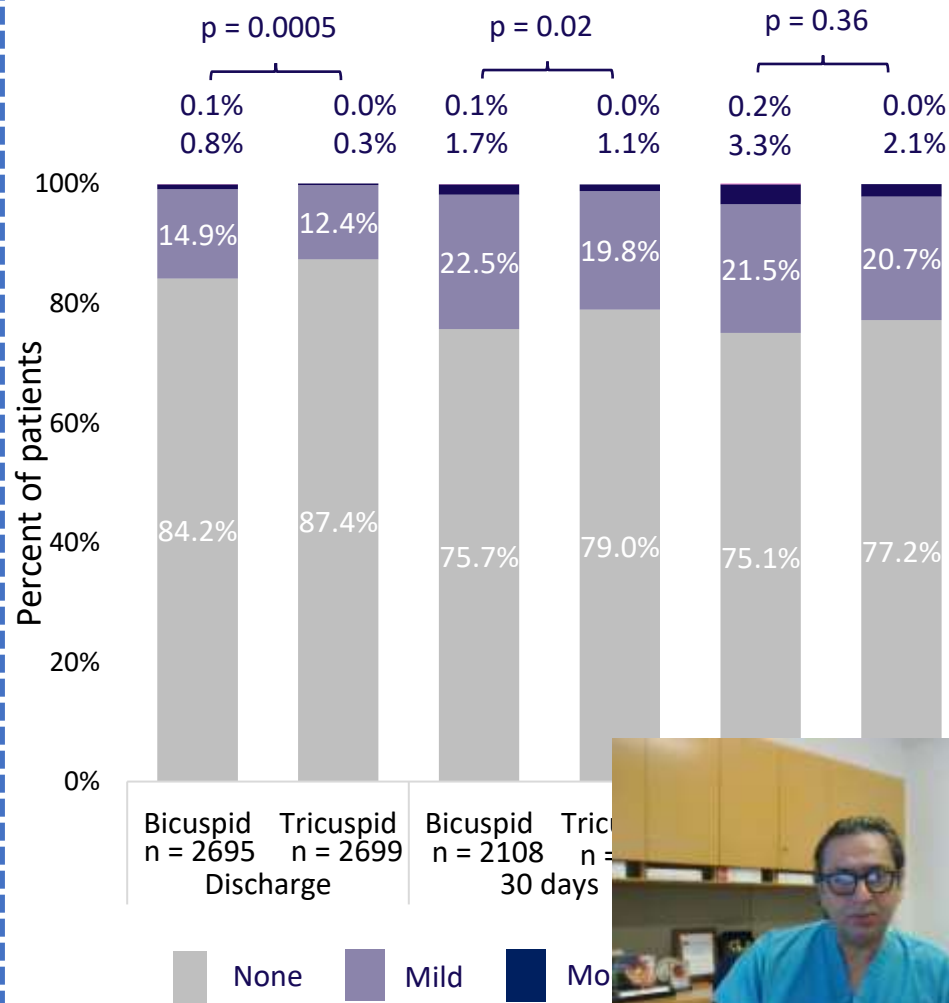
Outcome (KM estimate, %)	30 days			1 year		
	BICUSPID n = 3168	TRICUSPID n = 3168	p value	BICUSPID n = 3168	TRICUSPID n = 3168	p value
New pacemaker	7.91 (230)	6.71 (195)	0.06	8.85 (241)	7.77 (208)	0.08
New requirement for dialysis	0.25 (7)	0.31 (9)	0.64	0.34 (8)	0.70 (14)	0.24
New onset atrial fibrillation	1.39 (43)	0.99 (31)	0.16	1.39 (43)	0.99 (31)	0.16
Aortic valve reintervention	0.36 (11)	0.13 (4)	0.07	1.16 (20)	0.45 (14)	0.02
Any readmission	5.37 (154)	5.43 (158)	0.93	22.36 (361)	23.36 (361)	0.001



