Outcomes of Transcatheter Aortic Valve Replacement with Balloon-Expandable Sapien3 Valve in Bicuspid Aortic Stenosis:

An analysis of the STS/ACC TVT Registry

Raj R. Makkar*, Sung-Han Yoon, Martin B. Leon, Tarun Chakravarty, Sreekanth Vemulapalli, Michael Rinaldi, Pinak B. Shah, Eric R. Skipper, Vinod H. Thourani, Vasilis Babaliaros, Wen Cheng, Alfredo Trento, Samir R. Kapadia, Susheel Kodali, Michael J. Mack, Gilbert H. L. Tang, Tsuyoshi Kaneko

** Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles*

Disclosure Statement

Raj Makkar, MD

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	• Edwards Lifesciences, Abbott Inc., Medtronic, Boston Scientific
• Consulting Fees/Honoraria	• Edwards Lifesciences, Abbott Inc., Medtronic, Boston Scientific
• Major Stock Shareholder/Equity	• Entourage Medical

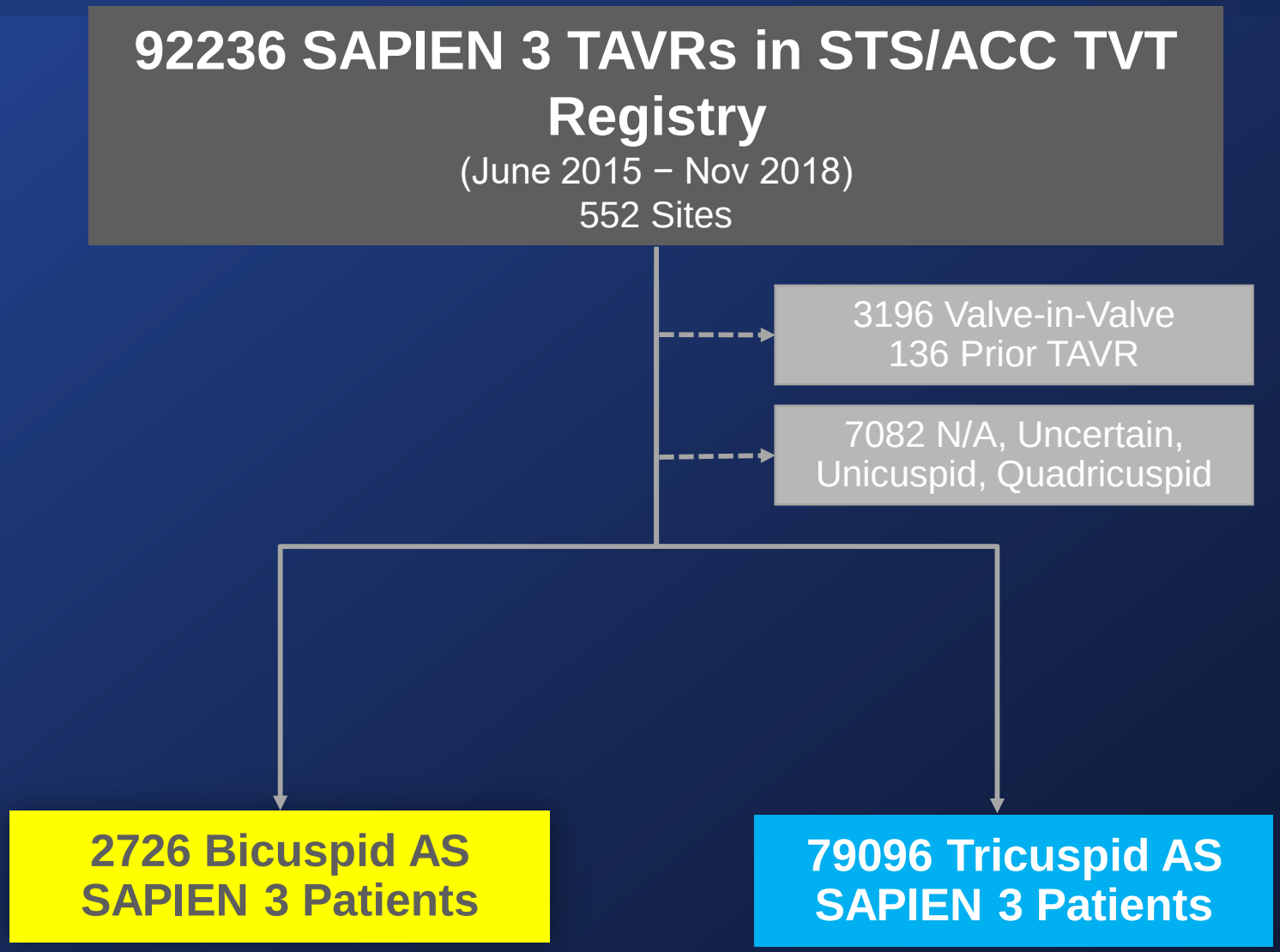
Statistical analyses were performed by Edwards Lifesciences. The views or opinions presented here do not represent those of the American College of Cardiology, The Society of Thoracic Surgeons, or the STS/ACC TVT Registry.

Background & Objective

- Bicuspid aortic valve accounts for up to 50% of patients requiring surgical aortic valve replacement in the younger population[1]
- As TAVR becomes a therapeutic option for younger and healthier patients, bicuspid aortic valves will be seen more often.
- Pivotal clinical trials, including the low risk trials enrolling younger patients, have excluded patients with bicuspid aortic valves.
- We sought to compare the outcomes of TAVR with balloon-expandable SAPIEN 3 valve in native bicuspid versus tricuspid aortic valve stenosis in the real-world STS/ACC TVT Registry.

[1] Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. Circulation. 2005;111(7):920-925

