Centre for
Heart Valve Innovation
St. Paul's Hospital, Vancouver

Is it Early to Tell TAVR in All Patients with Aortic Stenosis?

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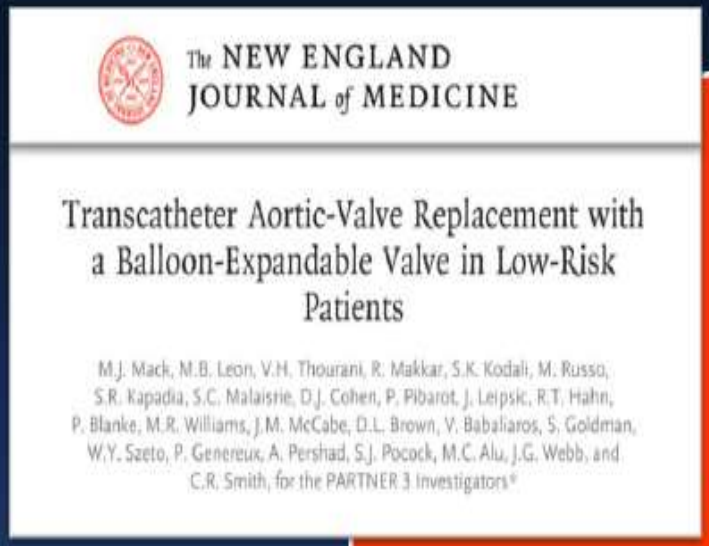
UBC

Disclosure

Consultant: **Edwards Lifesciences**

JC Medical Inc.

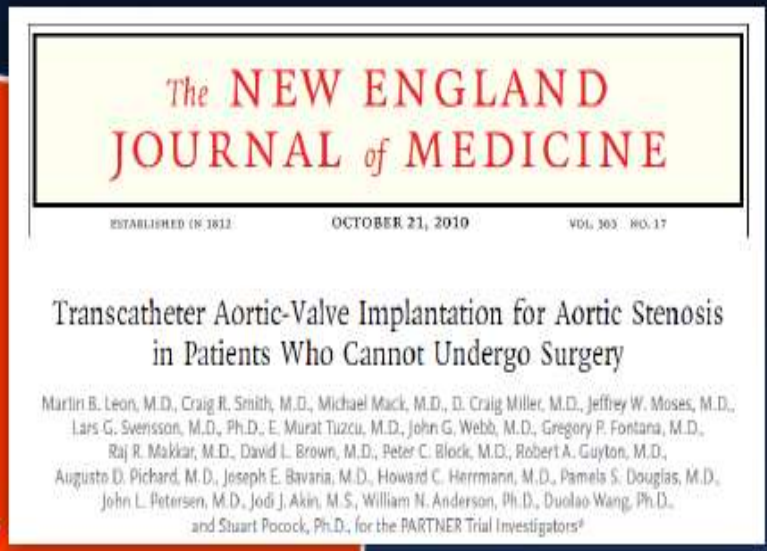
The PARTNER 3 Trial



The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

APRIL 28, 2016

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

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Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

THE PARTNER 3 TRIAL

Key Exclusion Criteria

Anatomic

- Aortic annulus diameter < 16 mm or > 28 mm (3D imaging)
- Bicuspid valve (CT imaging)
- Severe AR (> 3+) or MR (> 3+)
- Severe LV dysfunction (LVEF < 30%)
- Severe calcification of aortic valvar complex (esp. LVOT)
- Vascular anatomy not suitable for safe femoral access
- Complex CAD: ULM, Syntax score > 32, or not amenable for PCI
- Low coronary takeoff (high risk for obstruction)

Clinical

- Acute MI within 1 month
- Stroke or TIA within 90 days
- Renal insufficiency (eGFR < 30 ml/min) and/or renal replacement Rx
- Hemodynamic or respiratory instability
- Frailty (objective assessment; > 2/4+ metrics)

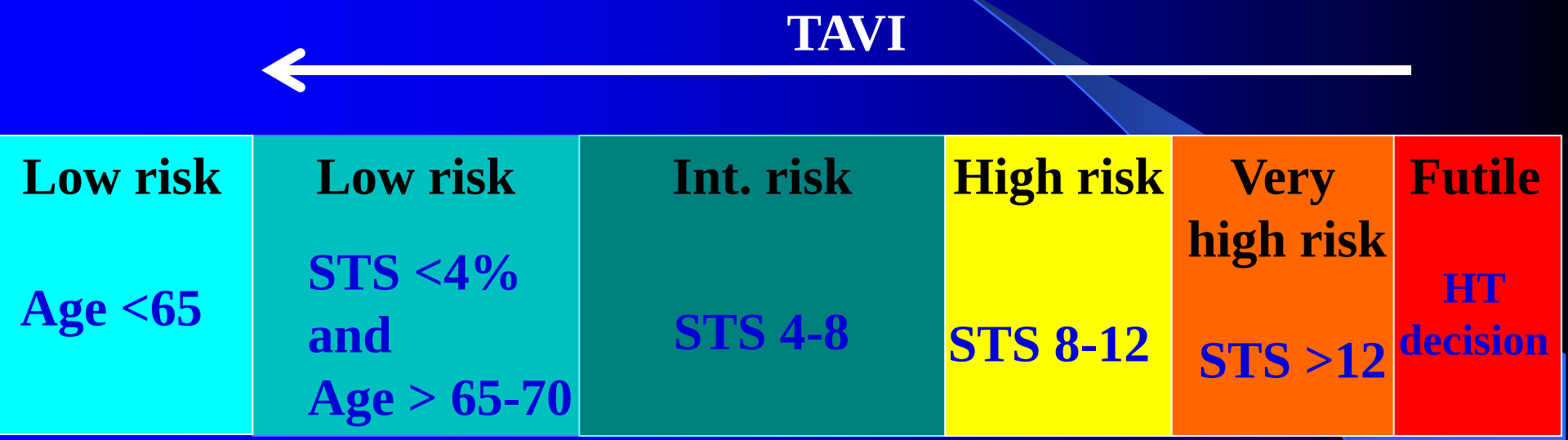
Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)
Age (years)	73.3 ± 5.8	73.6 ± 6.1