Aortic valve gradients and area



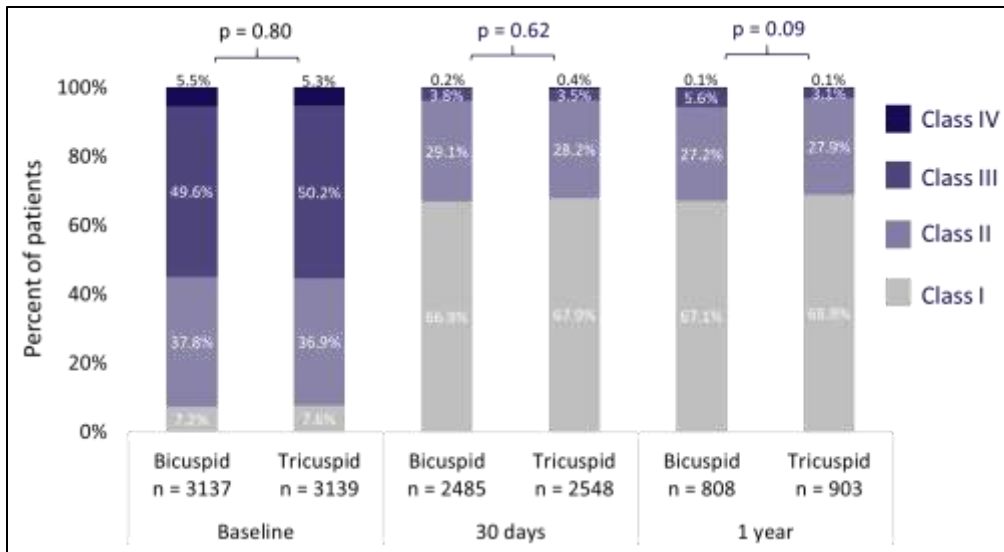
Paravalvular regurgitation



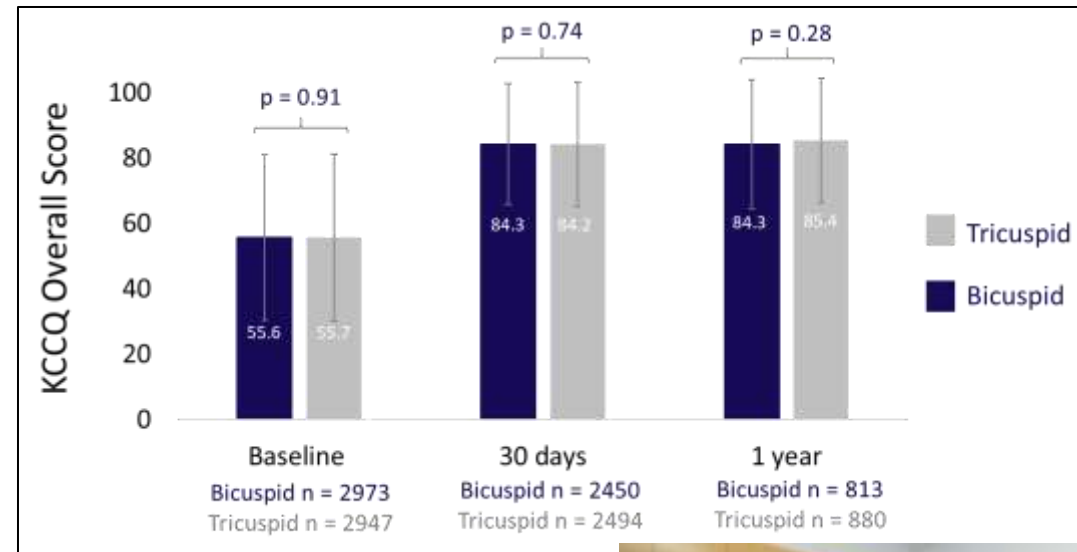
Aortic valve gradients	3135	2903	2318	734
	3133	2889	2338	839
Aortic valve area	3098	2505		
	3088	2473		

