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The US Pivotal Trial & Clinical Update

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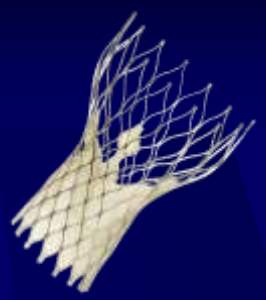
Hospital & Favaloro University Board
Associated Director of TCT
SCAI Board of Thrustees

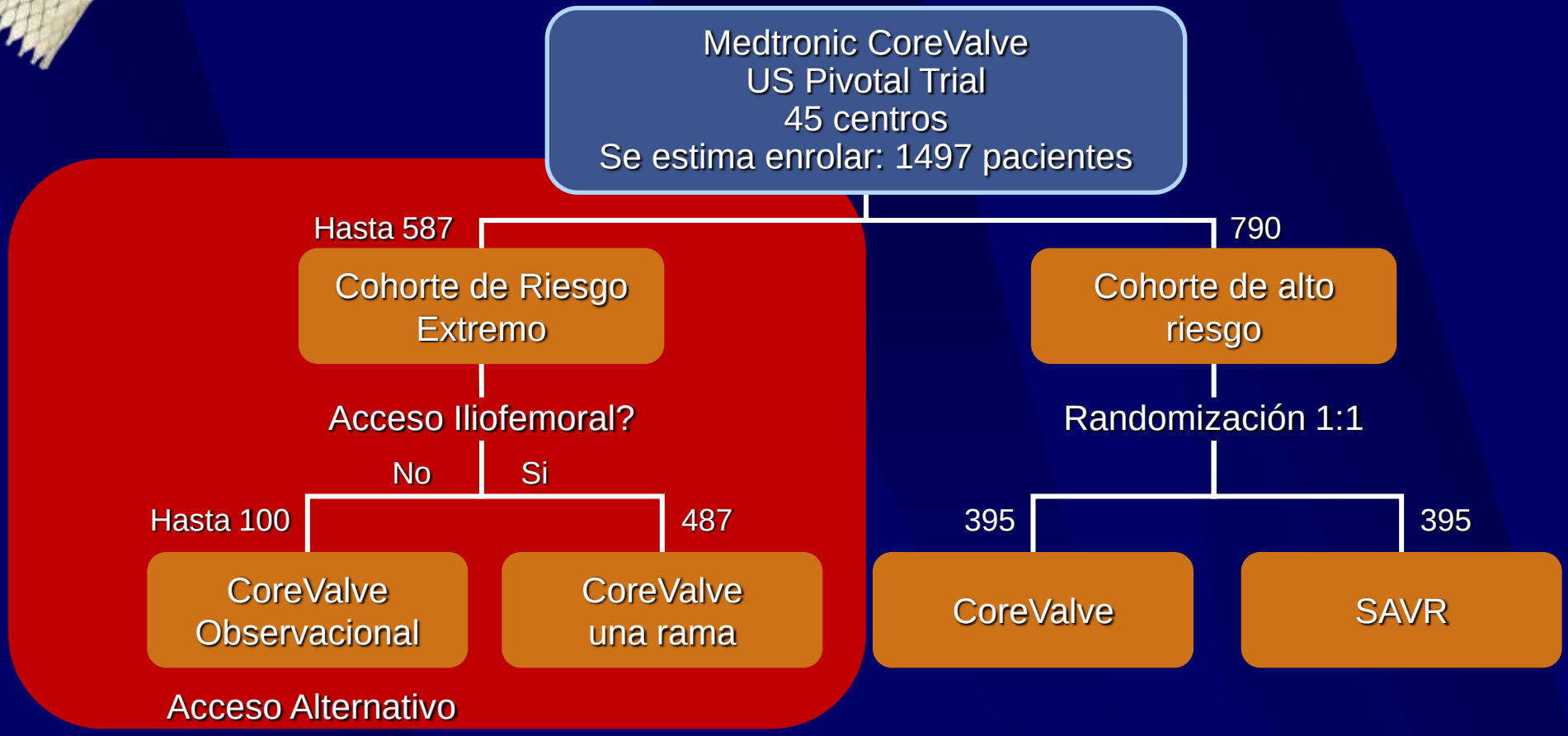
Disclosure

Nombre: Oscar A. Mendiz

- ☐ Consultant: Medtronic, Astra Zeneca.
- ☐ Meeting Sponsorship; Cook, Endologix, BSCI.



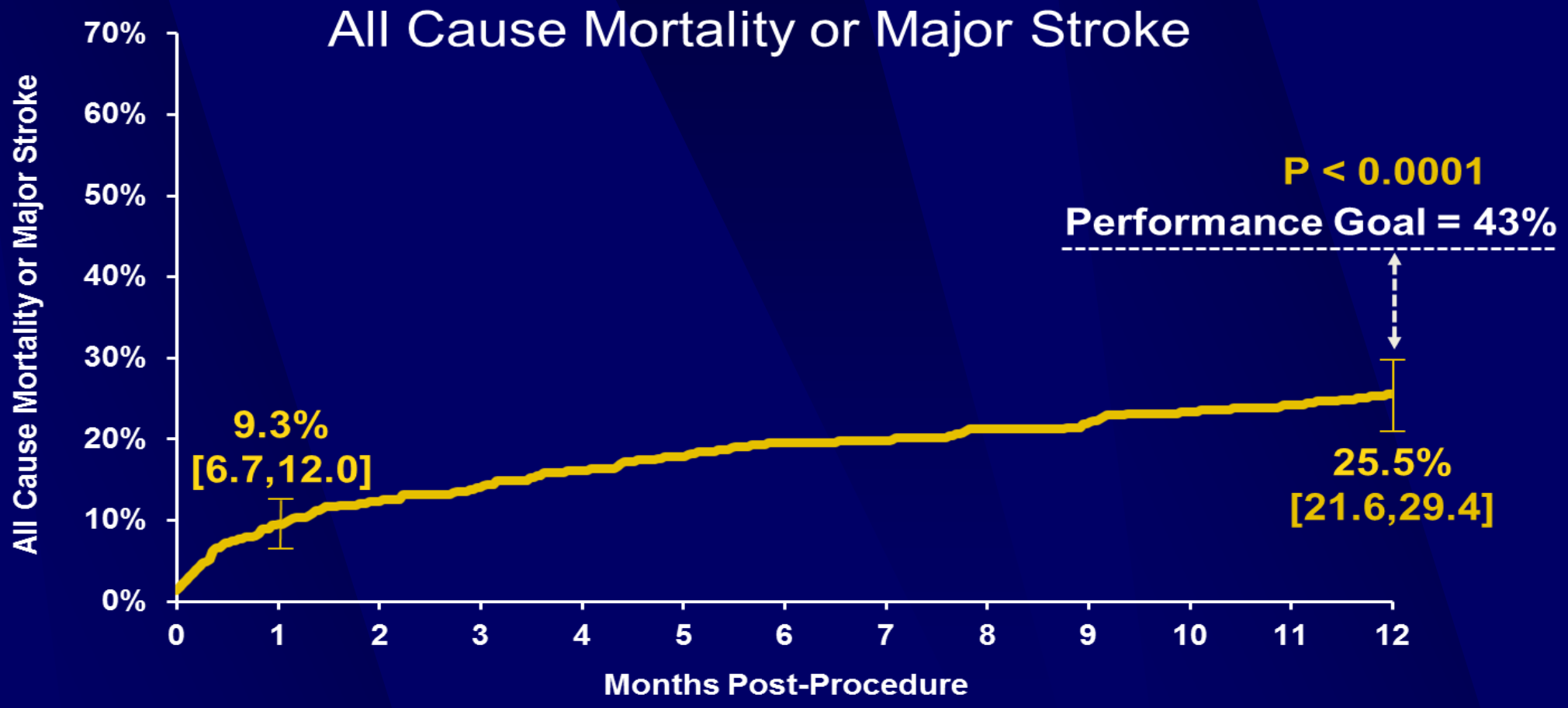
CoreValve® US Pivotal Trial
Diseño del estudio[1-3]



[a]Incluye pacientes con acceso iliofemoral y alternativo.
SAVR=reemplazo quirúrgico.

1. Medtronic CoreValve® U.S. Pivotal Trial. US National Institutes of Health Web site. http://clinicaltrials.gov/ct2/results?term=NCT01240902. Accessed 6/30/11.
2. *Medtronic CoreValve® U.S. Pivotal Trial (Extreme Risk Patients)*. Version 7.0. Mounds View, MN: Medtronic, Inc. Clinical Research; 2011.
3. *Medtronic CoreValve® U.S. Pivotal Trial (High Risk Patients)*. Version 6.0. Mounds View, MN: Medtronic, Inc. Clinical Research; 2011.

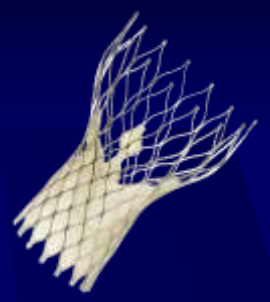
CoreValve® US Pivotal Trial : Primary end Point



Popma J, J Am Coll Cardiol. 2014;63(19):1972-1981

TAVR:

Surgical Candidates with High Surgical Risk



CoreValve® US Pivotal Trial
Diseño del estudio[1-3]

Medtronic CoreValve
US Pivotal Trial
45 centros
Se estima enrolar: 1497 pacientes

Hasta 587
Cohorte de Riesgo Extremo

Acceso Iliofemoral?

No
Hasta 100
CoreValve Observacional

Si
487
CoreValve una rama

Acceso Alternativo

790
Cohorte de alto riesgo

Randomización 1:1

395
CoreValve

395
SAVR

[a]Incluye pacientes con acceso iliofemoral y alternativo.
SAVR=reemplazo quirúrgico.