My Answer

Yes

It is Early to Tell TAVR in All Patients with Aortic Stenosis!

Evolution of Indication

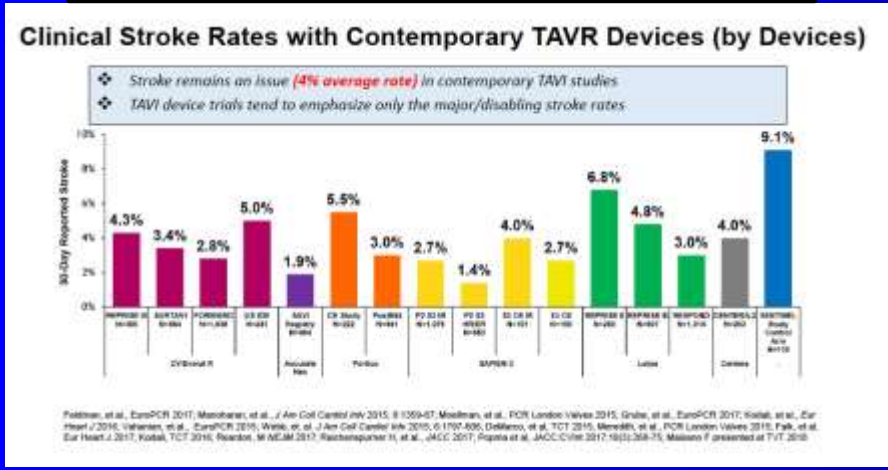


Potential Pitfalls of TAVI in Young Patients

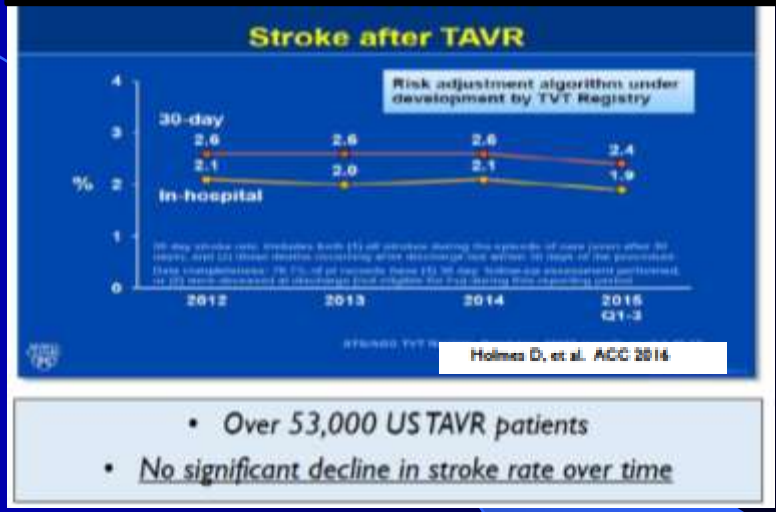
- Stroke and “Silent” embolic event
- Paravalvular leak
- Pacemaker
- Valve thrombosis
- Valve durability
- Redo AVR

Stroke remains an issue

Stroke rates: mean 4% (1.4-9.1%)

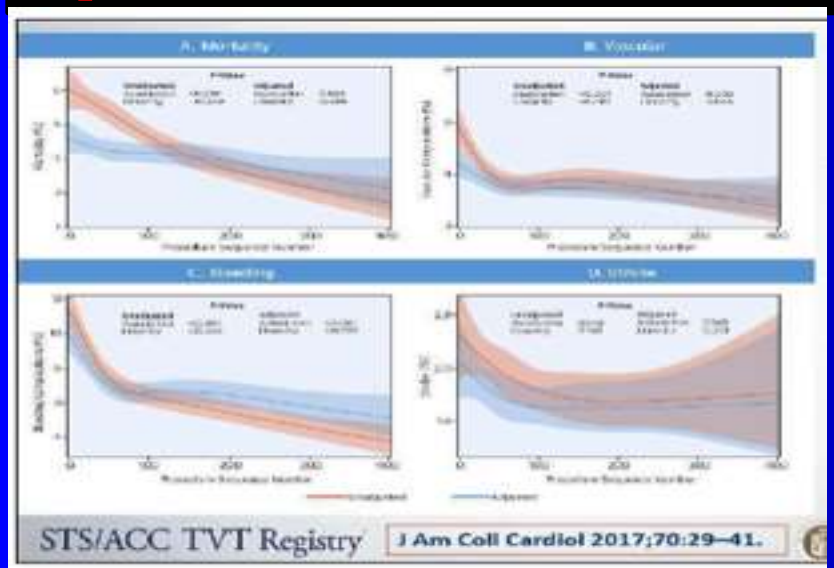


No significant decline in stroke rate



- *Over 53,000 US TAVR patients*
- *No significant decline in stroke rate over time*