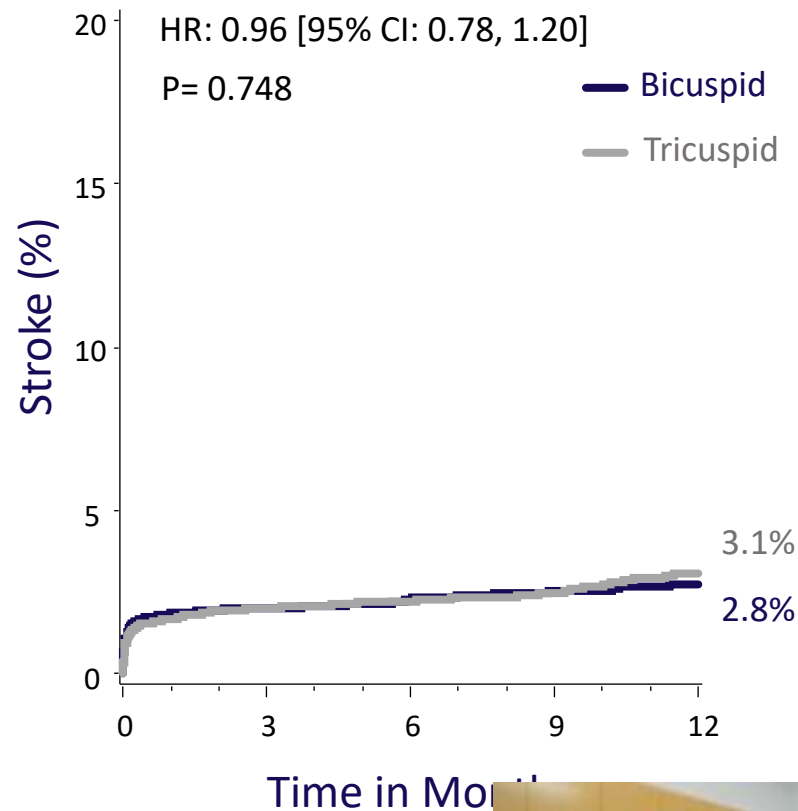
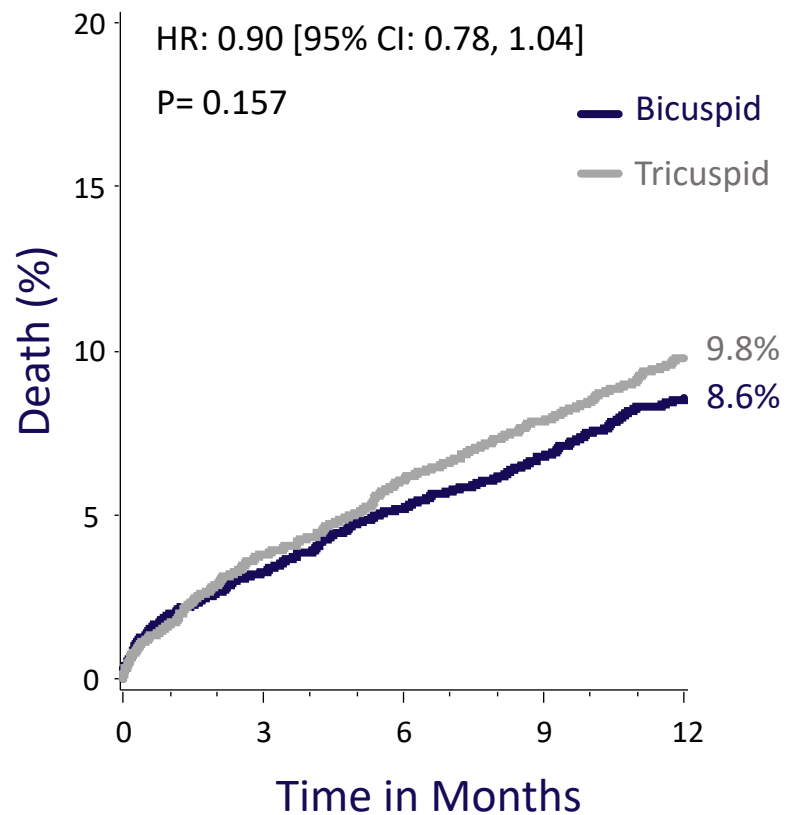