1. Medtronic CoreValve® U.S. Pivotal Trial. US National Institutes of Health Web site. http://clinicaltrials.gov/ct2/results?term=NCT01240902. Accessed 6/30/11.
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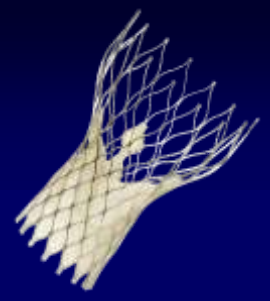
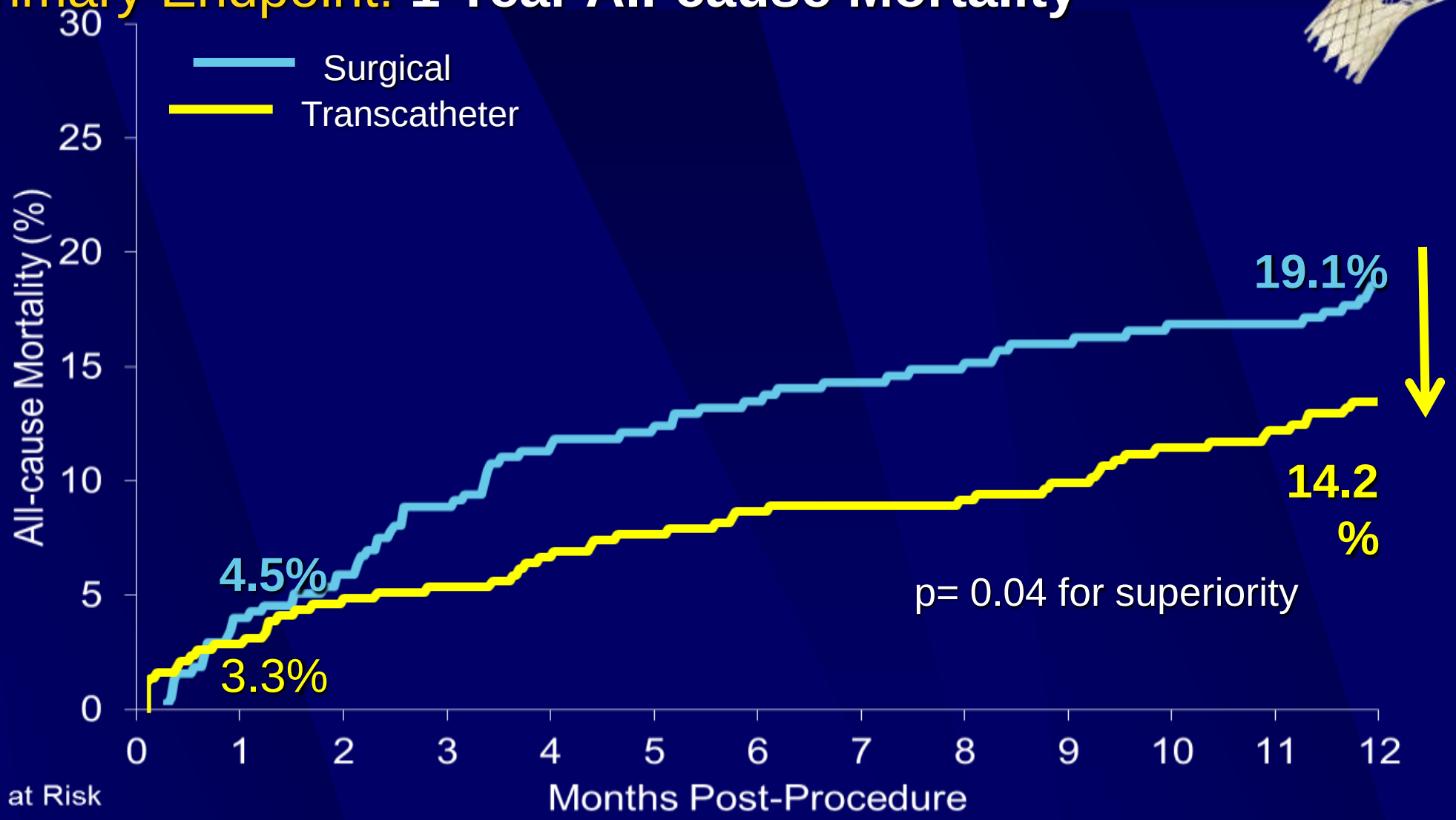
3. *Medtronic CoreValve® U.S. Pivotal Trial (High Risk Patients)*. Version 6.0. Mounds View, MN: Medtronic, Inc. Clinical Research; 2011.

CoreValve® US Pivotal Trial
Primary Endpoint: **1 Year All-cause Mortality**





No. at Risk												
Surgical	357	341				297						274
Transcatheter	390	377				353						329

Adams DH, et al; U.S. CoreValve Clinical Investigators. N Engl J Med. 2014 May 8;370(19):1790-8

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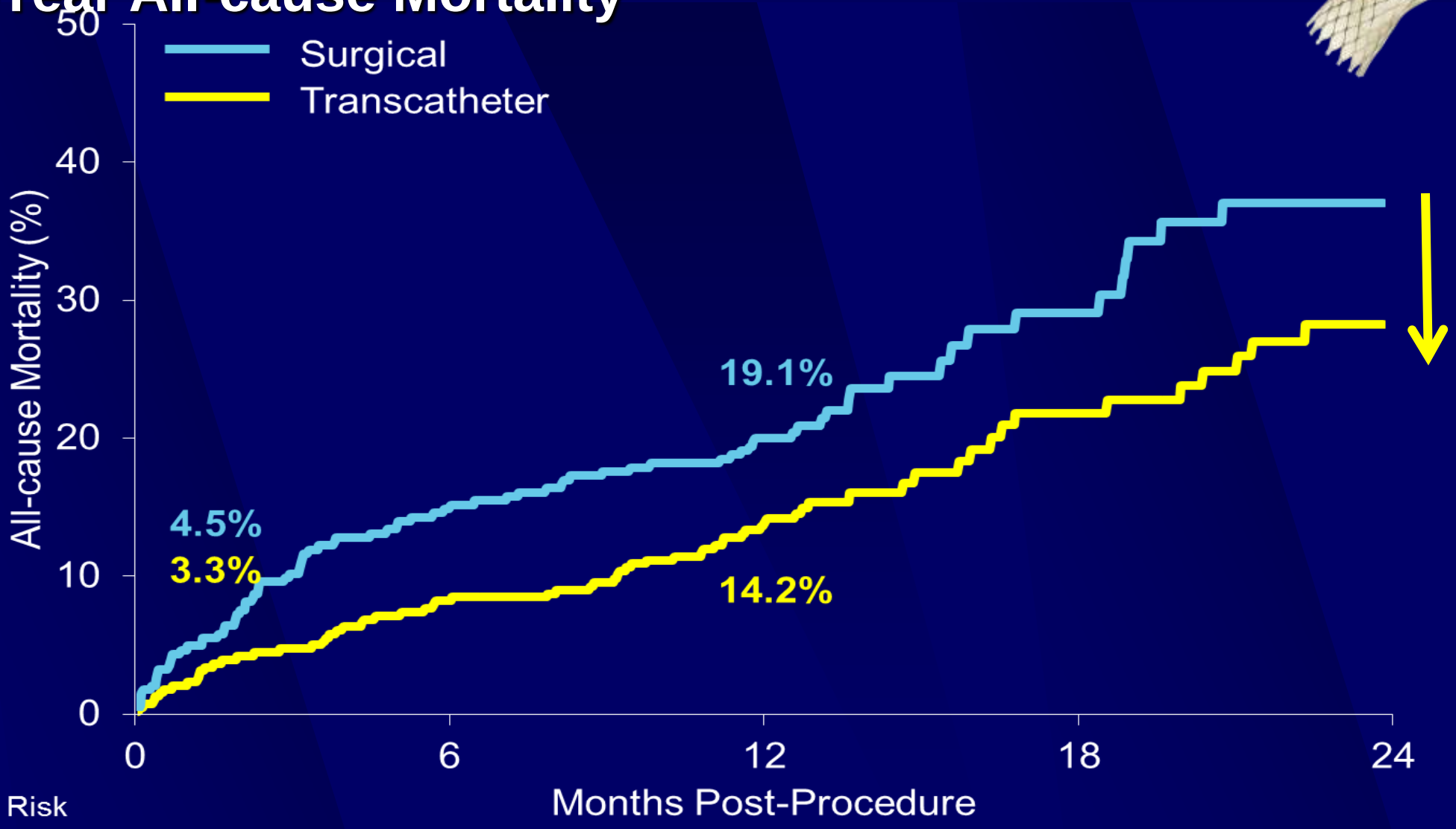
CoreValve® US Pivotal Trial