Stroke is independent of operator experience

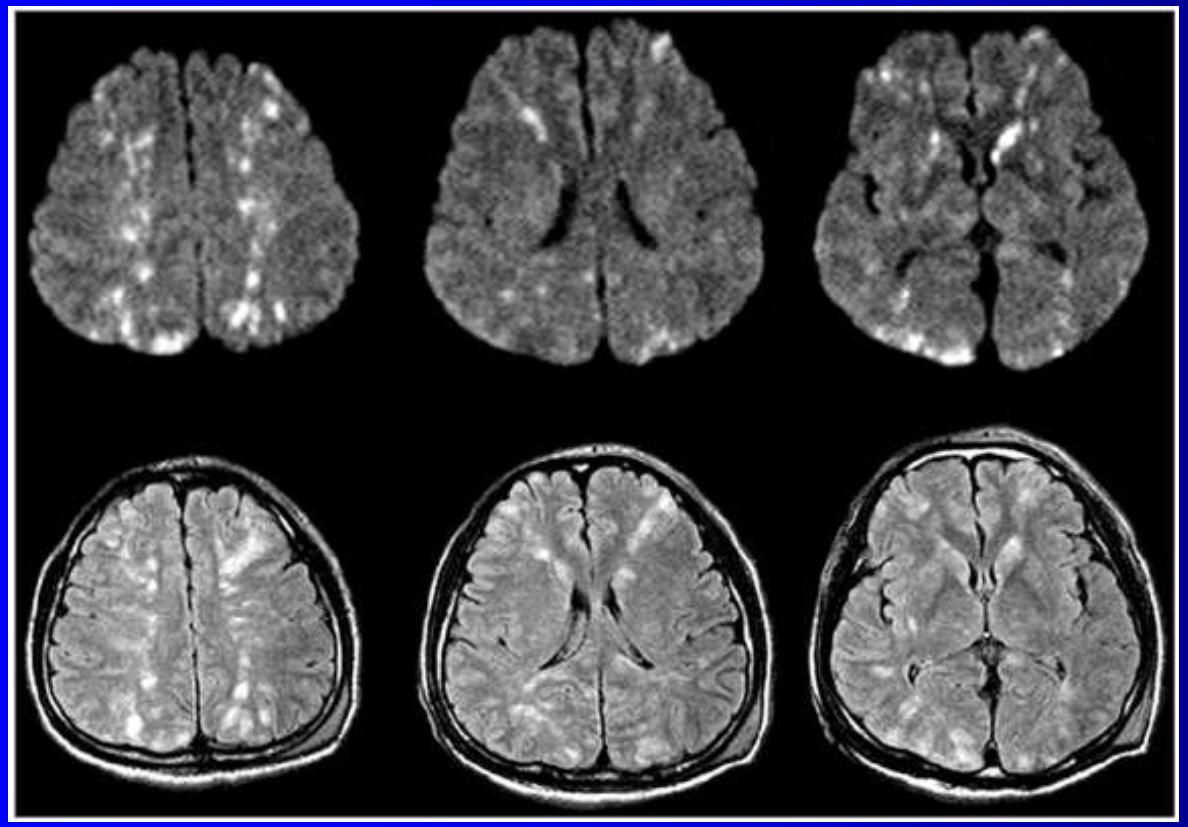


No decline in stroke rates with newer generation valves

	Early generation TAVI devices	Newer generation TAVI devices	Newer generation vs early generation	
			Crude	
	n=391	n=391	HR (95% CI)	P value
30-day follow-up				
Early safety composite end point, n (%)	83 (21.2)	81 (20.8)	0.98 (0.72 to 1.33)	0.876
All-cause death, n (%)	19 (4.9)	15 (3.9)	0.80 (0.41 to 1.58)	0.519
Cardiovascular death, n (%)	18 (4.6)	11 (2.8)	0.62 (0.29 to 1.31)	0.210
CVE, n (%)	17 (4.4)	17 (4.4)	1.00 (0.51 to 1.97)	0.989
Stroke	16 (4.1)	15 (3.9)	0.94 (0.47 to 1.91)	0.868
Disabling stroke	14 (3.6)	9 (2.3)	0.64 (0.28 to 1.49)	0.301
Non-disabling stroke	2 (0.5)	6 (1.6)	3.05 (0.61 to 15.09)	0.172
Transient ischaemic attack	1 (0.3)	2 (0.5)	2.02 (0.18 to 22.25)	0.567
Myocardial infarction, n (%)	2 (0.5)	2 (0.5)	1.00 (0.14 to 7.10)	1.000
All-cause death or CVE, n (%)	26 (6.7)	29 (7.5)	1.13 (0.66 to 1.91)	0.661