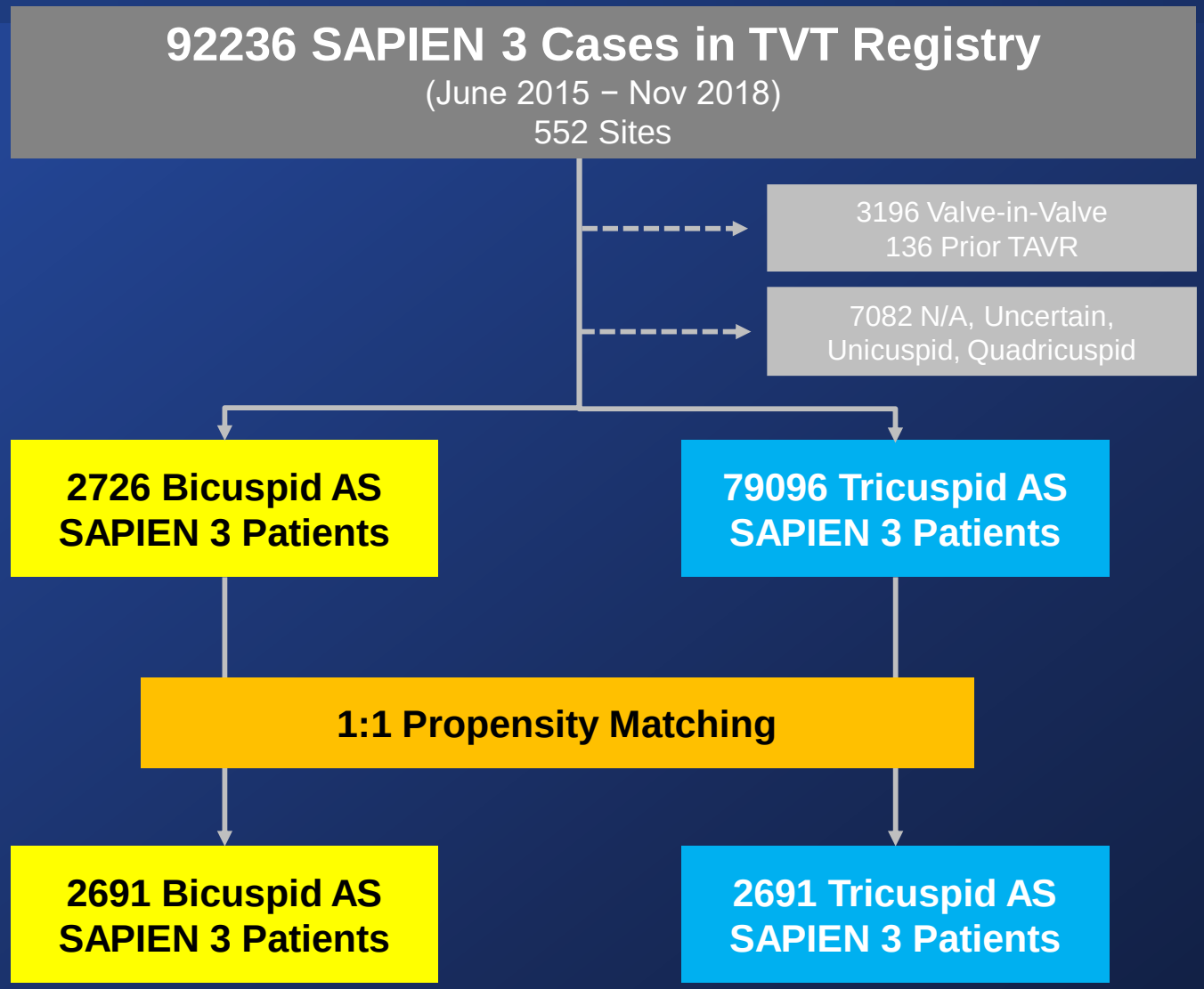
Study Population



Baseline Characteristics – Unadjusted

Characteristic % or mean ± SD	Bicuspid AS (n=2726)	Tricuspid AS (n=79096)	p-value
Age (years)	**73 ± 11**	**81 ± 8**	**<0.0001**
STS Risk Score (%)	**4.9 ± 4.0**	**6.5 ± 4.6**	**<0.0001**
Male	60.4	55.1	<0.0001
NYHA III/IV	74.3	75.4	0.20
BMI (kg/m^2)	29.2 ± 7.6	29.0 ± 7.3	0.13
Hypertension	84.1	91.2	<0.0001
Diabetes	35.7	38.8	0.001
Peripheral Arterial Disease	24.1	27.6	<0.0001
Carotid Stenosis	**14.8**	**25.2**	**<0.0001**
Atrial Fibrillation	**28.8**	**38.7**	**<0.0001**
Prior Stroke	10.2	11.5	0.04
Chronic Lung Disease	41.5	40.1	0.13
Prior PCI	25.2	34.0	<0.0001
Prior CABG	**15.7**	**20.8**	**<0.0001**
Porcelain Aorta	2.7	3.4	0.05
GFR (mL/min/1.73 m^2)	**65.3 ± 28.7**	**59.3 ± 24.5**	**<0.0001**
5MWT (seconds)	7.5 ± 4.2	8.4 ± 5.4	<0.0001

Study population



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	5 Meter Walk Test
Atrial Fibrillation	Access Site
Prior Stroke	KCCQ
Immunocompromised	Hemoglobin
GFR	

Baseline Characteristics – Matched

Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Age (years)	73 ± 10	73 ± 11	**0.47**
STS Risk Score (%)	4.9 ± 4.0	5.1 ± 4.2	**0.09**
Male	60.3	61.5	**0.35**
NYHA III/IV	74.4	74.1	**0.83**
BMI (kg/m^2)	29.2 ± 7.6	29.4 ± 7.4	**0.30**
Hypertension	84.5	84.2	**0.80**
Diabetes	35.8	36.8	**0.43**
Peripheral Arterial Disease	24.3	24.5	**0.90**
Carotid Stenosis	15.0	15.6	**0.63**
Atrial Fibrillation	29.0	29.4	**0.73**
Prior Stroke	10.2	10.2	**0.96**
Chronic Lung Disease	41.7	42.0	**0.79**
Prior PCI	25.5	26.6	**0.34**
Prior CABG	15.9	17.2	**0.18**
Porcelain Aorta	2.7	3.1	**0.37**
GFR ($mL/min/1.73\ m^2$)	65.0 ± 28.4	64.4 ± 27.2	**0.39**
5MWT (seconds)	7.6 ± 4.2	7.6 ± 4.0	**0.79**

Methods

- **Primary end-point:** Mortality and Stroke at 30-days and 1-year.

- **Secondary end-point:** Procedural complications, in-hospital adverse events, post-procedural echocardiographic assessment of the valve, functional status and health status at 30 days and 1 year.

- To compare death and stroke between bicuspid and tricuspid cohorts, the patients in the study cohort were linked with Centers for Medicare and Medicaid Services (CMS) claims data, in addition to the follow-up obtained from the TVT registry.