2-Year All-cause Mortality

Adams D; et al. ACC 2014



No. at Risk					
Surgical	357	341	274	28	
Transcatheter	390	377	329	38	

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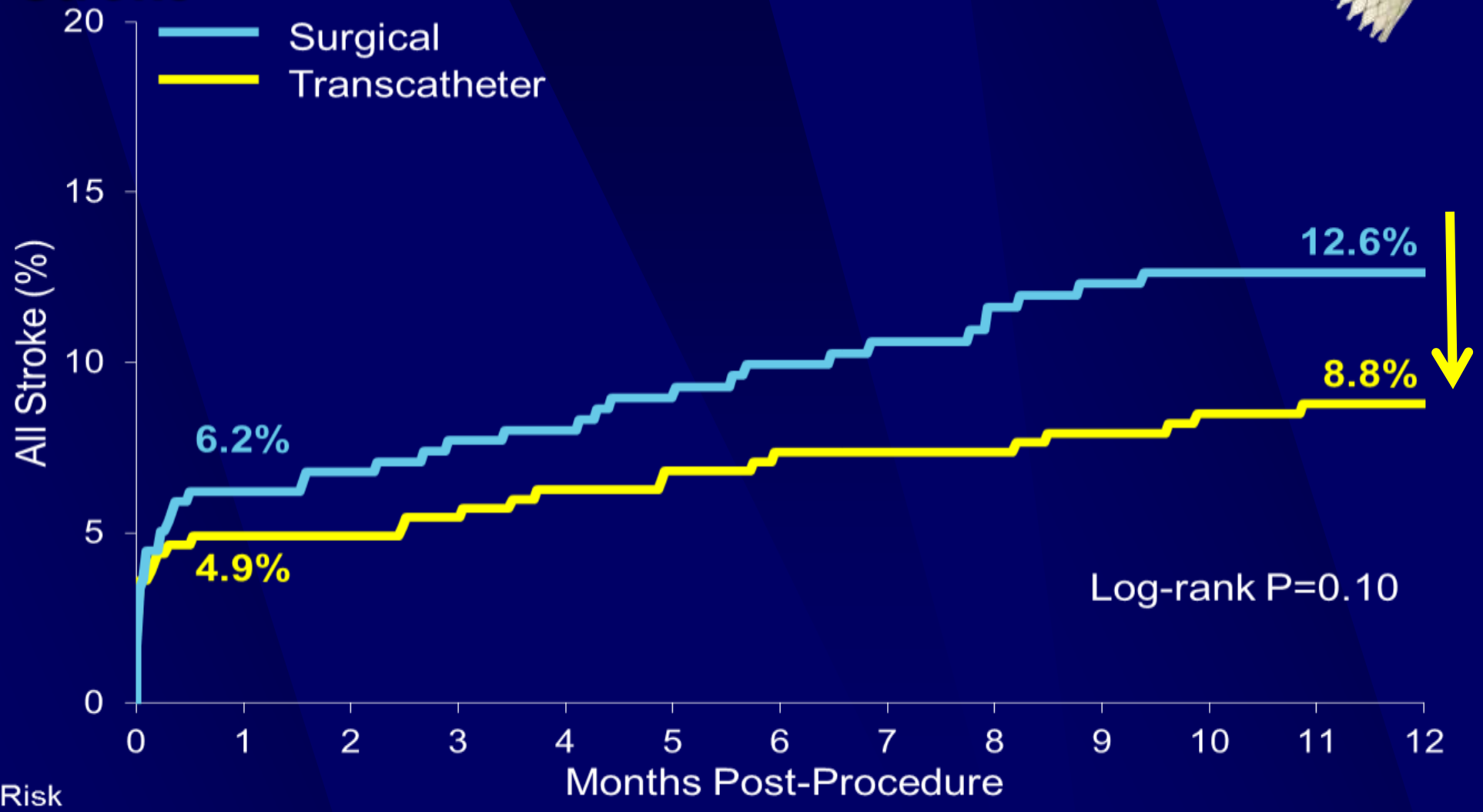
CoreValve® US Pivotal Trial:
All Stroke

Adams D; et al. ACC 2014



No. at Risk

Surgical	357	322	274	249	
Transcatheter	390	363	334	314	

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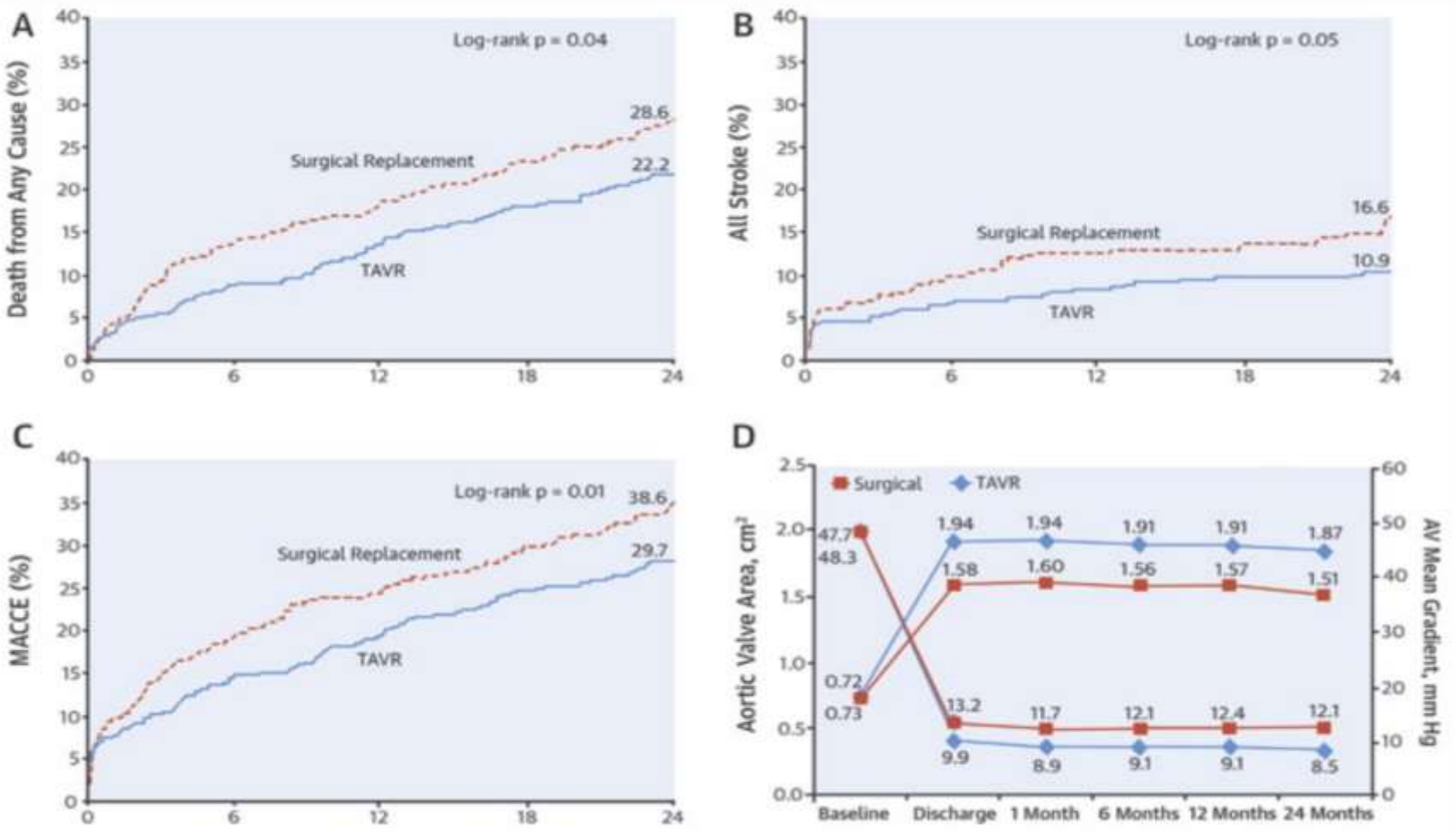
TAVR: for High Risk Surgical Ptes

- Two Studies and several registries support TAVR as and alternative to SAVR for this indication
- TAVR for surgical candidates at high risk (IIaB):
  - Similar outcomes (mortality: PARTNER = ; CoreValve ↓)
  - Durability would be questionable in case of younger Ptes.
  - More AR
  - More PPM
  - Stroke ? (PARTNER ↑ - CoreValve ↓)
- Cost/Effectiveness: ???

TAVR:

Durability

2-Year Outcomes in Patients Undergoing Surgical or Self-Expanding Transcatheter Aortic Valve Replacement



Reardon, M.J. et al. J Am Coll Cardiol. 2015; 66(2):113-21.

Michael J. Reardon. J Am Coll Cardiol. 2015;66(2):113-121. doi:10.1016/j.jacc.2015.05.017

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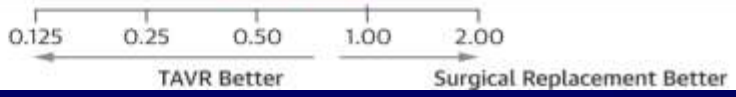
2-Year Outcomes in Patients Undergoing Surgical or Self-Expanding Transcatheter Aortic Valve Replacement

Subgroup	TAVR	Surgical Replacement	Hazard Ratio (95% CI)	p Value for Interaction
	No. of patients with event / total no. of patients (%)			
Age				0.26
≤85 yr	36/204 (17.8)	52/195 (27.7)	0.62 (0.40, 0.95)	
>85 yr	49/187 (27.0)	47/164 (29.7)	0.87 (0.58, 1.29)	
Sex				0.47
Male	49/207 (24.0)	52/188 (28.9)	0.82 (0.55, 1.21)	
Female	36/184 (20.1)	47/171 (28.3)	0.66 (0.43, 1.02)	
Body-mass index				0.71
≤30	67/284 (24.2)	72/247 (30.2)	0.75 (0.54, 1.05)	
>30	18/107 (17.0)	27/112 (25.1)	0.66 (0.37, 1.21)	
STS PROM estimate				0.11
≤7%	30/202 (15.0)	45/181 (26.3)	0.56 (0.35, 0.89)	
>7%	55/189 (29.9)	54/178 (31.1)	0.91 (0.63, 1.33)	
Left ventricular ejection fraction				0.26
≤60%	57/244 (23.9)	62/238 (26.9)	0.85 (0.59, 1.21)	
>60%	28/147 (19.4)	36/120 (31.7)	0.60 (0.36, 0.98)	
Hypertension				0.11
Yes	81/372 (22.2)	91/345 (27.4)	0.78 (0.58, 1.05)	
No	4/19 (21.1)	8/14 (59.8)	0.29 (0.09, 0.95)	
Previous CABG				0.67
Yes	20/115 (17.6)	27/113 (24.5)	0.66 (0.37, 1.18)	
No	65/276 (24.1)	72/246 (30.6)	0.77 (0.55, 1.07)	
Peripheral vascular disease				0.82
Yes	33/159 (21.2)	42/150 (29.1)	0.70 (0.44, 1.11)	
No	50/229 (22.2)	56/207 (28.1)	0.75 (0.51, 1.10)	
Diabetes				0.97
Yes	25/136 (18.9)	40/162 (25.6)	0.71 (0.43, 1.18)	
No	60/255 (23.9)	59/197 (31.1)	0.72 (0.50, 1.03)	