NYHA Adjusted cohort



KCCQ Adjusted cohort





Pts at risk 6995 3282 3154 3088 2248

Pts at risk 6995 3567 3437 3349 2453

Pts at risk 6995 3226 3099

Pts at risk 6995 3510 3376



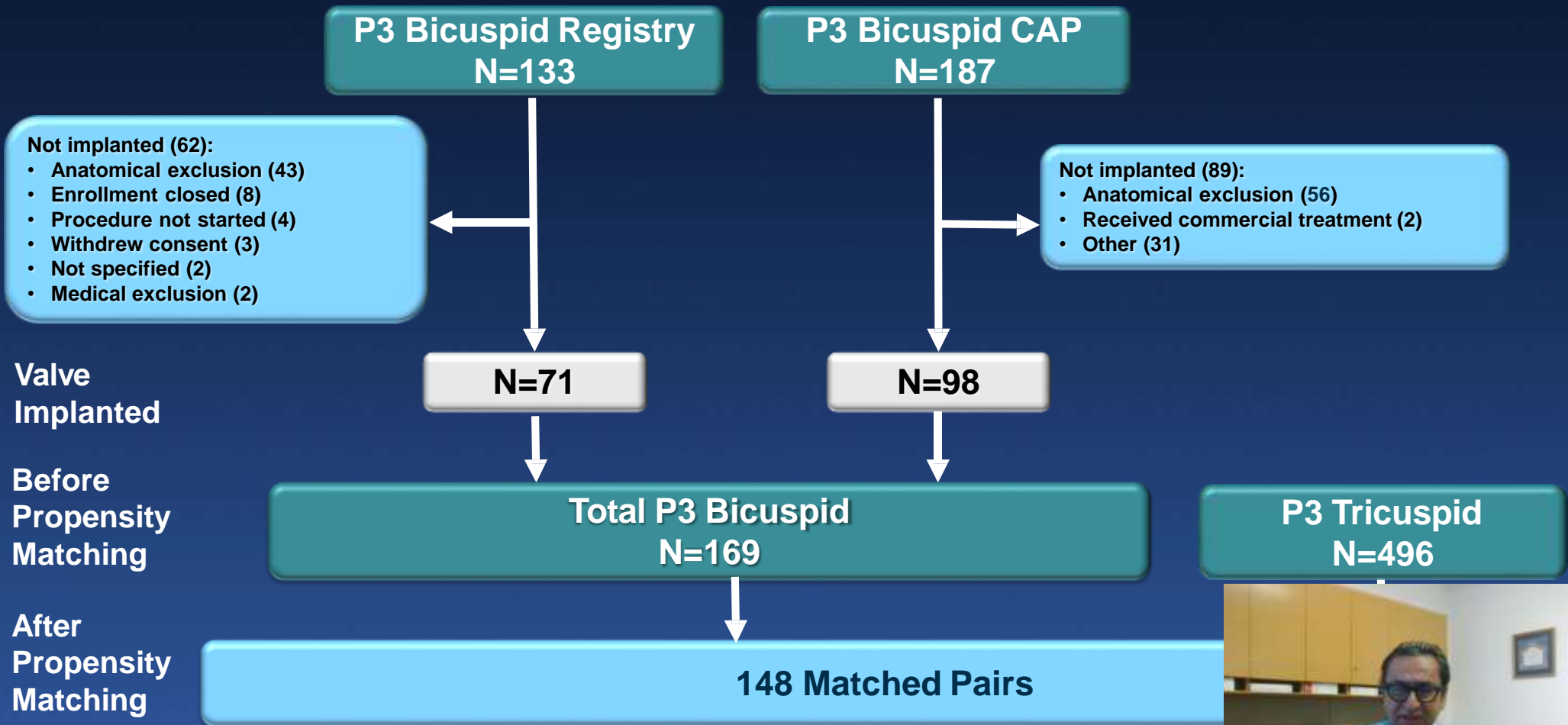
The PARTNER 3 Bicuspid Registry and CAP for SAPIEN 3 TAVR in Low-risk Patients

- Prospective registries, 30 centers, CT core lab adjudicated Bicuspid AS, Central echo core lab and CEC in
- Patients with Severe Bicuspid AS and STS<4
- Key exclusion-hostile anatomy and Aortic dimension>40 mm
- Total of 237 patients presented, 64 excluded mostly due to anatomical reasons, 173 enrolled in both registries

Co-Pis: Mathew R. Williams, MD
John G. Webb, MD



Patient Disposition



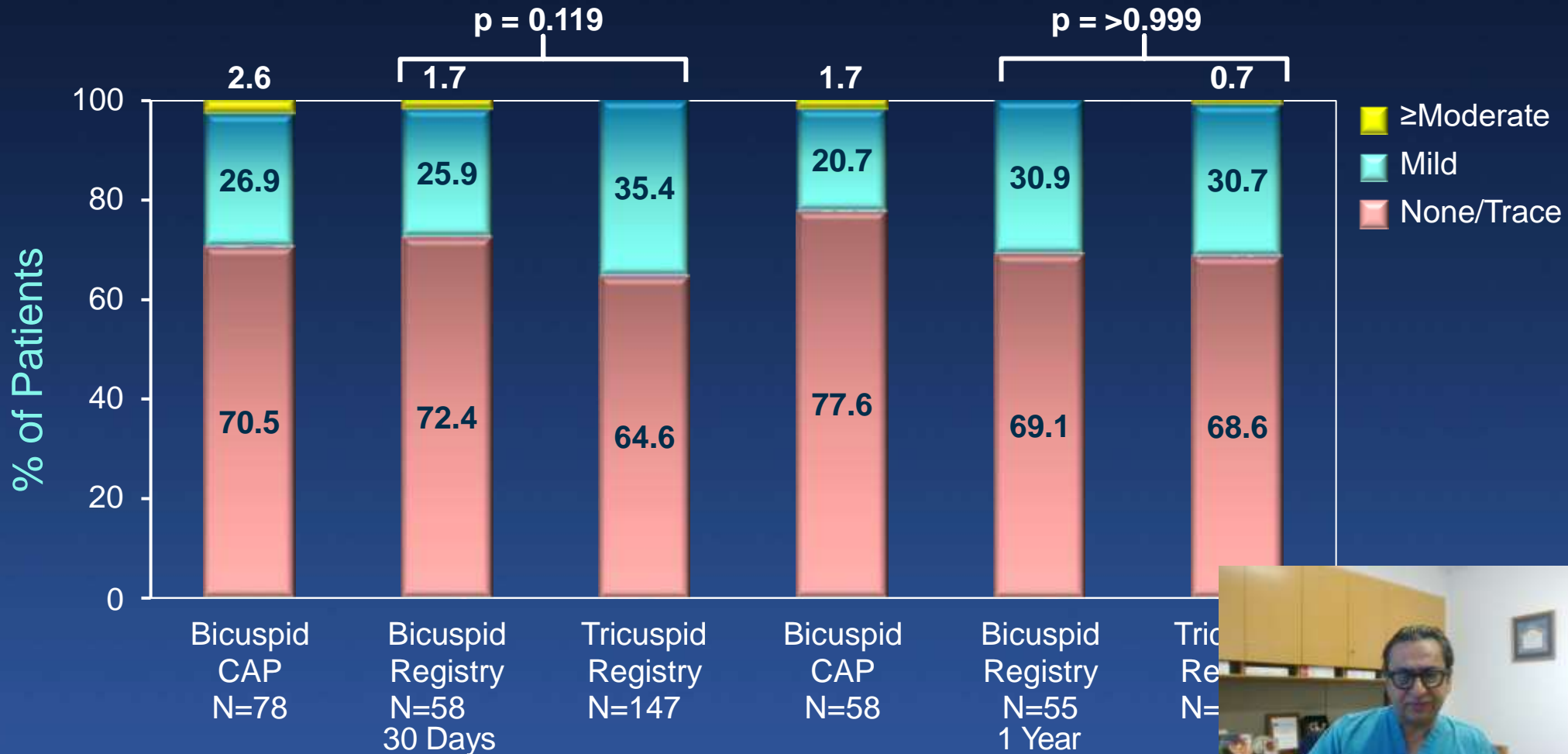
Clinical Outcomes: Average 71 yrs, STS 1.4