Baseline Echo

Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
AV Mean Gradient (mmHg)	45.2 ± 15.0	44.9 ± 15.2	0.51
AV Area (cm^2)	0.71 ± 0.23	0.71 ± 0.21	0.15
LVEF (%)	53.5 ± 14.7	52.5 ± 15.0	0.02
Annular Size (mm)	**25.1 ± 3.2**	**24.6 ± 3.0**	**<0.0001**
Mitral Regurgitation (mod/sev) (%)	20.6	21.7	0.39
Tricuspid Regurgitation (mod/sev) (%)	14.0	14.1	0.86

Procedural Data

Characteristic %	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Transfemoral access	93.6	93.9	0.65
Conscious Sedation	42.8	44.1	0.33
Valve Size			<0.0001
20mm	2.7	3.1	0.33
23mm	**23.0**	**28.5**	**<0.0001**
26mm	**39.1**	**42.0**	**0.03**
29mm	**35.2**	**26.4**	**<0.0001**

Procedural Outcomes

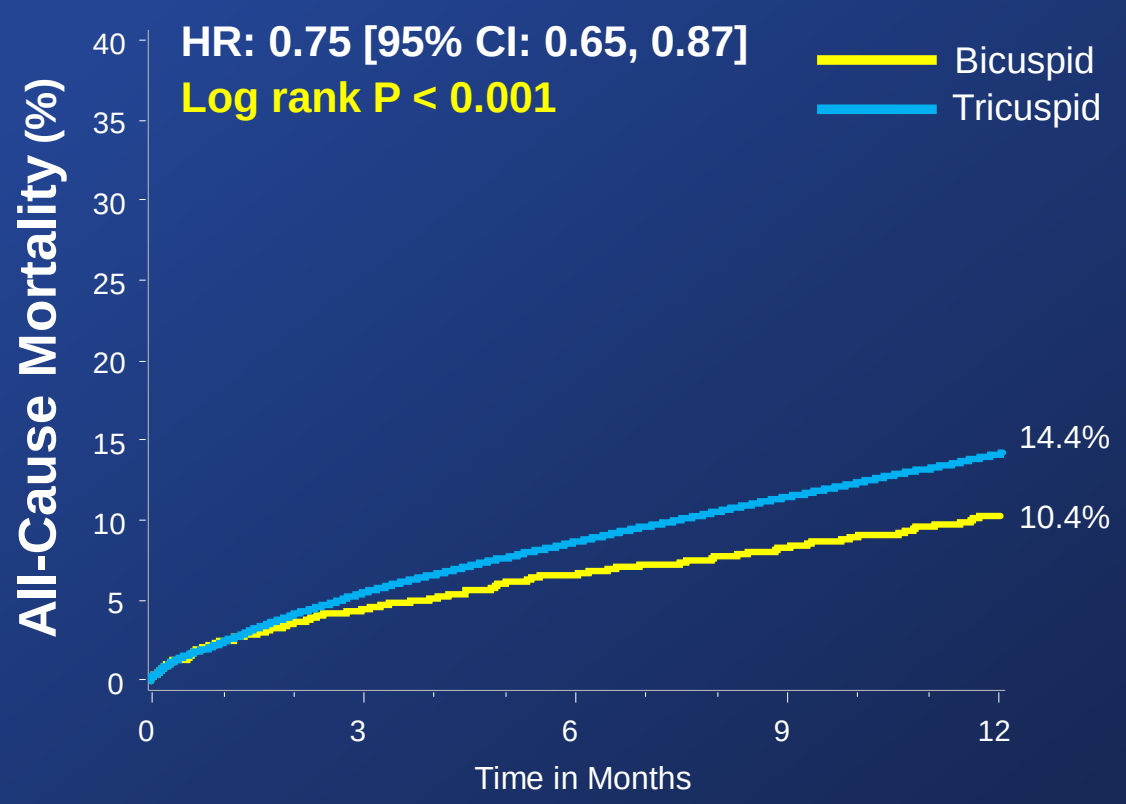
Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Device success	96.5	96.6	0.87
Procedure Time, min	100.7 ± 51.8	98.2 ± 52.1	0.08
Fluoroscopy Time, min	18.5 ± 11	17.1 ± 10.2	<0.0001
Conversion to open surgery	**0.9**	**0.4**	**0.03**
Annulus Rupture	**0.3**	**0.0**	**0.02**
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**	**0.16**

30-Day Outcomes

KM estimate %	Bicuspid	Tricuspid AS	p-value
All-cause mortality	2.6	2.5	0.82
All stroke	**2.4**	**1.6**	**0.02**
Life-threatening bleeding	0.1	0.1	0.99
Major vascular complication	0.9	1.0	0.68
New pacemaker	**9.1**	**7.5**	**0.03**
Aortic valve reintervention	0.2	0.3	0.79