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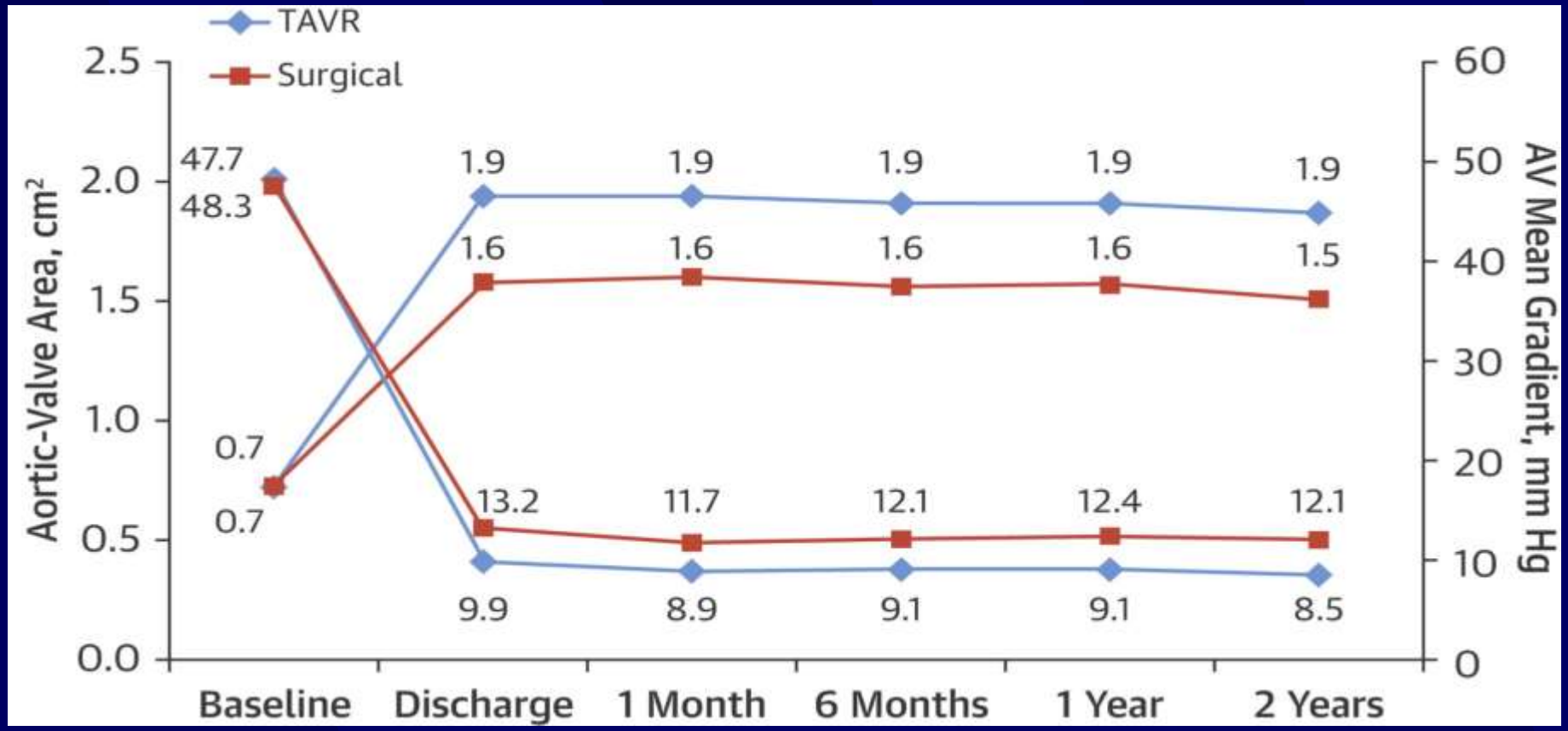
2-Year Outcomes in Patients Undergoing Surgical or Self-Expanding Transcatheter Aortic Valve Replacement



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JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 8, NO. 8, 2015

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2015.03.024

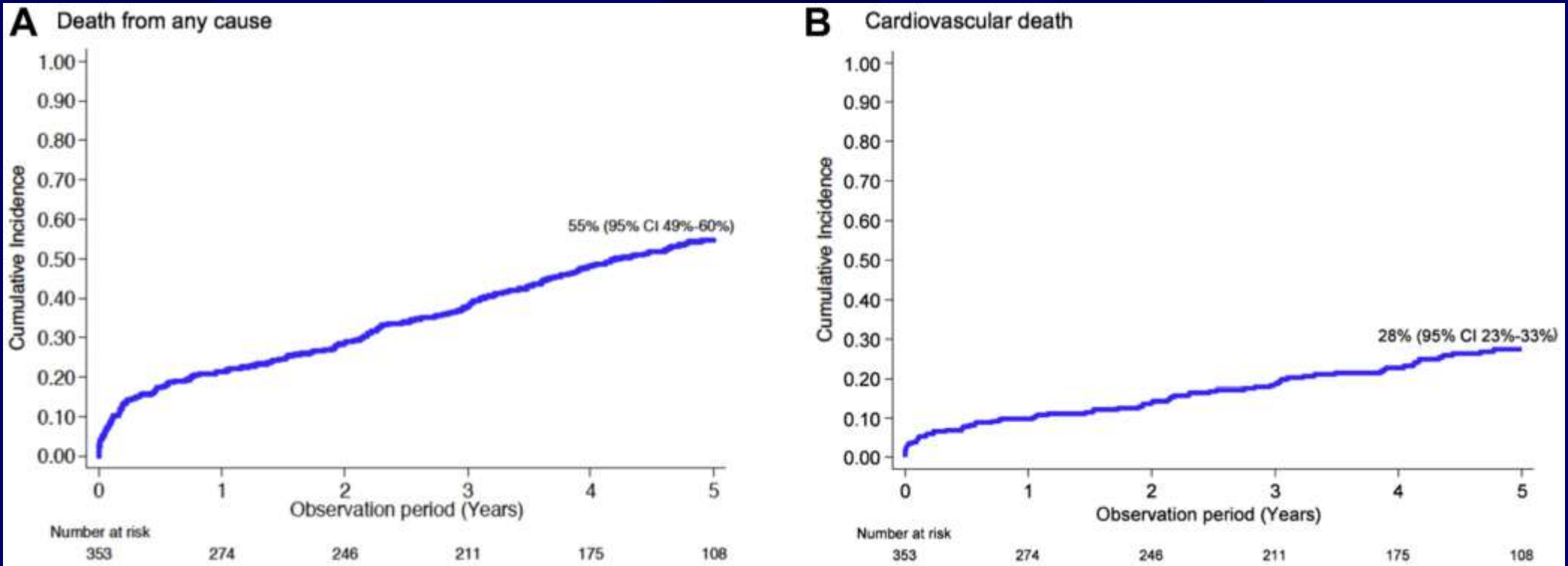
STRUCTURAL

5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis

Marco Barbanti, MD,*† Anna Sonia Petronio, MD,‡ Federica Ettori, MD,§ Azeem Latib, MD,‖ Francesco Bedogni, MD,¶ Federico De Marco, MD,# Arnaldo Poli, MD,** Carla Boschetti, MD,†† Marco De Carlo, MD,‡ Claudia Fiorina, MD,§ Antonio Colombo, MD,‖ Nedy Brambilla, MD,¶ Giuseppe Bruschi, MD,# Paola Martina, MD,** Claudia Pandolfi, MD,†† Cristina Giannini, MD,‡ Salvatore Curello, MD,§ Carmelo Sgroi, MD,*† Simona Gulino, MD,* Martina Patanè, MD,* Yohei Ohno, MD,* Claudia Tamburino, MD,* Guilherme F. Attizzani, MD,* Sebastiano Immè, MD,* Alessandra Gentili, MS,‡‡ Corrado Tamburino, MD, PhD*†

5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis

8 Italian Centers; n=353 Ptes



Marco Barbanti., et al. **J Am Coll Cardiol Intv. Published online June 24, 2015. doi:10.1016/j.jcin.2015.03.024**