Matched

Outcome (KM estimate as %)	30 Days			1 Year		
	Bicuspid N=148	Tricuspid N=148	p value	Bicuspid N=148	Tricuspid N=148	p value
Death, Stroke, or Rehospitalization	6.8%	4.7%	0.44	10.9%	10.2%	0.80
Death	0.0%	0.0%	NA	0.7%	1.4%	0.58
Stroke	1.4%	1.4%	0.99	2.1%	2.0%	0.99
Rehospitalization	5.4%	4.1%	0.58	9.6%		
New pacemaker	6.1%	6.8%	0.81	6.8%		



Paravalvular Regurgitation *Matched*



Primary Results From the Evolut Low Risk Bicuspid Study

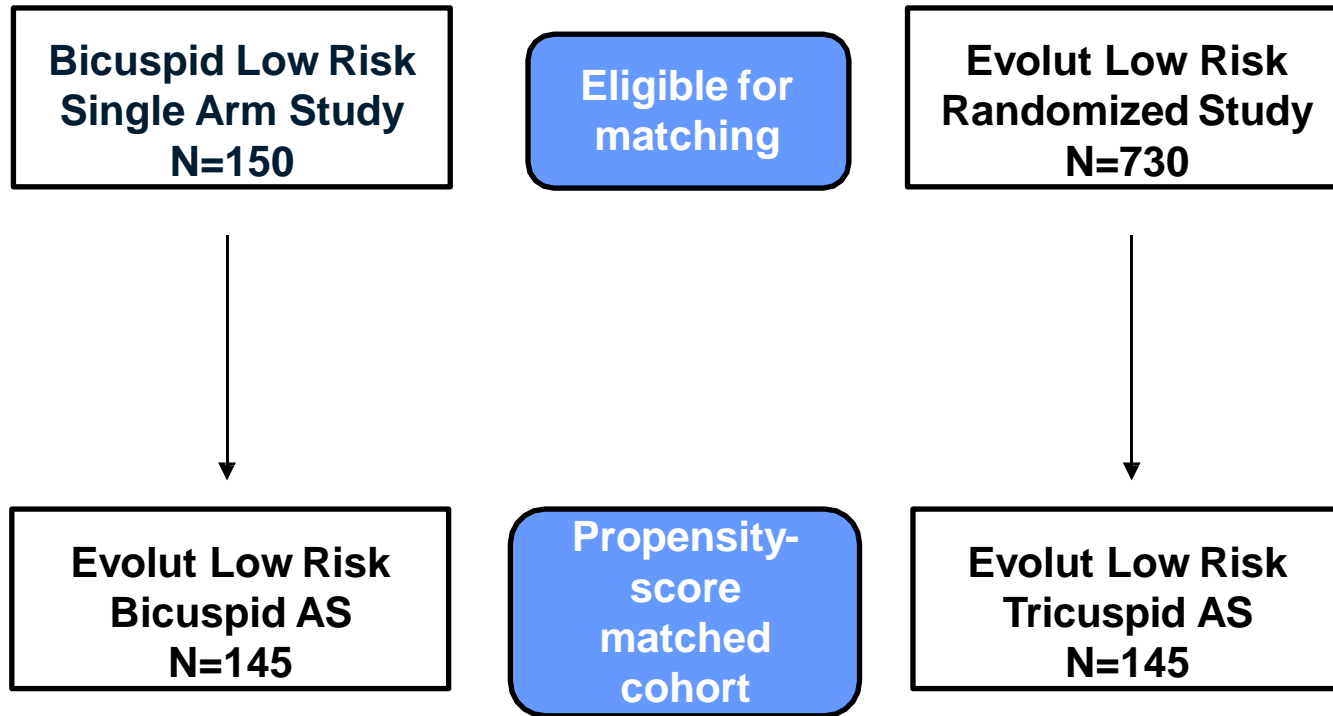
- Multicenter, prospective, interventional, single-arm study
- Baseline MSCT to confirm bicuspid morphology
- Patient eligibility reviewed by local Heart Team & Screening Committee
- Key Inclusion: Bicuspid AS and STS<3
- Key Exclusion: <60y, Aorta.4.5 cms, prohibitive LVOT calcium
- 222 patients screened, 150 attempted, 149 implanted
- Type 0-10%, Type 1-90%
- Key endpoint-30d death and stroke
- F/U to 10 years