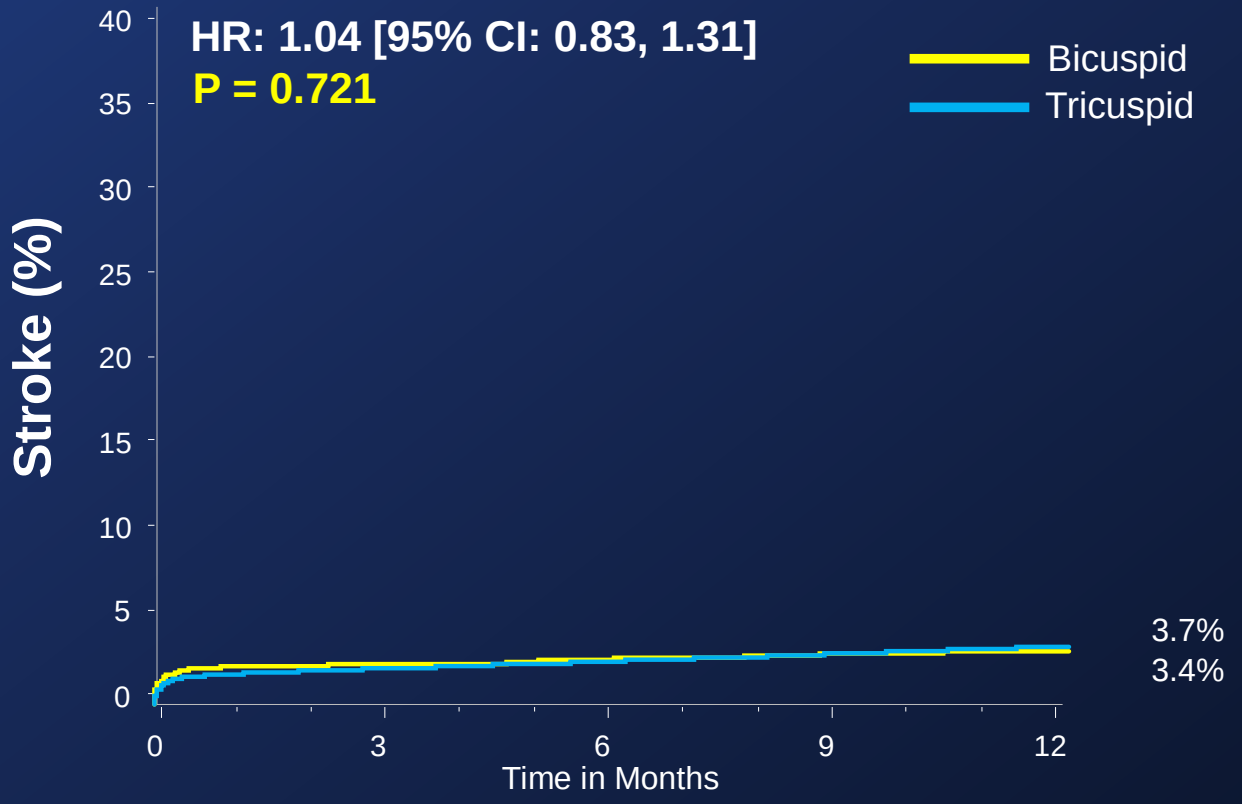
1-year Mortality and All Stroke

Unadjusted Cohort



Bicuspid	2726	1272	1235	1175	947
Tricuspid	79096	41830	40133	37794	30309

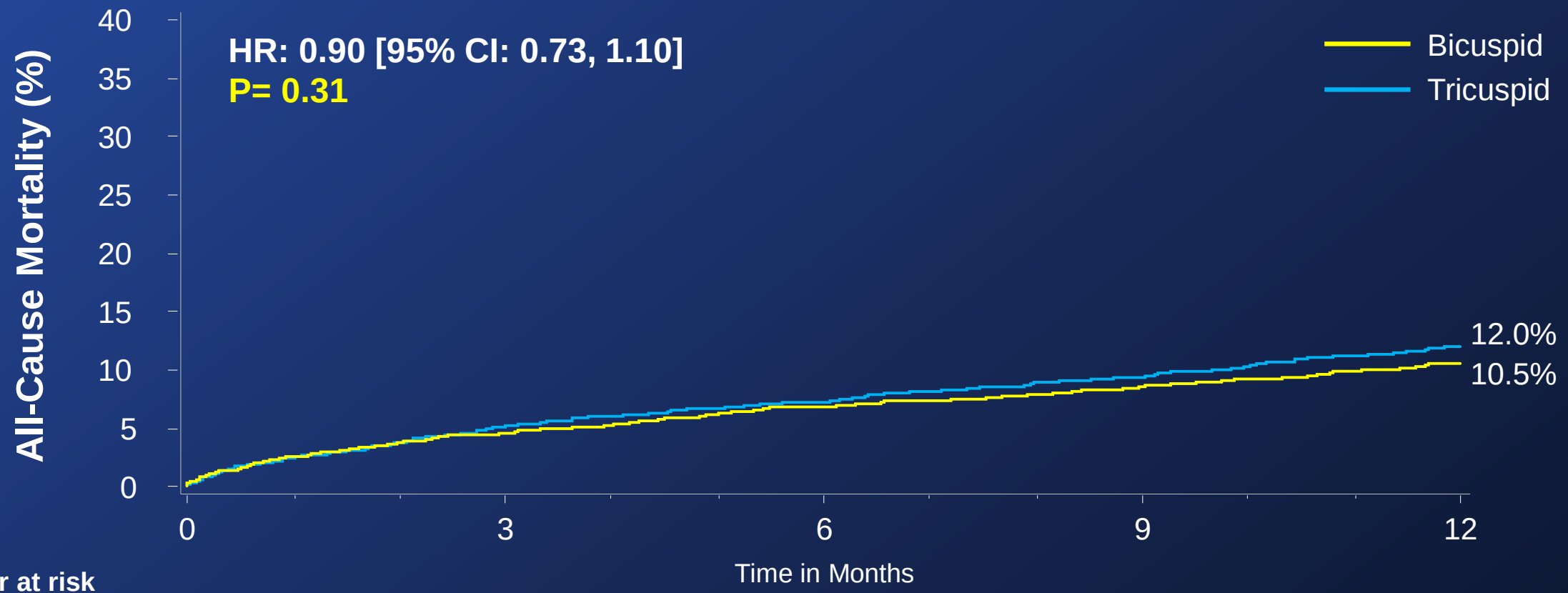
Number at risk



Bicuspid	2726	1247	1209	1148	923
Tricuspid	79096	41050	39266	36851	29459

Number at risk

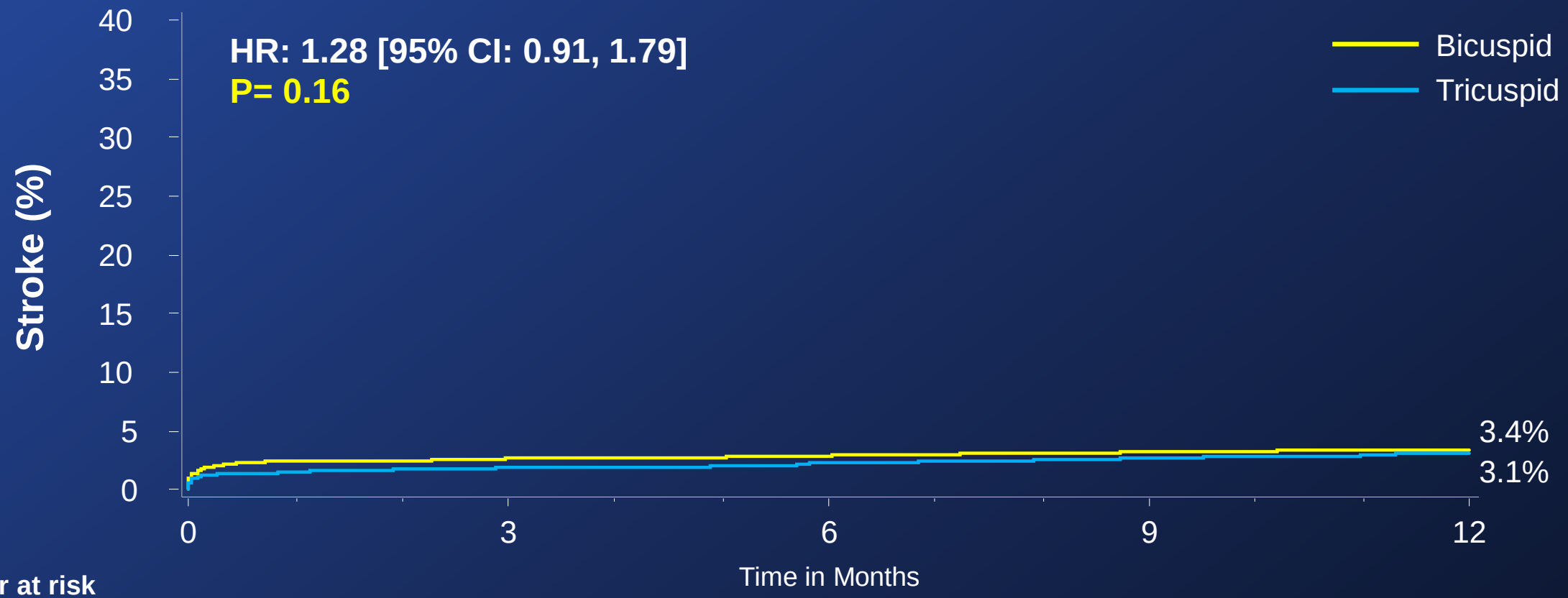
1-Year Mortality – Matched



Number at risk

Bicuspid	**2691**	**1259**	**1222**	**1162**	**934**
Tricuspid	**2691**	**1367**	**1326**	**1256**	**977**