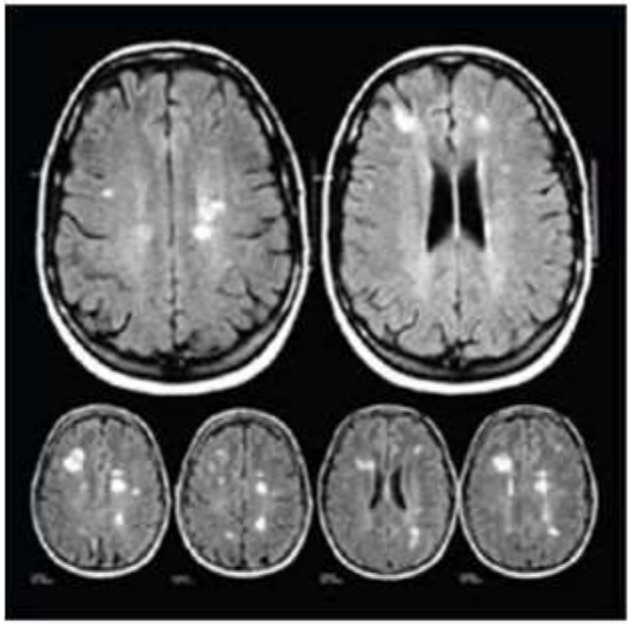
30-day outcomes were adjudicated by an independent CEC. Pilgrim T. *et al. Open Heart* 2018;5:e000695

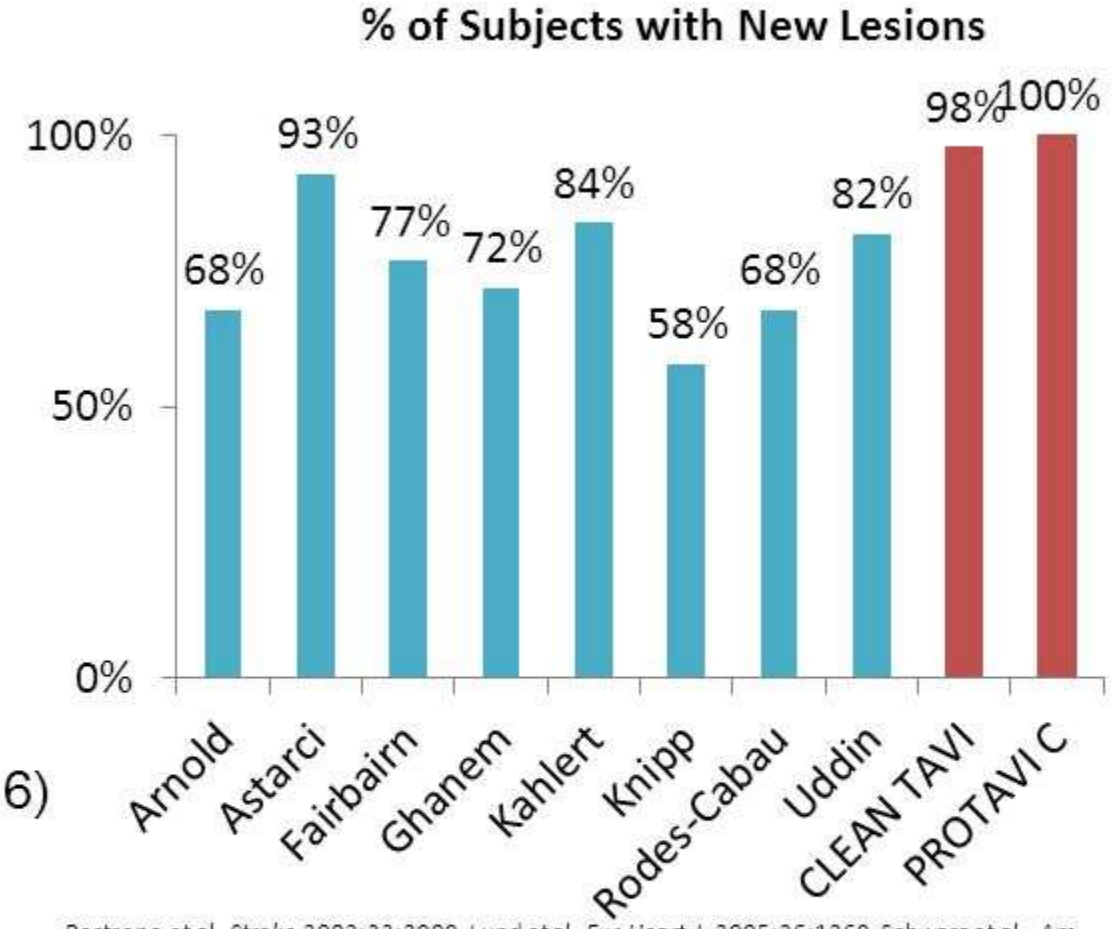
"Silent" stroke is a major concern in young patients!