CO-Pis Basel Ramlawi, MD and

Forrest J et al. JAMA



Patients

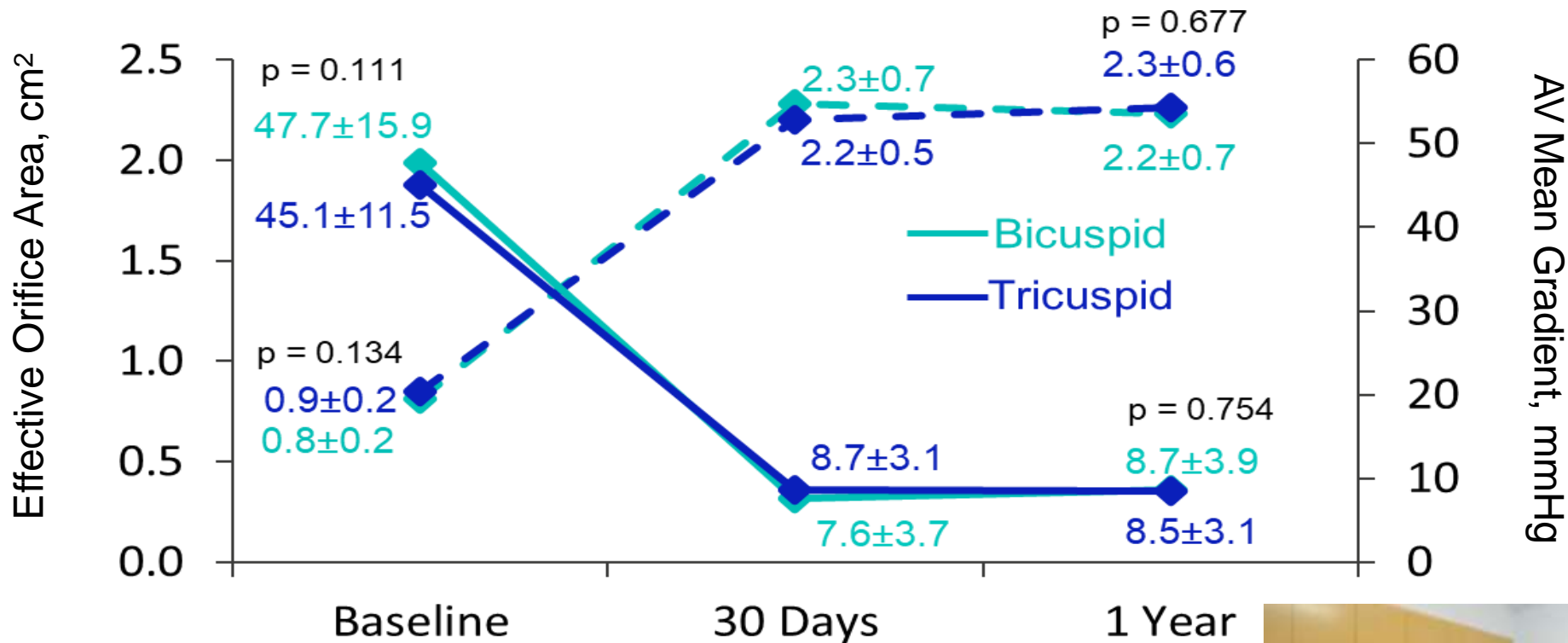


Clinical Outcomes in Matched Patients

No. (KM rates as %)	30 Days			1 Year		
	Bicuspid N=145	Tricuspid N=145	p Value	Bicuspid N=145	Tricuspid N=145	p Value
Death or disabling stroke	2 (1.4)	1 (0.7)	0.565	2 (1.4)	4 (2.8)	0.413
All-cause mortality	1 (0.7)	0 (0.0)	0.317	1 (0.7)	3 (2.1)	0.317
Disabling stroke	1 (0.7)	1 (0.7)	0.998	1 (0.7)	1 (0.7)	0.998
Major bleeding	2 (1.4)	4 (2.8)	0.409	2 (1.4)	4 (2.8)	0.409