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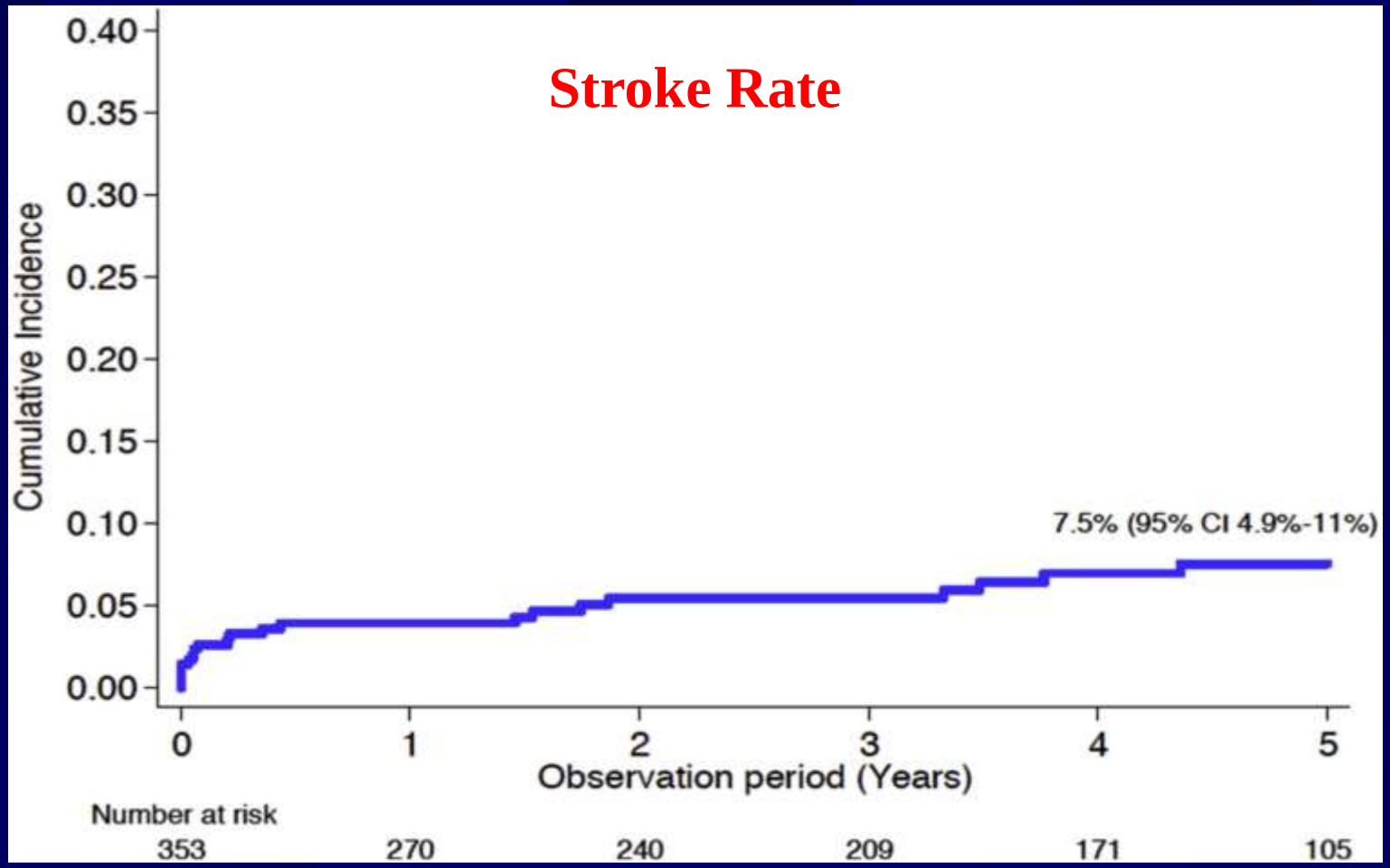

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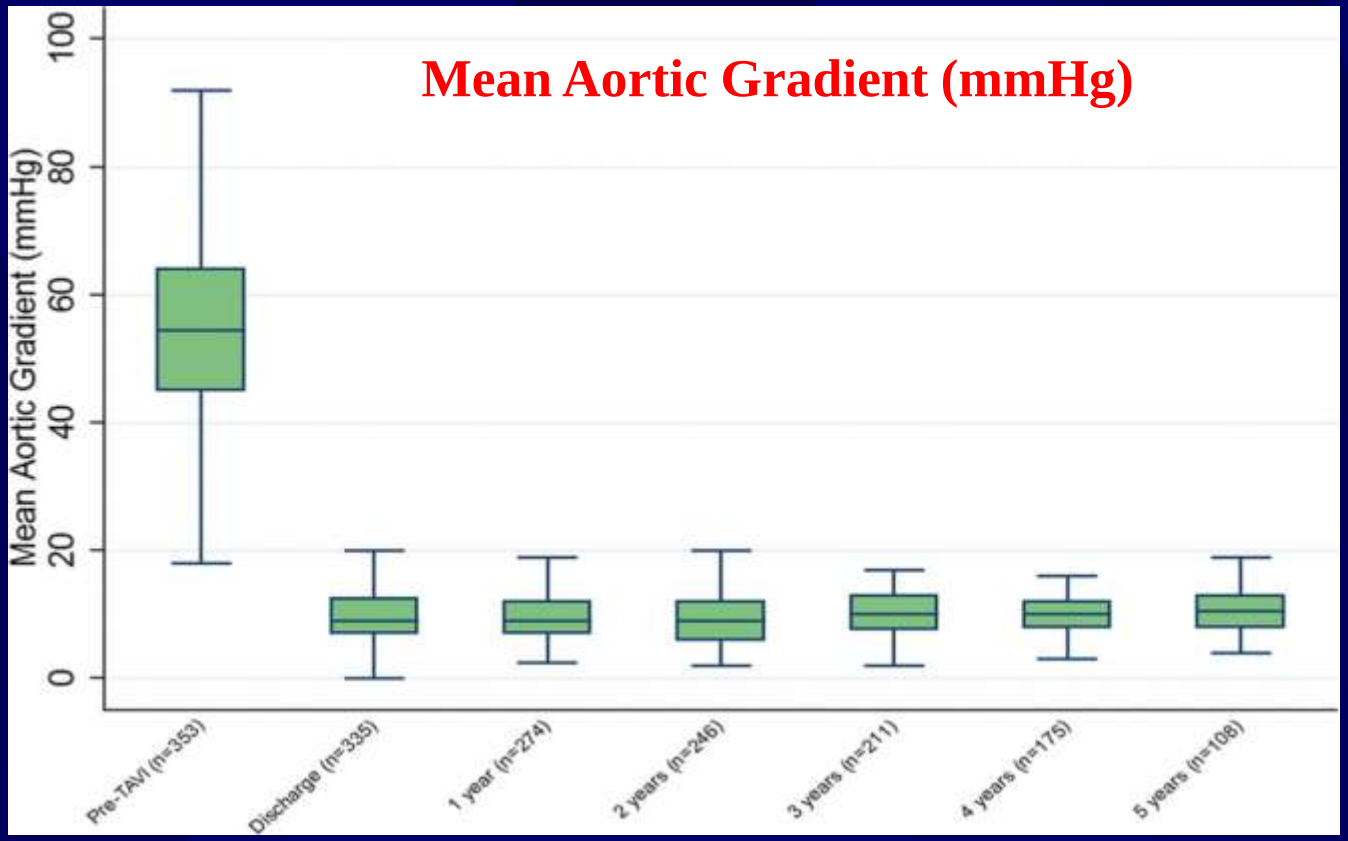
5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis

Prosthesis Performance

Time trends in transaortic mean gradient. TAVI = transcatheter aortic valve implantation.



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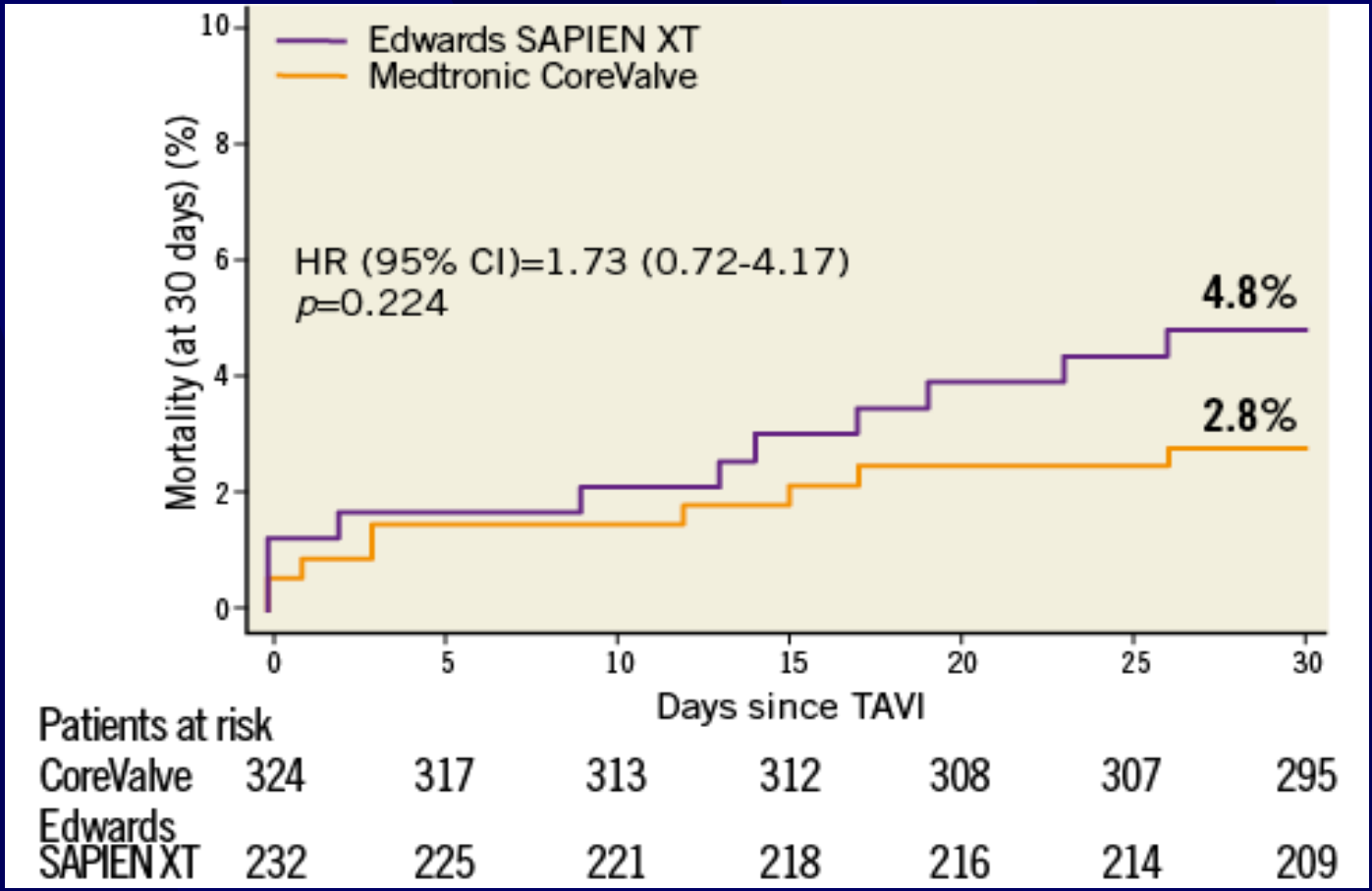
TAVR:

Real Live Outcomes

Short-term clinical outcomes among patients undergoing transcatheter aortic valve implantation in Switzerland: the Swiss TAVI registry



Wenaweser P, et al. EuroIntervention 2014;10:982-989 published online ahead of print April 2014

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ADVANCE | Procedural Results

Procedural Parameters	
N=996	**%**
Successful vascular access, delivery & deployment of device & successful retrieval of the delivery system	97.5
Correct position of the device in the proper anatomical location	98.7
Mean aortic valve gradient < 20 mmHg (discharge echo)	96.2
One valve used	96.0

Major Complications, Valve Related	
N=996	**%**
Annulus Rupture	0.0
Valve Embolization	0.2
Conversion to open AVR	0.1
Coronary Compromised	0.1

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ADVANCE | Primary Endpoint

Endpoint	1 Month	1 Year	2 Years	3 Years
N=996	%*	%*	%*	%*
MACCE	8.0	21.0	30.1	38.5
All-cause Mortality	4.5	17.6	25.5	33.7
Myocardial Infarction	0.2	0.9	2.5	2.6
Emergent Cardiac Surgery or Percutaneous Re-intervention	1.3	1.6	1.9	2.4
Stroke	3.0	4.4	5.6	6.5
Minor	1.8	2.3	3.0	3.3
Major	1.2	2.1	2.9	3.5

*Kaplan-Meier Estimates

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ADVANCE | Additional VARC 1 Endpoints

Endpoint	1 Month	1 Year	2 Year	3 Year
N=996	%*	%*	%*	%*
Cardiovascular Mortality	3.4	11.6	16.7	22.3
Bleeding	29.0	32.0	33.8	35.3
Life Threatening or Disabling Bleeding	4.0	4.9	5.6	6.1
Major Bleeding	9.7	11.2	12.5	12.7
Minor Bleeding	17.4	19.3	20.1	21.1
Vascular Complications	20.7	21.8	22.0	22.0
Major	10.9	12.0	12.3	12.3
Minor	10.2	10.3	10.3	10.3
Acute Kidney Injury—Stage III†	0.4	0.6	0.6	0.6
New Pacemaker Implantation	26.3	29.1	30.5	31.4

*Kaplan-Meier Estimates
†New AKI that occurred outside of the 72 hr post-TAVI window are included

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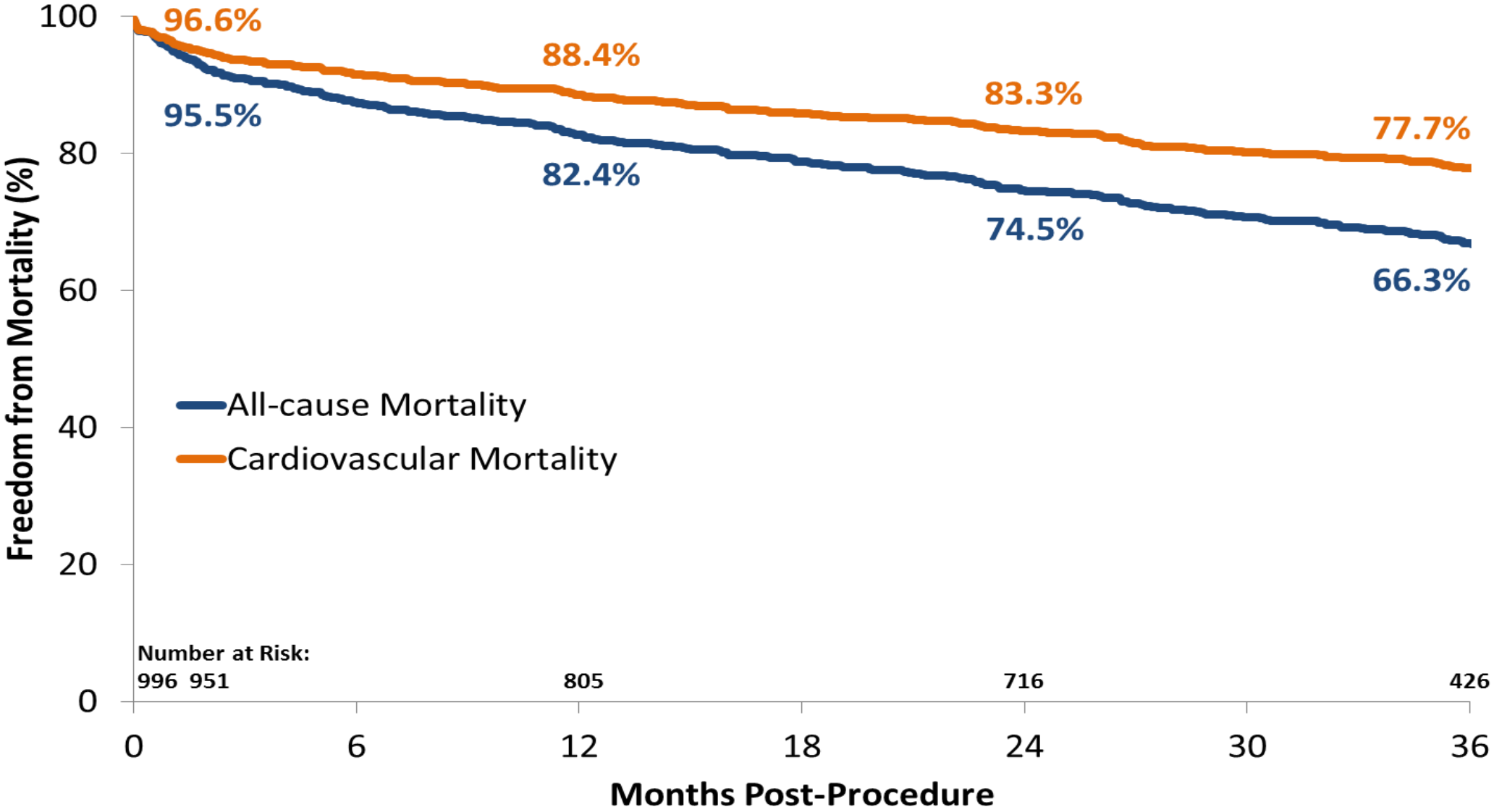
ADVANCE | 3-Year Survival



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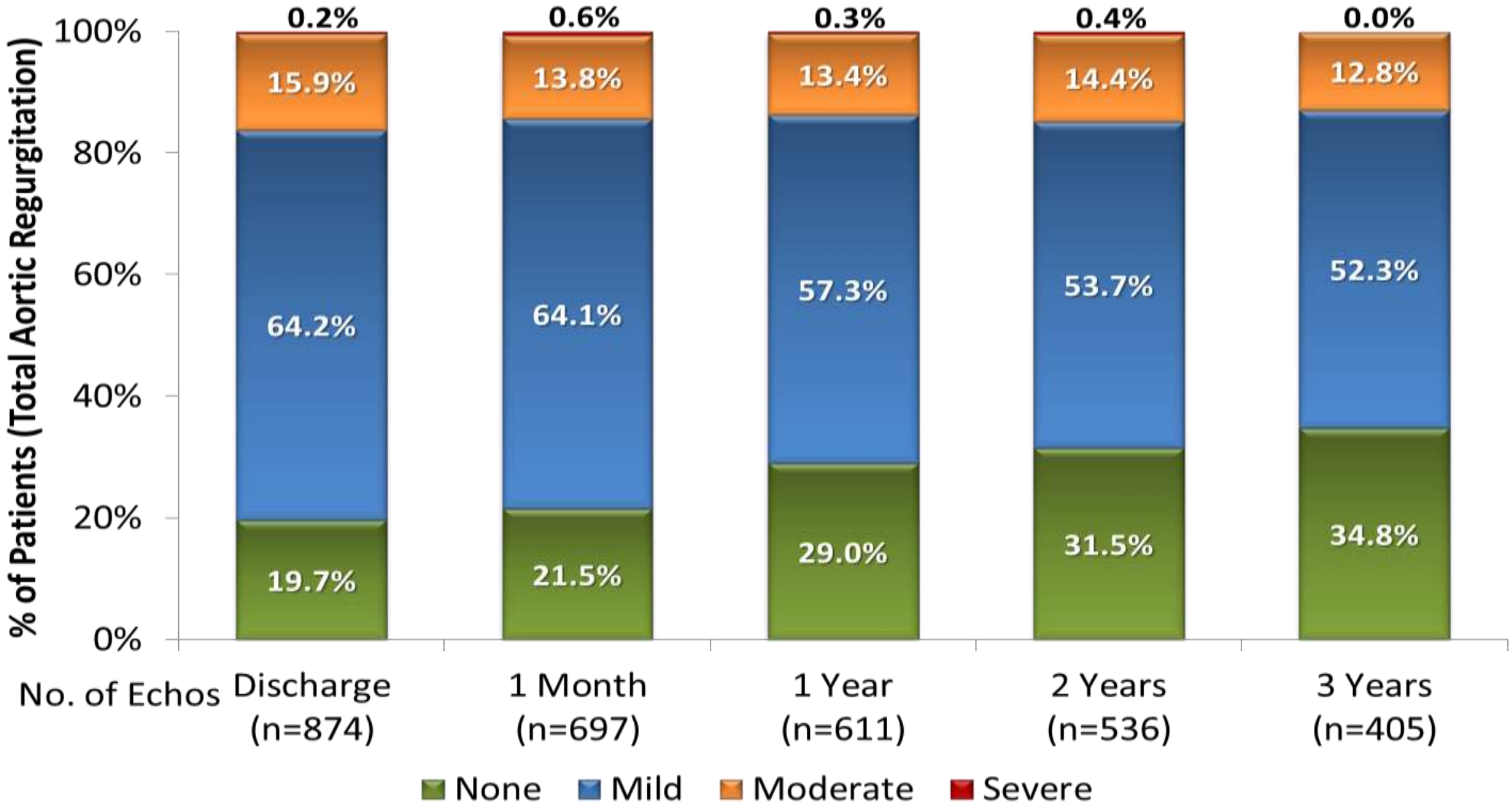
ADVANCE | Aortic Regurgitation