Captured by embolic protection devices in 80-85% TAVI patients

Silent Embolic Events on DW-MRI after TAVR





- Affect 58-100% of patients
- Multiple infarcts (≤36, $\bar{x}$ = 4.6)
- Associated with:
  - Neurocognitive decline
  - >2 fold risk of dementia
  - **>3 fold risk of stroke**

Restrepo et al. *Stroke* 2002;33:2909, Lund et al. *Eur Heart J.* 2005;26:1269, Schwarz et al. *Am Heart J* 2011;162:756, Knipp et al. *Ann Thorac Surg* 2008;85:872, Vermeer et al. *NEJM* 2003; 348:1215, Vermeer et al. *Stroke* 2003; 34:1126, Arnold et al. *JACC Cardiovasc Interv.* 2010;3:1126, Astarci et al. *J Heart Valve Dis.* 2013;22:79, Fairbairn et al. *Heart* 2012;98:18, Ghanem et al. *EuroIntervention.* 2013;8:1296, Kahlert et al. *Circ.* 2010;121:870, Knipp et al. *Interact Cardiovasc Thorac Surg.* 2013;16:116, Linke et al. TCT 2014, Rodes-Cabau et al. *JACC Cardiovasc Interv* 2014;7:1146

High rate of PPM is not acceptable in health young patients!

17.4% PPM in the CoreValve low risk trial

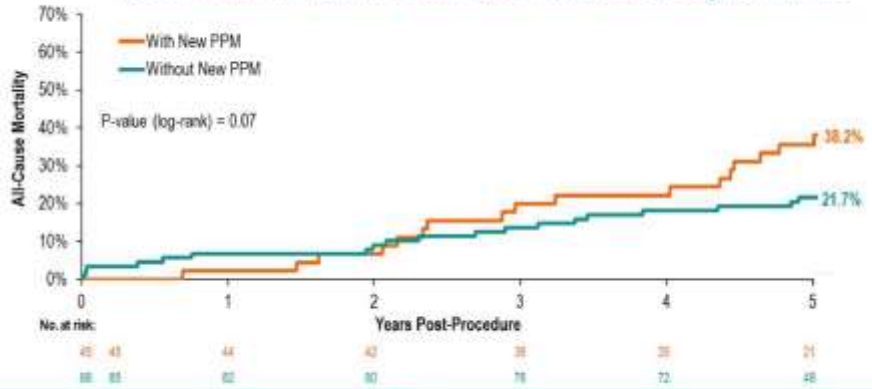
NOTION Trial

Secondary Outcomes

5-Year Outcome, Kaplan-Meier %	TAVR	SAVR	p-value
Death, any cause	27.7	27.7	0.90
Death, cardiovascular	21.0	22.5	0.75
Stroke	10.5	8.2	0.67
TIA	6.8	4.1	0.35
Myocardial infarction	8.6	8.7	0.87
Atrial fibrillation	25.2	62.2	<0.001
Pacemaker	41.8	8.4	<0.001
Aortic valve re-intervention	2.5	0.0	0.09
Valve endocarditis	11.3	5.8	0.10

ACC.18

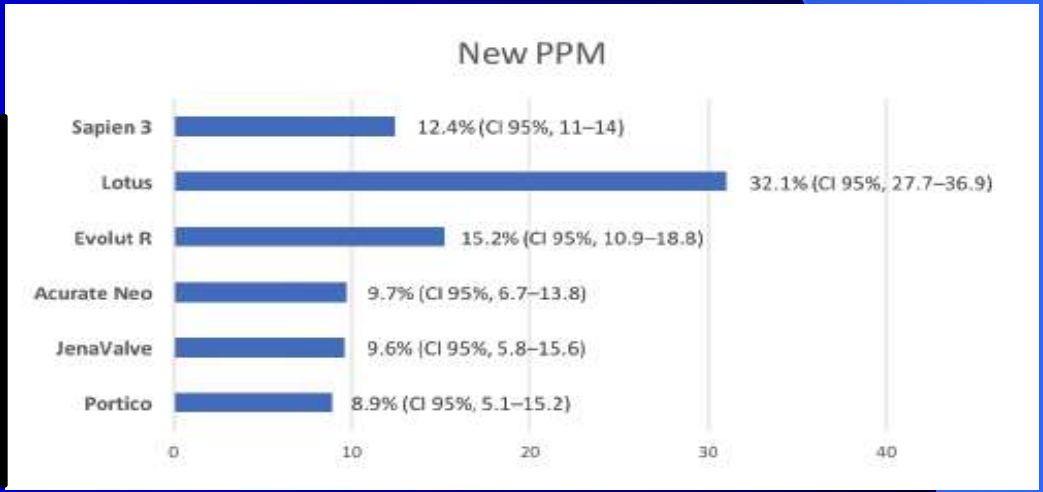
Association of New Pacemaker with Mortality for TAVR