Pacemaker implanted	21 (14.5)	25 (17.2)	0.526	24 (16.6)	26 (17.9)	0.741
AV rehospitalization	3 (2.1)	1 (0.7)	0.314	5 (3.5)	7 (4.9)	0.560
Valve thrombosis	1 (0.7)	0 (0.0)	0.317	2 (1.4)	1 (0.7)	0.568

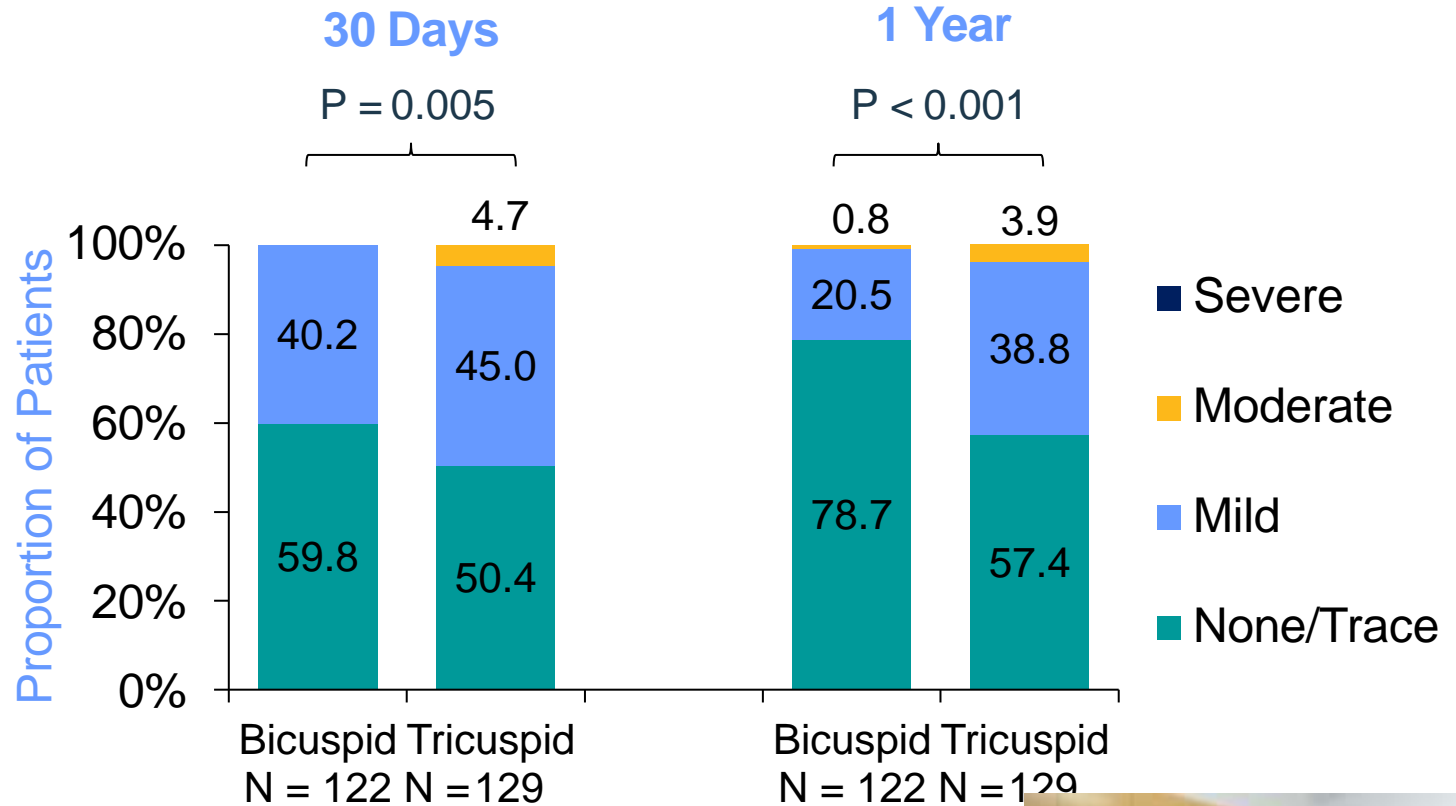


Valve Hemodynamics



Paravalvular Regurgitation for Matched Patients

- Data presented for patients with PVL measured at both time points.
- At 1 year, fewer patients with bicuspid AV had \geq mild PVL (21.3% vs. 42.6%, $p < 0.001$).