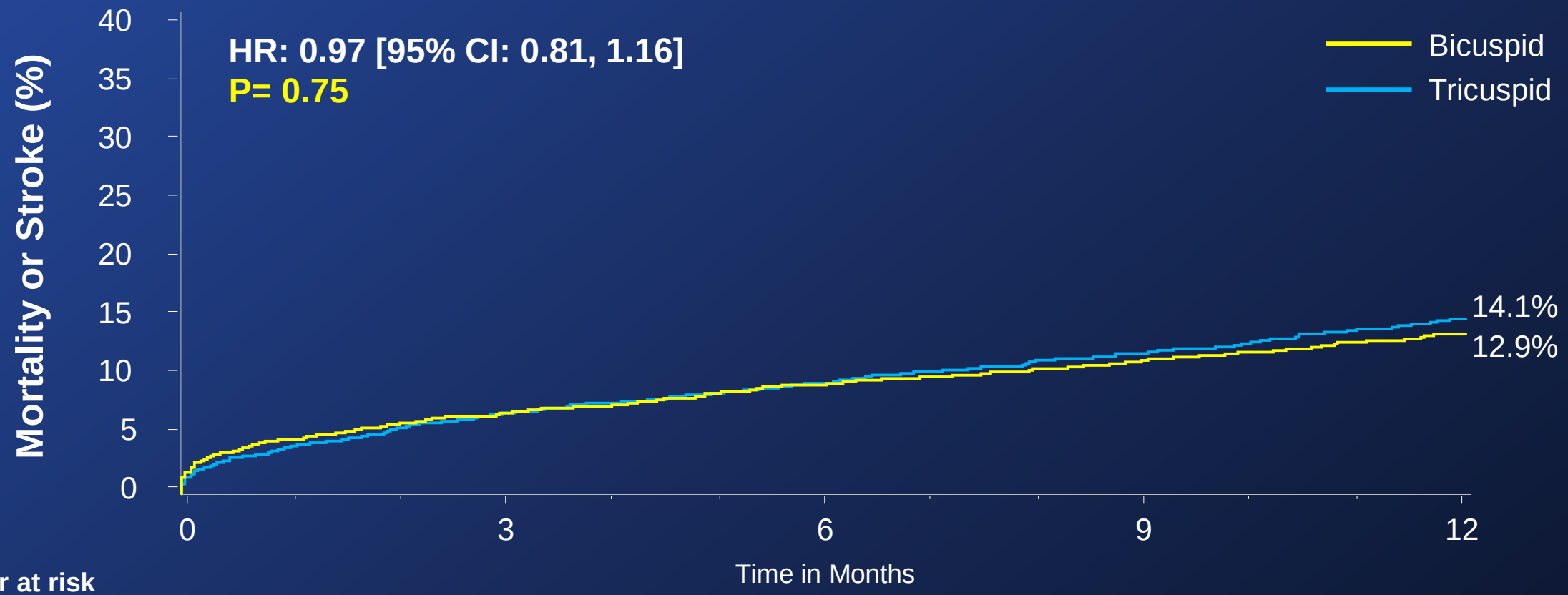
1-Year Stroke – Matched



Number at risk

Bicuspid	**2691**	**1234**	**1196**	**1135**	**910**
Tricuspid	**2691**	**1341**	**1296**	**1226**	**952**