ACC.18

Meta-analysis

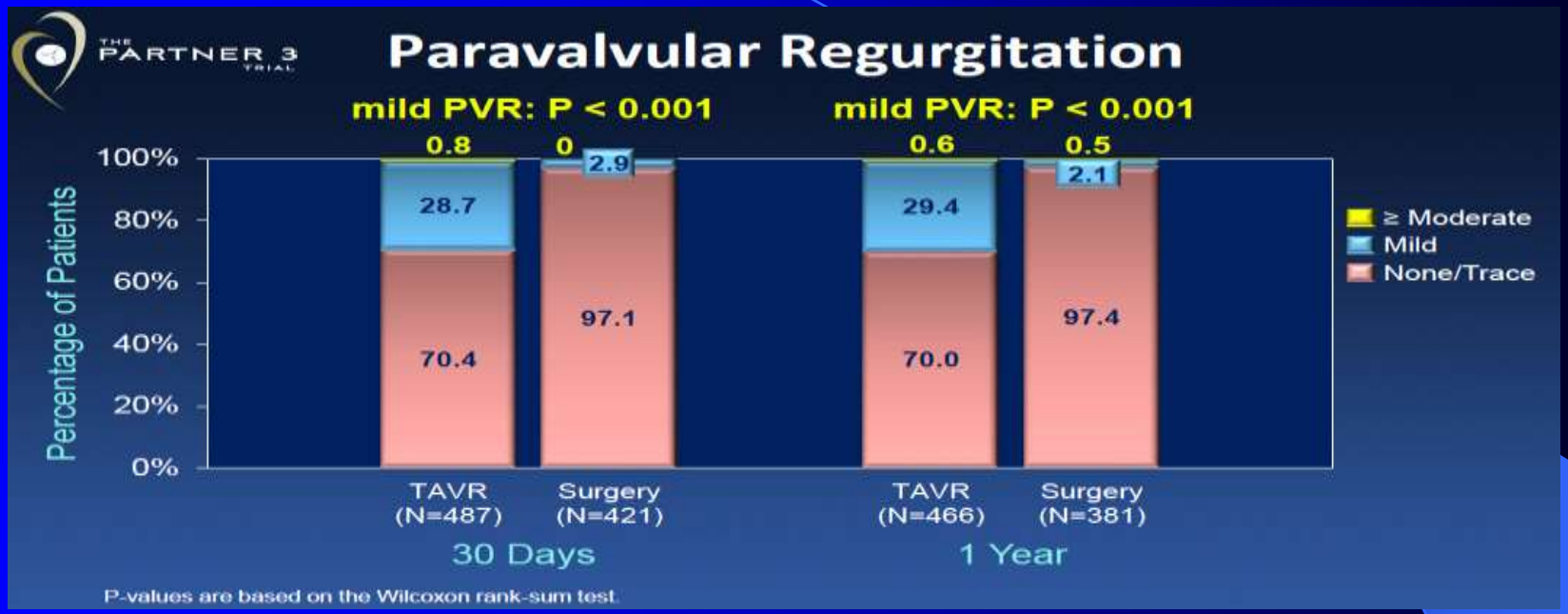
Outcomes from a weighted meta-analysis of 30 studies including 5,923 patients achieved with a comprehensive search of multiple Database from January 2011 to March 2016.



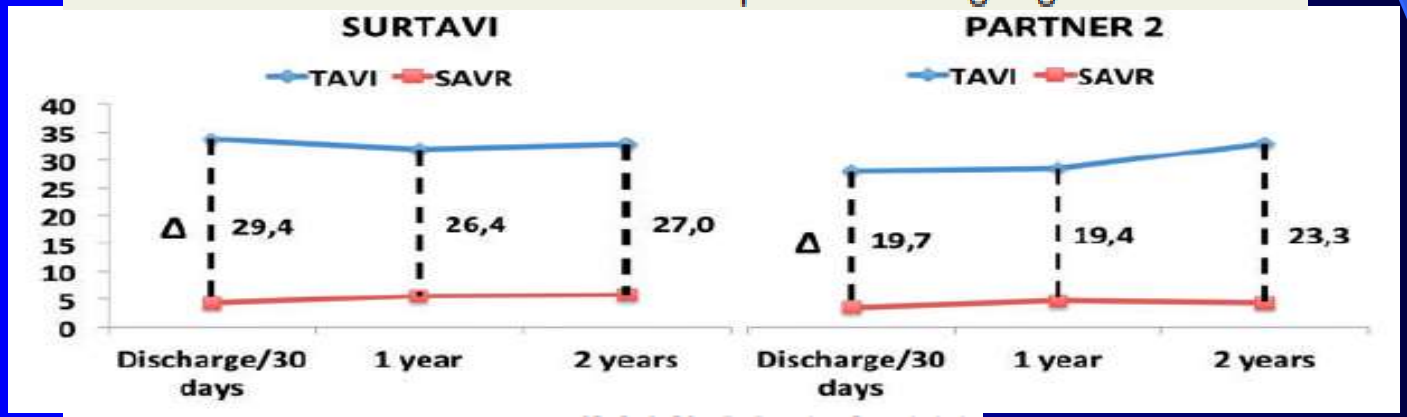
CARDIAC INTERVENTIONS TODAY MARCH/APRIL 2017 VOL. 11, NO. 2

Mild Paravalvular leak is still higher in TAVI

Is mild PVL a concern in young patient?