Bicuspid Aortic Valve Morphology and Outcomes After Transcatheter Aortic Valve Replacement

- A total of **1034** patients with CT-confirmed Bicuspid anatomy from 24 sites
- Mean age 74.7 ± 9.3 yrs, mean STS score of $3.7 \pm 3.3\%$, transfemoral TAVR 94.3%
- Type 0 BAV: 10.3%, Type 1 Non-calcified raphe: 45.1%, Type 1 Calcified raphe 44.6%
- Sapien 3 740 (71.6%), Evolut R/Pro 188 (18.2%)
- 30 day Mortality 2%, Stroke-2.4%

A total of 1034 CT-confirmed Bicuspid patients
undergoing TAVR with current generation devices

Yoon et al: JACC



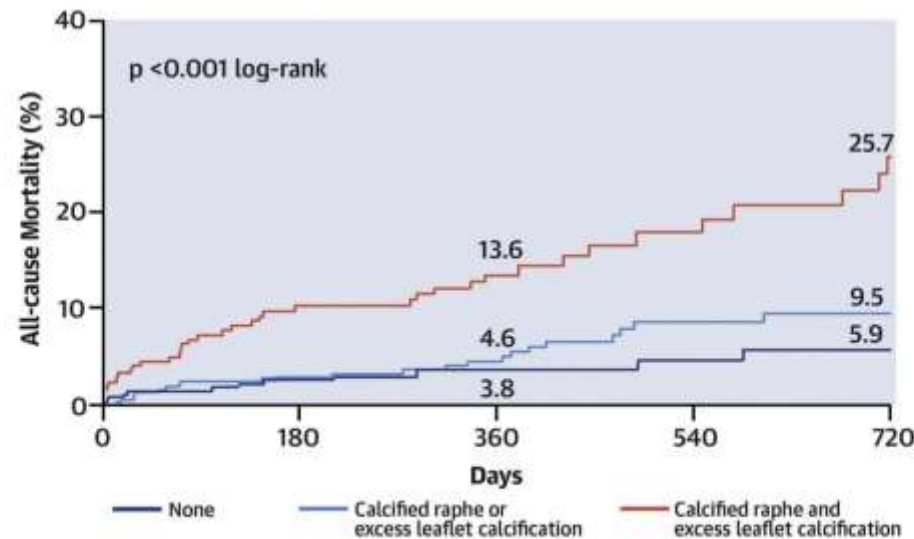
Procedural and Clinical Outcomes According to Valve Morphology

	Overall (n = 1034)	None (n = 324)	Calc Raphe OR Excess Leaflet Ca (n = 441)	Calc Raphe Plus Excess Leaflet Ca (n = 269)	P value
Conversion to surgery	9 (0.9)	1 (0.3)	2 (0.5)	6 (2.2)	0.028
Aortic root injury	18 (1.7)	3 (0.9)	3 (0.7)	12 (4.5)	<0.001
Second valve	14 (1.4)	4 (1.2)	3 (0.7)	7 (2.6)	0.10
PVL ≥ mild	291 (28.6)	63 (19.8)	130 (29.7)	98 (37.3)	<0.001
PVL ≥ moderate	33 (3.2)	5 (1.6)	11 (2.5)	17 (6.5)	0.002
New permanent pacemaker	118 (12.2)	31 (10.3)	50 (11.9)	37	
30-day Mortality	21 (2.0)	5 (1.5)	5 (1.1)	11	



Bicuspid Morphology and Mortality After TAVR

CENTRAL ILLUSTRATION: Death From Any Cause According to Morphological Features



Yoon, S.-H. et al. J Am Coll Cardiol. 2020;76(9):1018-30.



Summary

- Favorable outcomes with TAVR in carefully selected patients with Sapien and Evolut in real life TVT and sponsored prospective registries
- CT phenotyping is important in patient selection and procedure planning.
- While Bicuspid TAVR is justifiable irrespective of surgical risk, high risk anatomical features (extreme calcium, heavy-calcified raphe) and/or concomitant aortopathy should prompt consideration for surgical AVR in low-risk patients
- Randomized trials/prospective registries especially in patients with lower surgical risk are needed.
- Important to take life-time management of patients into consideration when we decide between TAVR vs SAVR in younger patients who require multiple procedures over lifetime