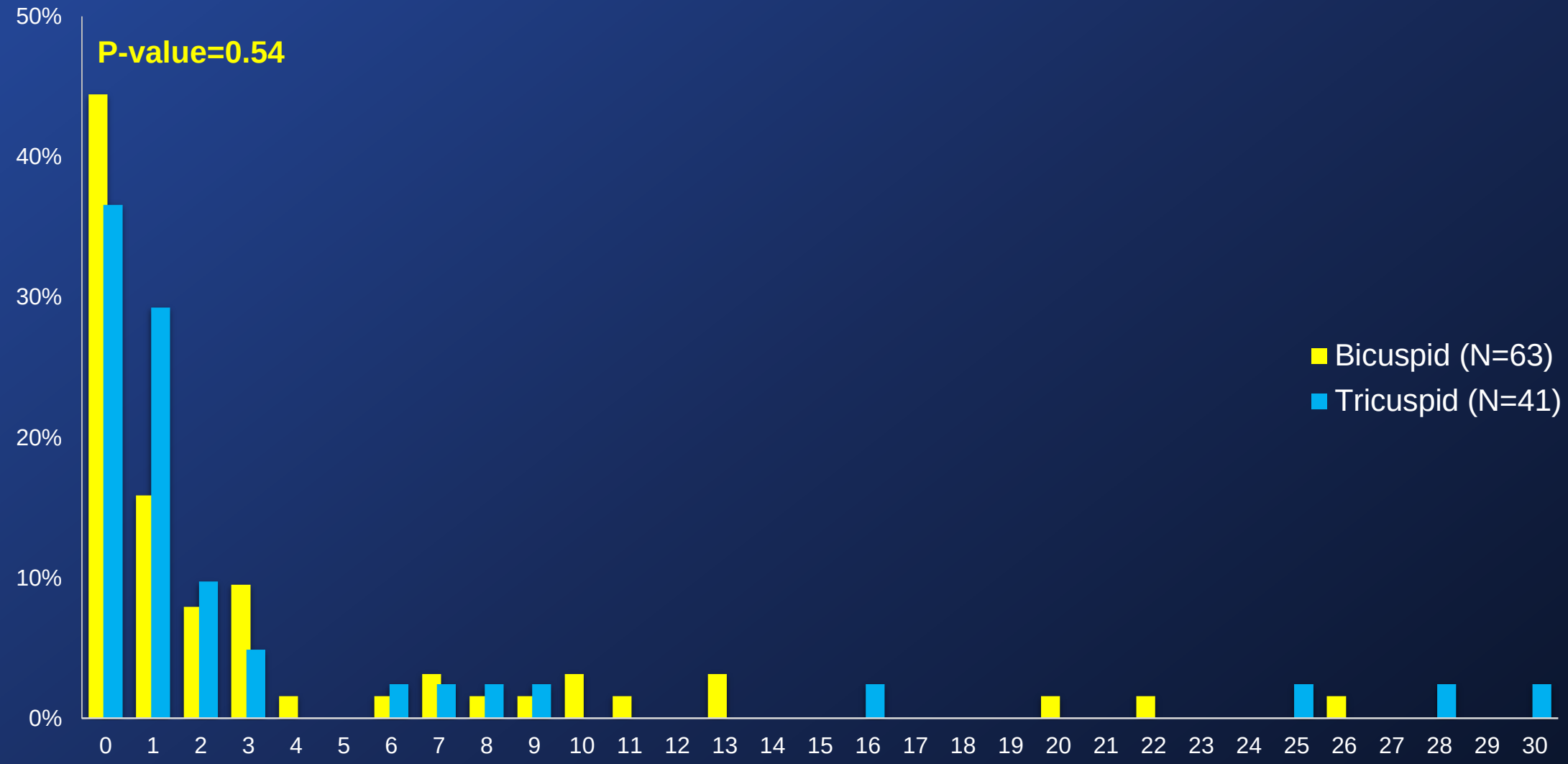
1-Year Mortality or Stroke – Matched



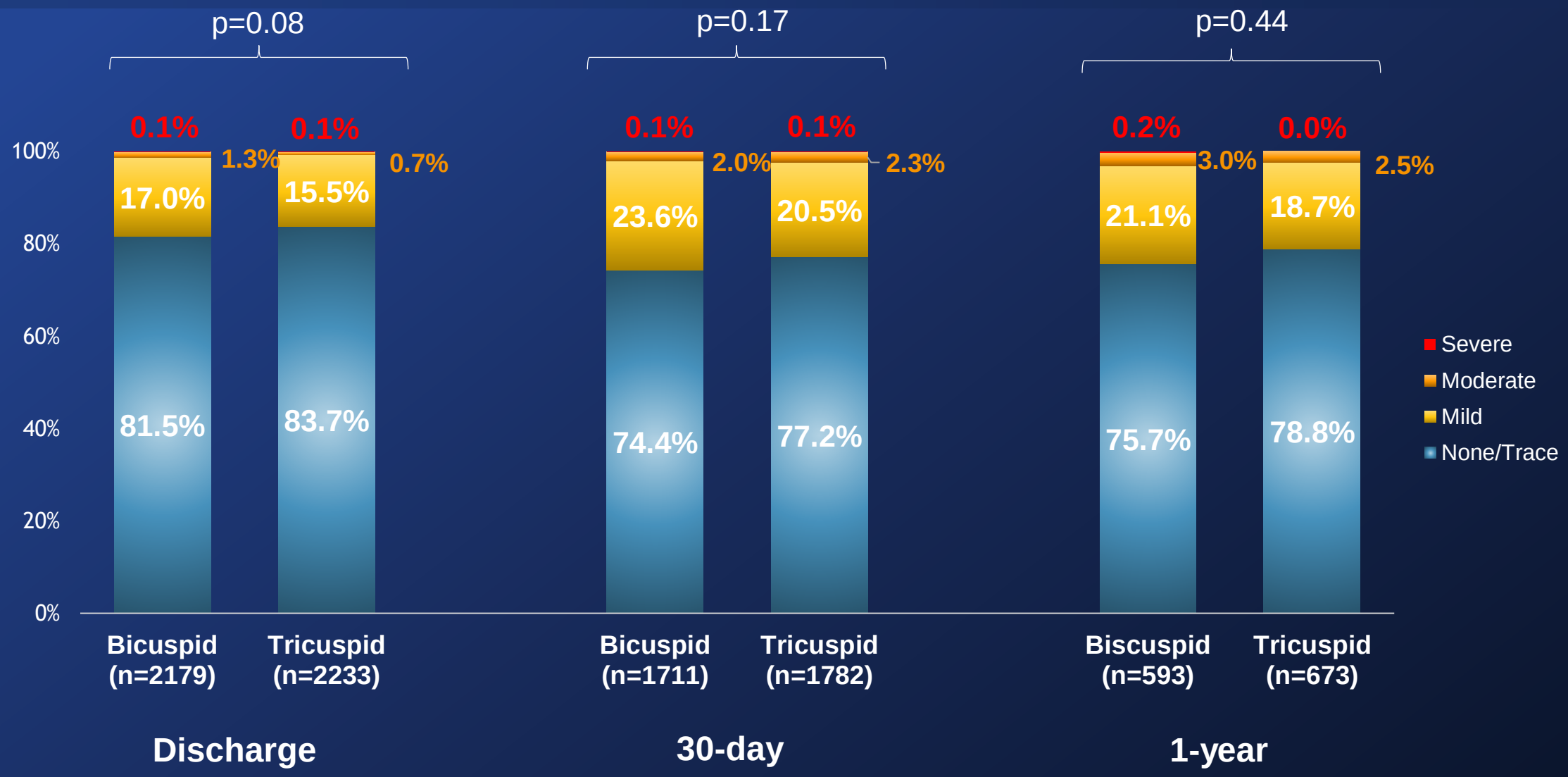
Number at risk

Bicuspid	**2691**	**1234**	**1196**	**1135**	**910**
Tricuspid	**2691**	**1341**	**1296**	**1226**	**952**