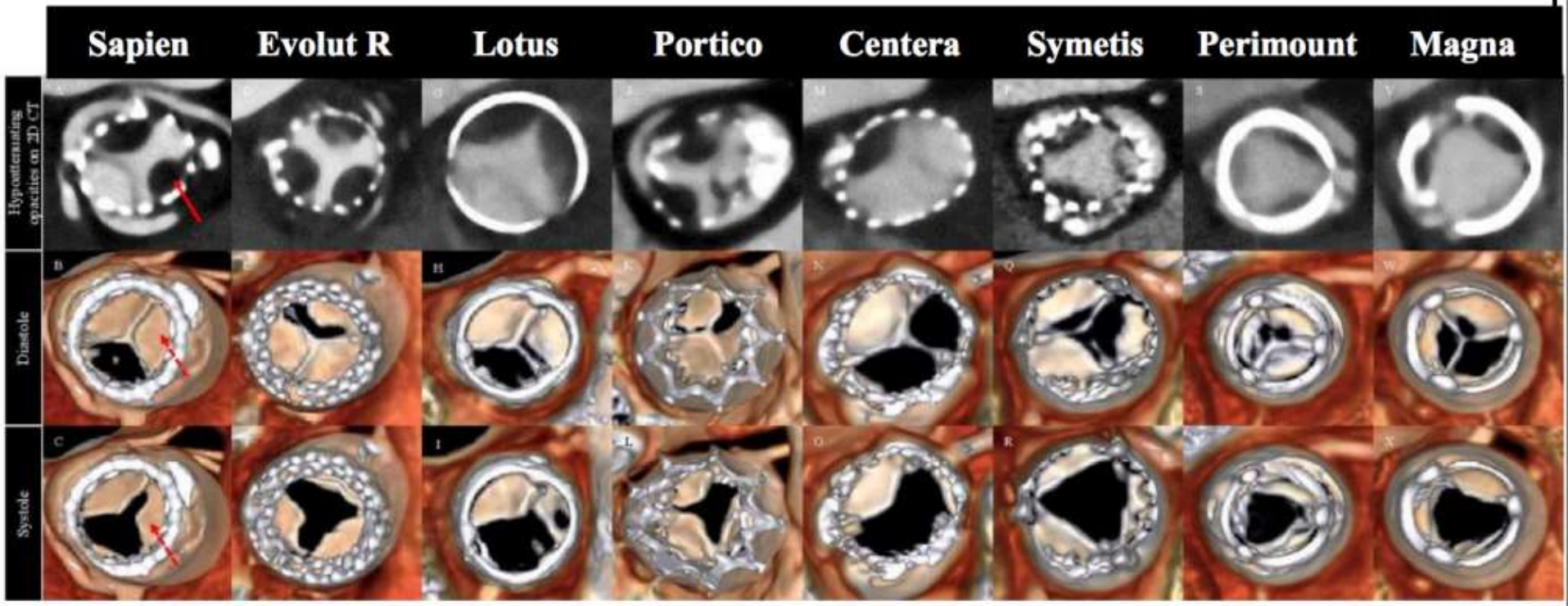
Incidence of mild PVL in intermediate-risk patients undergoing SAVR or TAVI



European Heart Journal (2018) **39**, 658–666

Higher Rate of Valve Thrombosis

TAVR ~13% SAVR ~5%



Likely reduce valve durability!

Valve durability is important in healthy young patients!

Surgically explanted Sapien and CorveValve THVs

Martin B Leon, MD

Columbia University Medical Center
NewYork-Presbyterian

Durability of bioprostheses is poor in young patients

Surgical bioprostheses

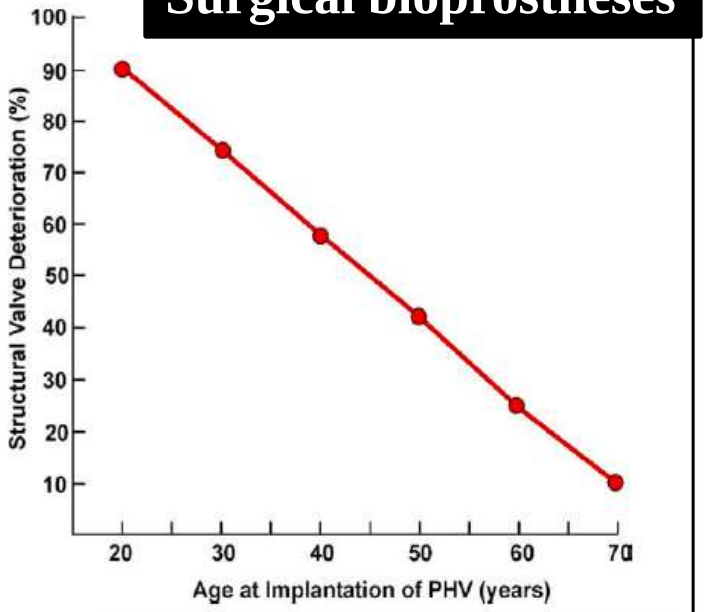
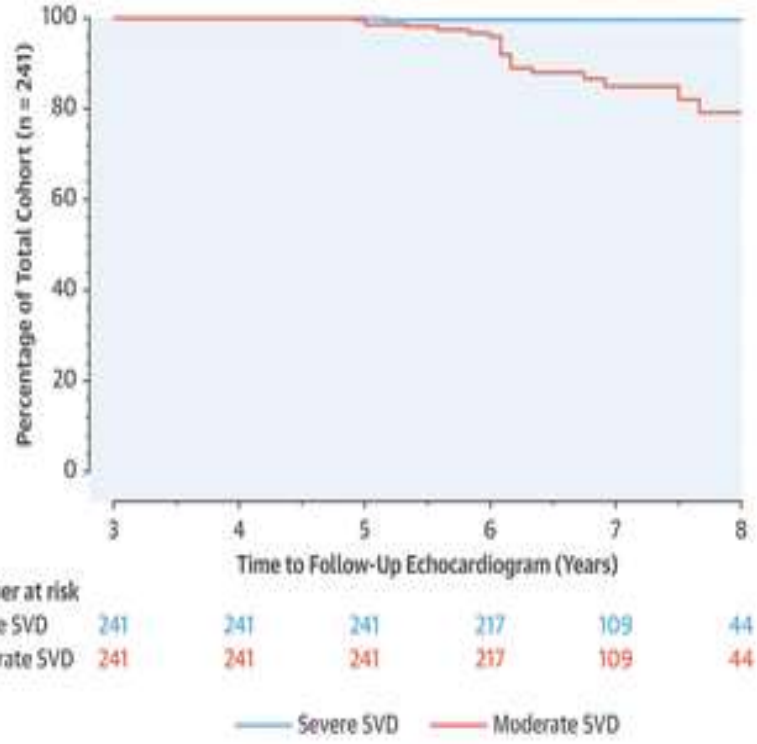