Echo Assessment



TAVR: Fundación Favaloro Experience

Population	**n=160**
Inclusion Period	10/2009-05/2015
Age (years)	80.7±7.3
>80 years (%)	92 (57,5)
Male (%)	80 (50)
Logistic EuroScore (%)	21.4%±0.5
Valve-in-Valve (%)	2 (1.2)
Combined (PCI + TAVR within 3 months)	56 (35%)

TAVR: Fundación Favaloro Experience
30-day Outcomes

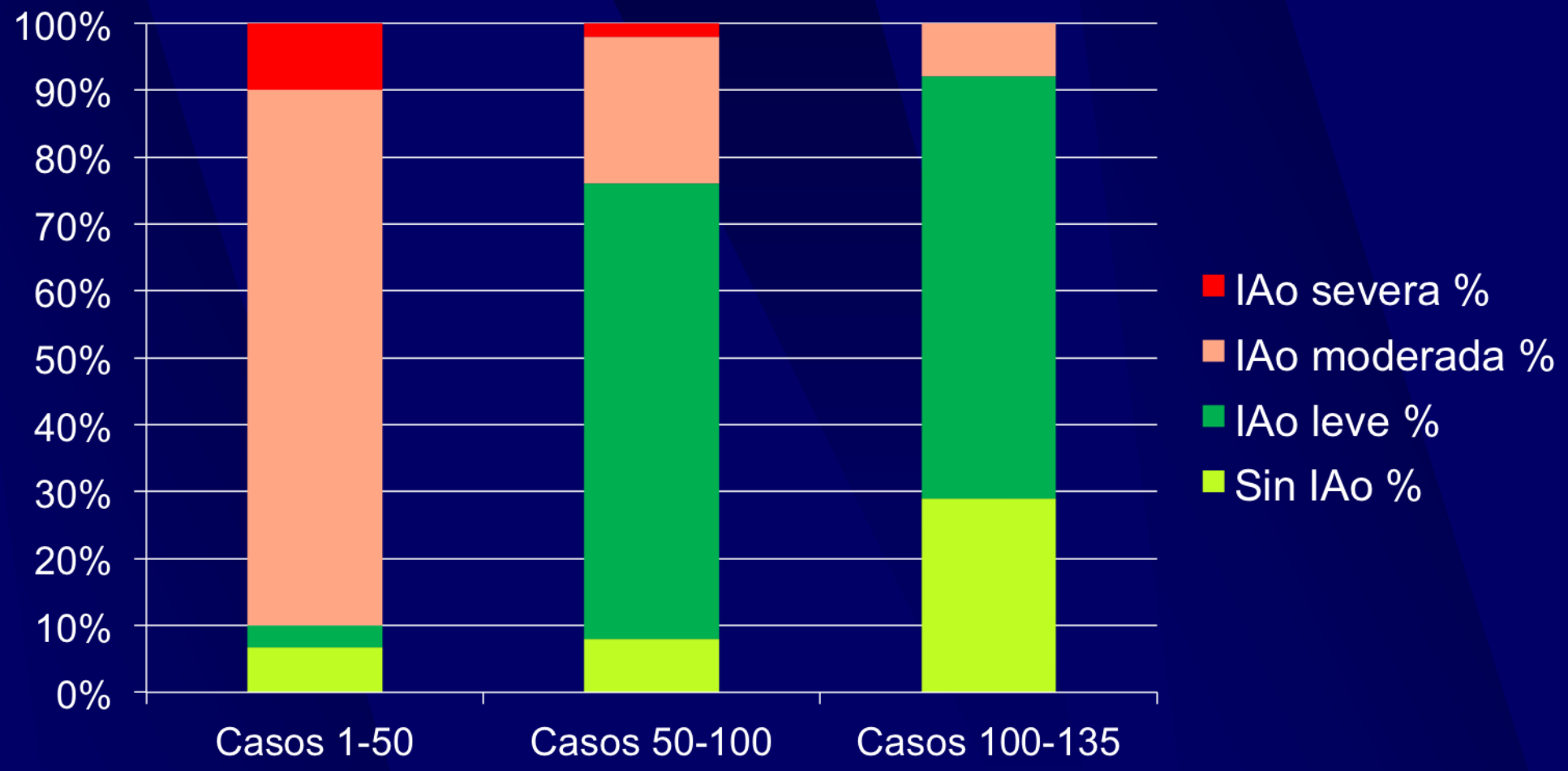
30-days Outcomes (10/2009 ~ 6/2015)	n=160
30-day Overall Mortality (%)	7 (4.4)
Surgical Convertion (%)	-
Need of a Second Valve (%)	3 (1.9)
Pericardiocentesis (%)	6 (3.8)
Major ACV (%)	2 (1.2)
Minor ACV (%)	2 (1.2)
Marcapaso definitivo (%)	61 (38.1)
Insuficiencia aórtica moderada a severa	9 (5.6)
Período de internación (días)	5.1±4

TAVR: Fundación Favaloro Experience

Follow-Up Evolution

Follow-Up Evolution	n=144 (94%)
Follow-Up (months)	12.6 ±10 (1-48)
MACE (%)	18 (12.5)
Mortality at Follow-up (%)	16 (11.1)
Related Mortality (%)	7 (4.9)
Stroke (%)	2 (1)
PPM Implantation (>30 días) (%)	9 (6.3)
Asymptomatic (%)	106 (7.4)

AR and Team Experience



Mendiz O, unpublished

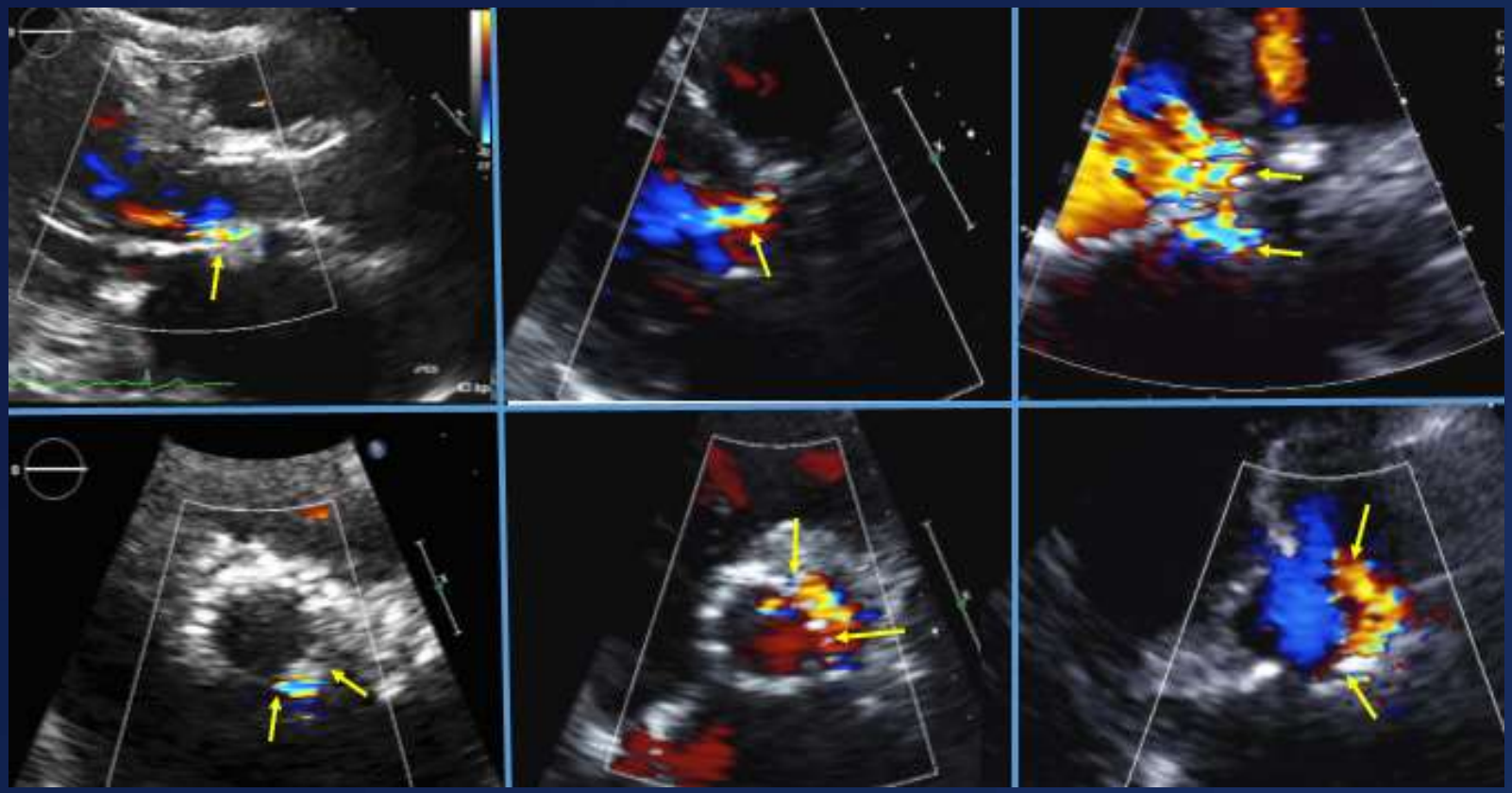
CoreValve US Pivotal Trial

Remodeling of Self-Expanding Transcatheter Aortic Valve Is Responsible for Regression of Paravalvular Aortic Regurgitation: An Observation from CoreValve US Pivotal Trial