Timing of All-Stroke Events

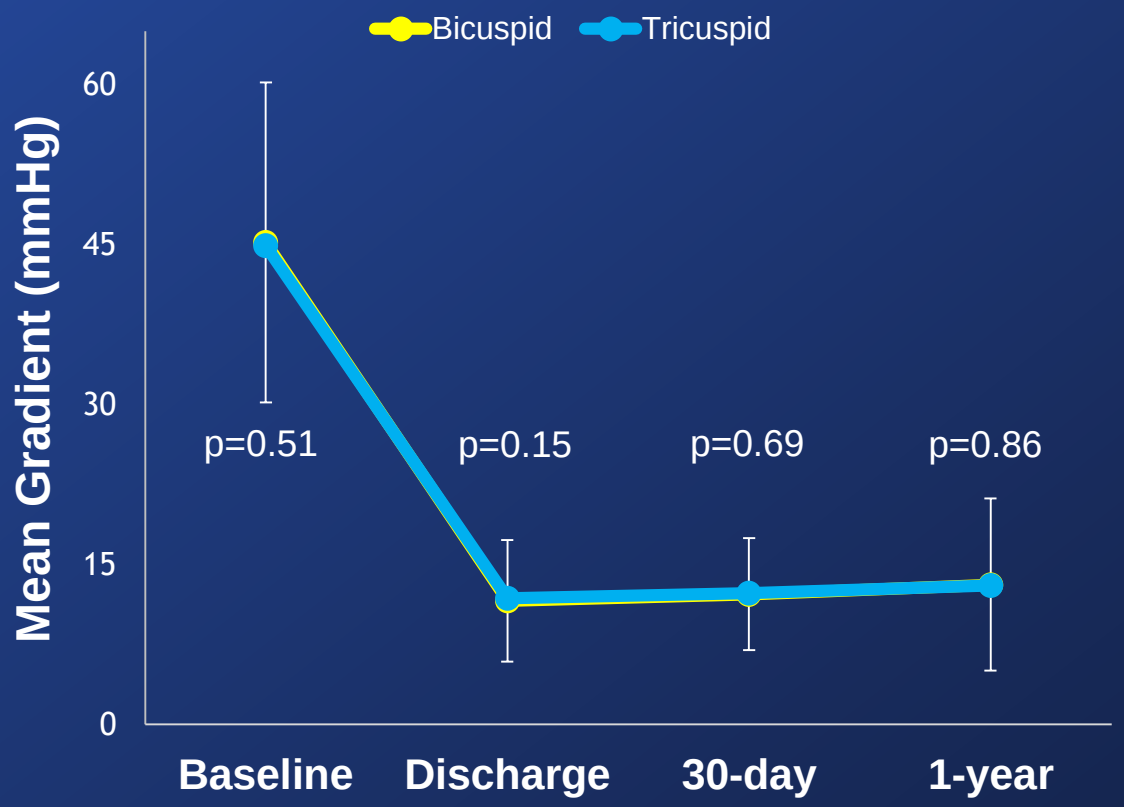


Paravalvular Leak – Matched

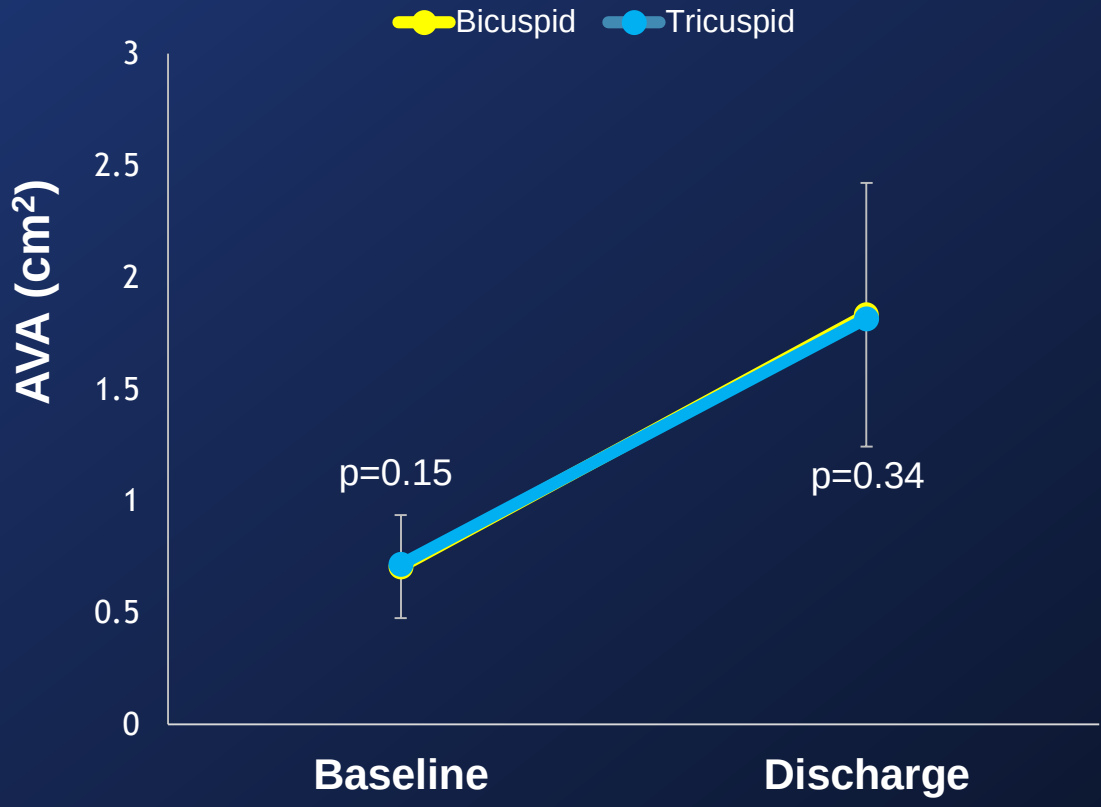


Hemodynamics – Matched

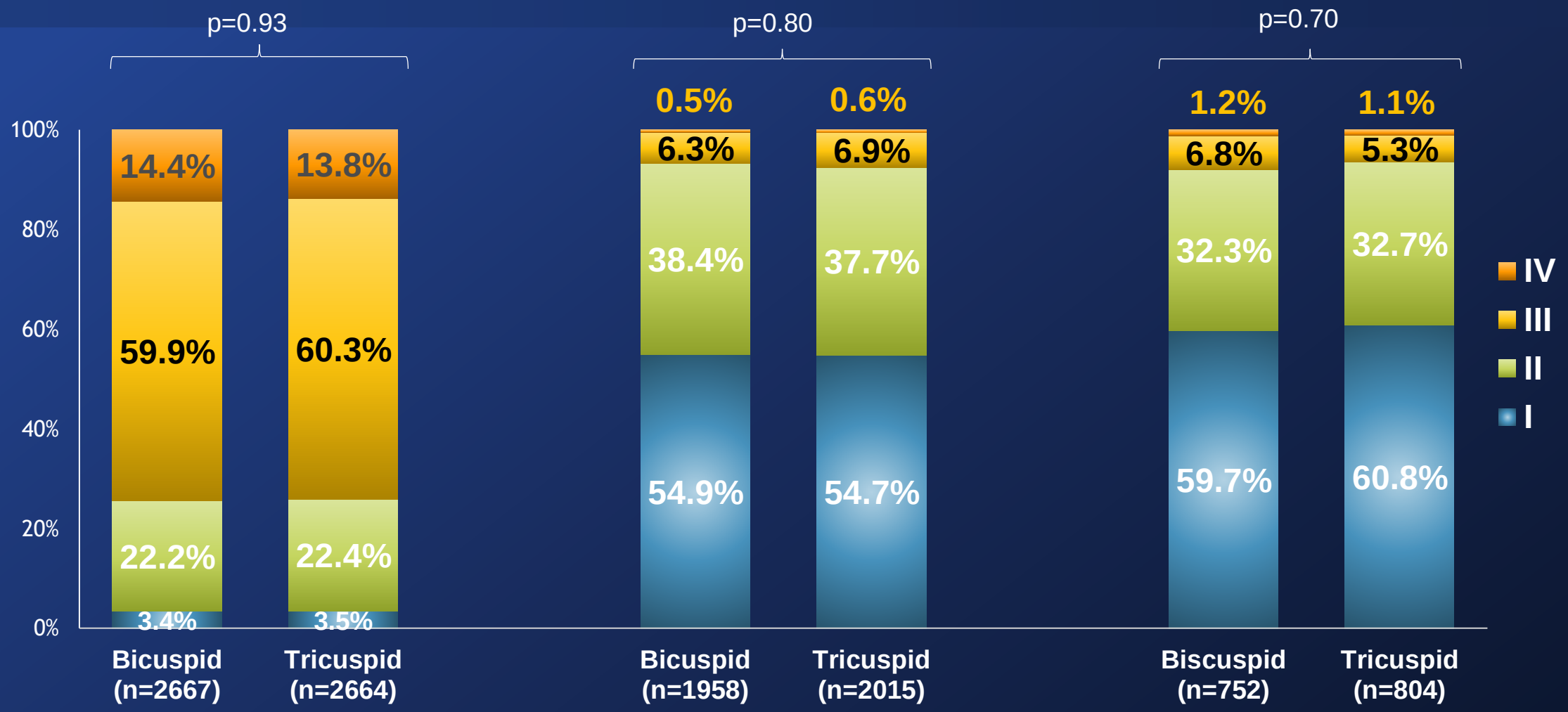
Mean Gradient



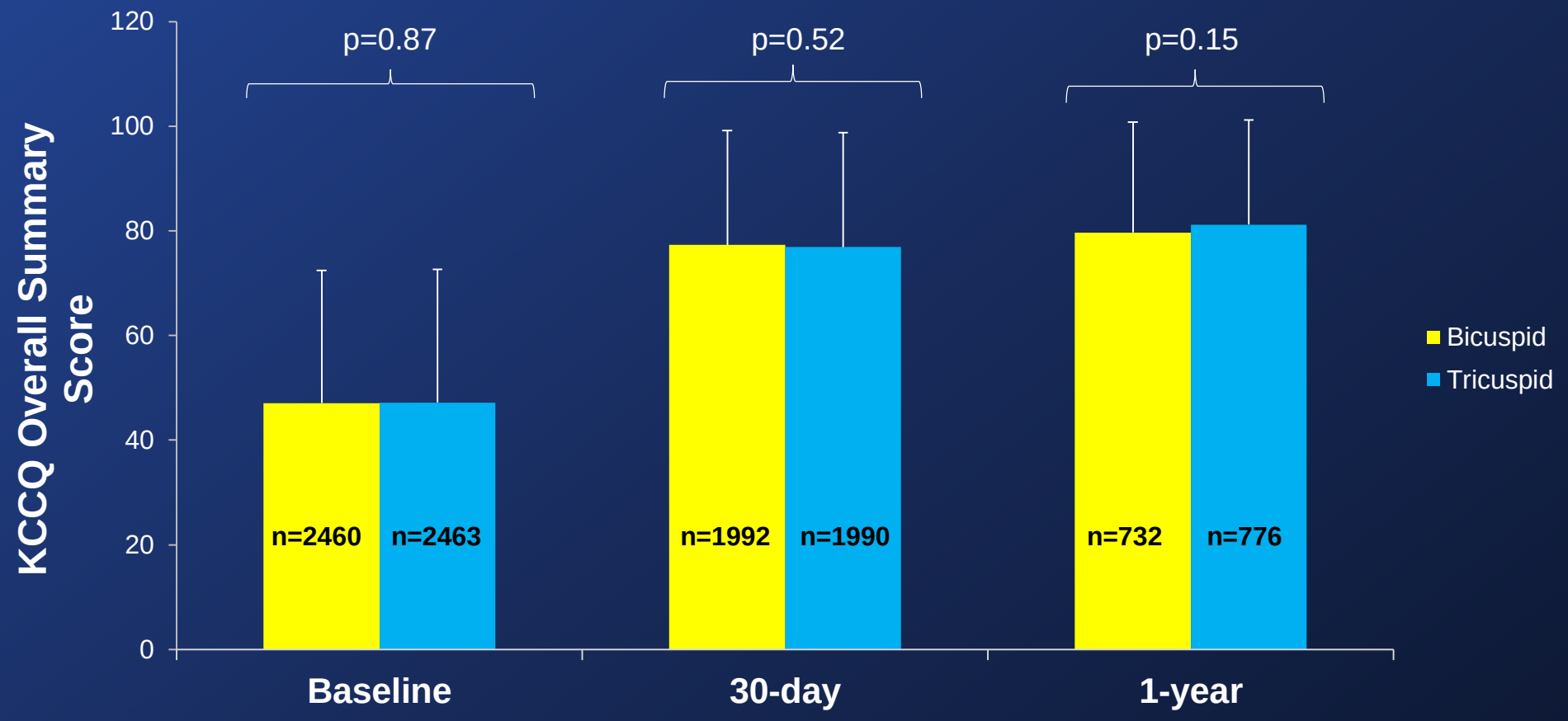
Aortic Valve Area



NYHA Class – Matched



KCCQ – Matched



Limitations

- Lack of center-independent adjudication of adverse events as well as potential under-reporting of adverse events.
- Bicuspid AS represents a heterogeneous anatomic cohort, It is possible that the operators selected the most favorable anatomic subsets while excluding patients with highest risk anatomical features
- Lack of a control group of bicuspid AS patients treated surgically
- Impact of aortopathy on outcomes could not be assessed

Summary

- In this largest real life registry of all consecutive TAVRs in the US, TAVR with balloon expandable Sapien 3 valve for Bicuspid AS, compared to tricuspid AS, was associated with
  - Similar survival at 30 days and 1 year
  - Increased risk of aortic root injury and conversion to open heart surgery; although overall rate was still low (<1.0%).
  - Increased peri-procedural and 30 day stroke rates
  - Equivalent hemodynamics (Similar and significant reduction in transaortic gradients, improvement in aortic valve areas and frequency of paravalvular leak rates)
  - Similar improvement in Quality of Life metrics (NYHA class and KCCQ scores)

Clinical Implications

- This analysis suggests that select bicuspid anatomy is amenable to TAVR with current generation balloon-expandable TAVR technology with acceptable clinical outcomes.

- These data provide an argument for TAVR to be a reasonable alternative for bicuspid AS in patients who are intermediate or high risk for surgical aortic valve replacement and provide a sound basis to conduct a randomized clinical trial in young patients with bicuspid AS who are low risk for surgery.