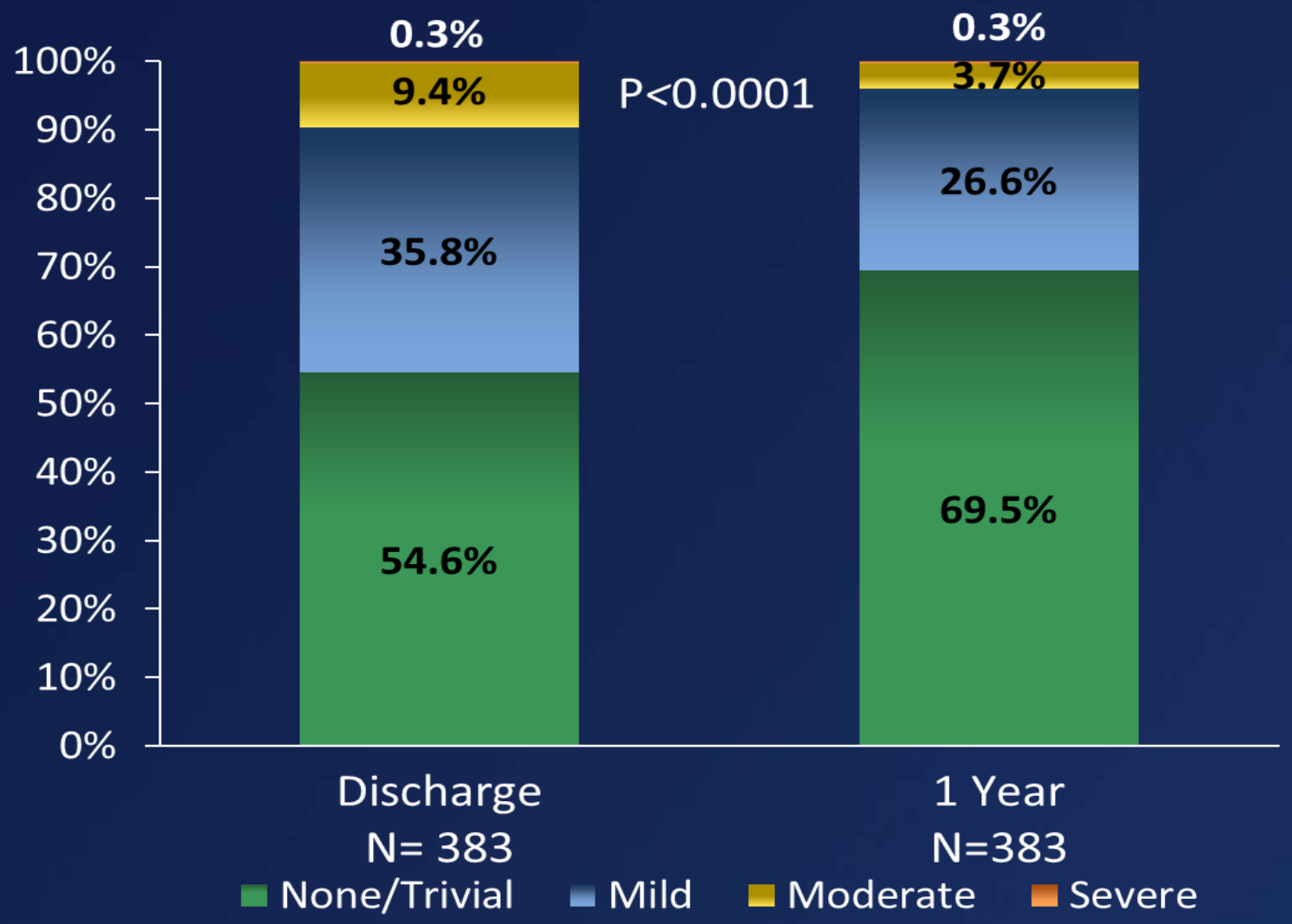
Jae K. Oh, MD

Determination of PVAR Severity by Integrating Multiple Parameters

	Mild	Moderate	Severe
VARC-1	<10% (<36°)	10 – 20% (36-72°)	>20% (>72°)

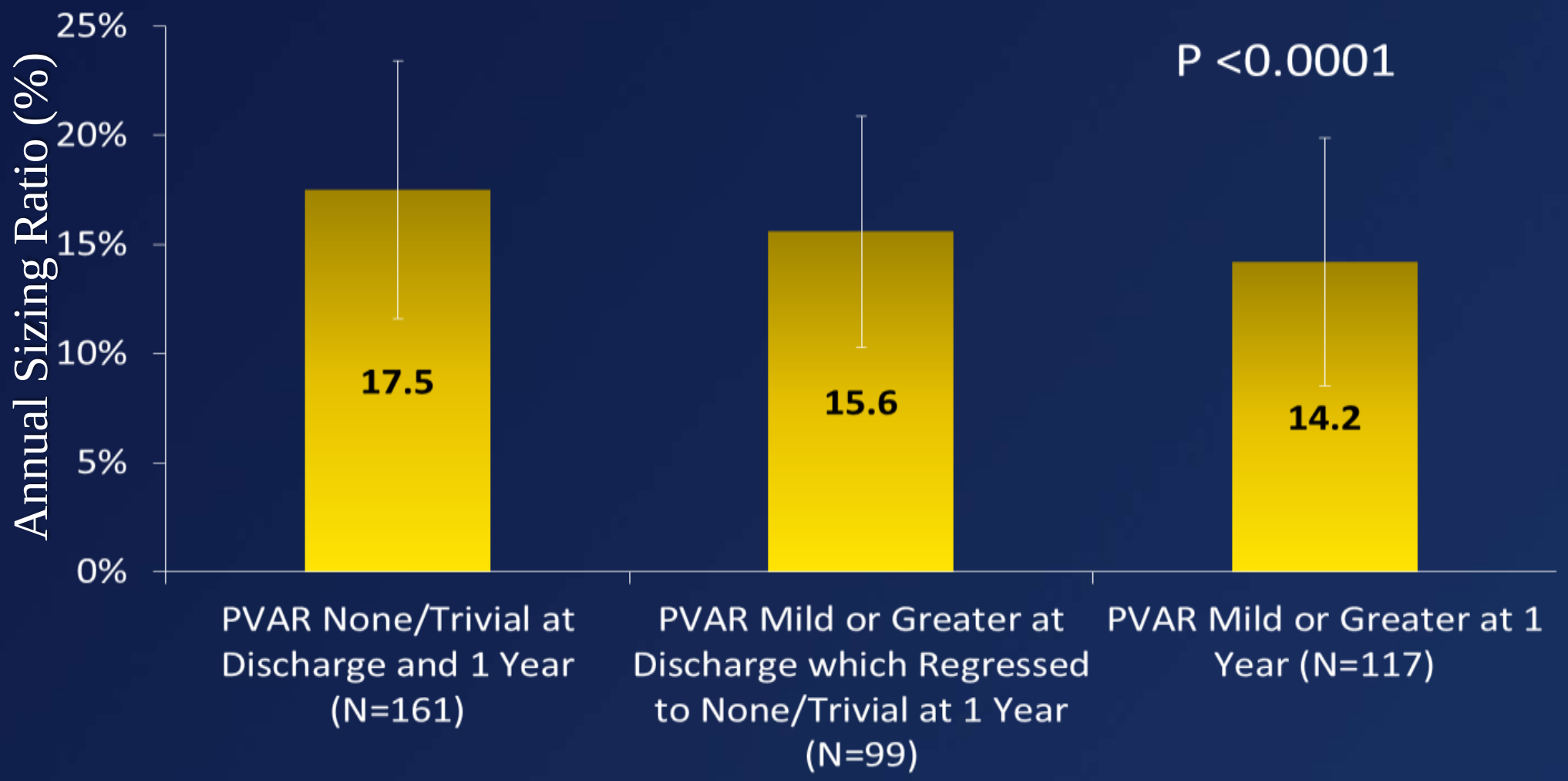


PVAR Paired Comparison at Discharge and 1 Year



Annulus Sizing Ratio

$$\frac{\text{Valve Perimeter} - \text{Annulus Perimeter}}{\text{Annulus Perimeter}} \times 100$$



Conclusions

- TAVR with CoreValve at RCT has:
  - Lower mortality rate than medical treatment for inoperable Ptes.
  - Lower mortality & stroke rate that SAVR at 2 years for high surgicla risk Ptes..
- TAVR with CoreValve in real life practice has shown similar outcomes to RCT according to different registries ans series.
- CoreValve over 3-5 year F-Up has:
  - Excellent valve performance (large EOAs and low mean gradients).
  - Low Stroke rate
  - Sustained moderate PVL rates and trends towards mild PVL reducing over time

Gracias por su Atención

Thank you for your Attention