Figure 6 SVD of Biological Valves at 15 to 20 Years Based on Patient Age at Time of PHV Implantation

(J Am Coll Cardiol 2010;55:2413–26)

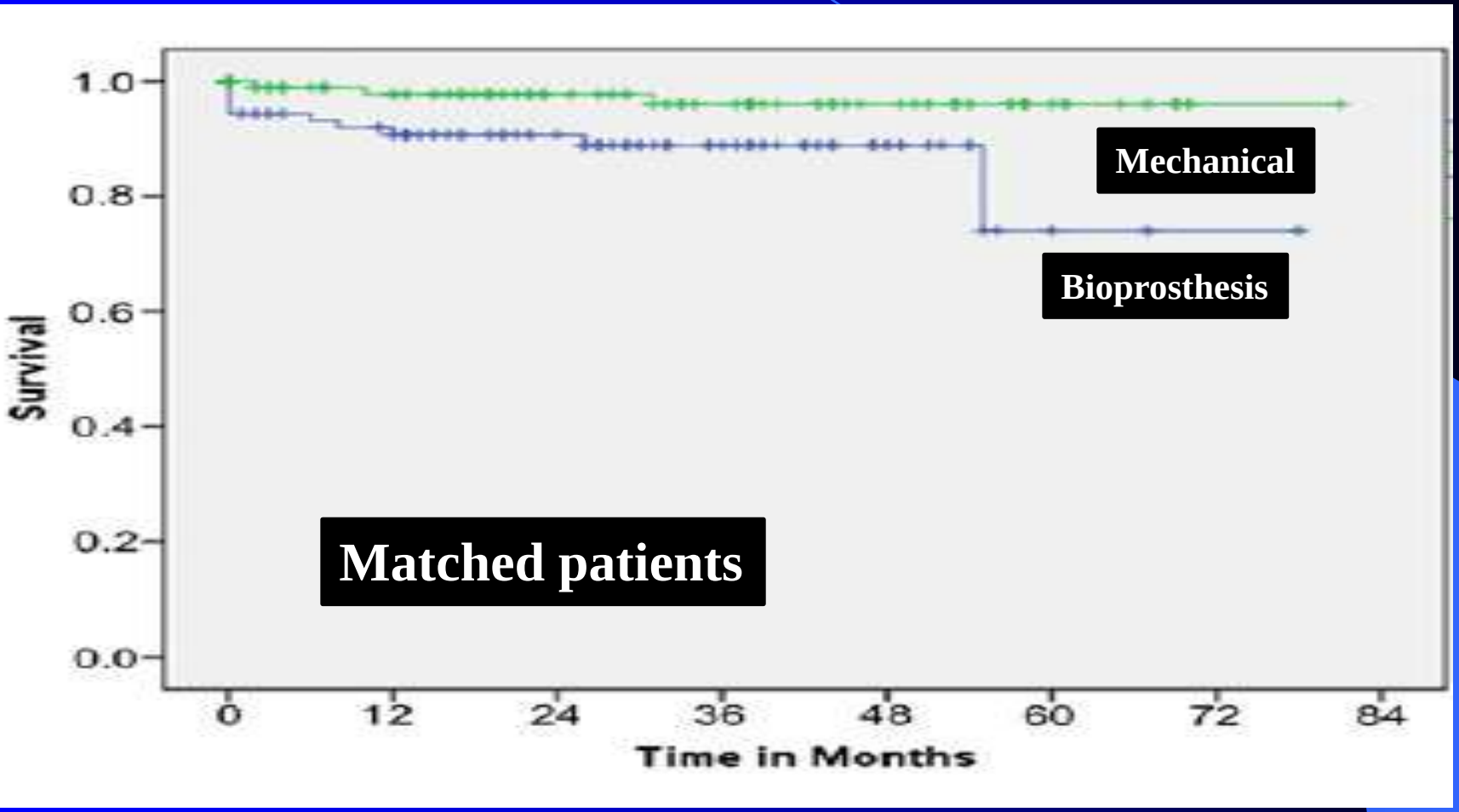
CENTRAL ILLUSTRATION: Freedom From Structural Valve Deterioration Over Time: Kaplan-Meier Curve



Blackman, D.J. et al. J Am Coll Cardiol. 2019;73(5):537-45.

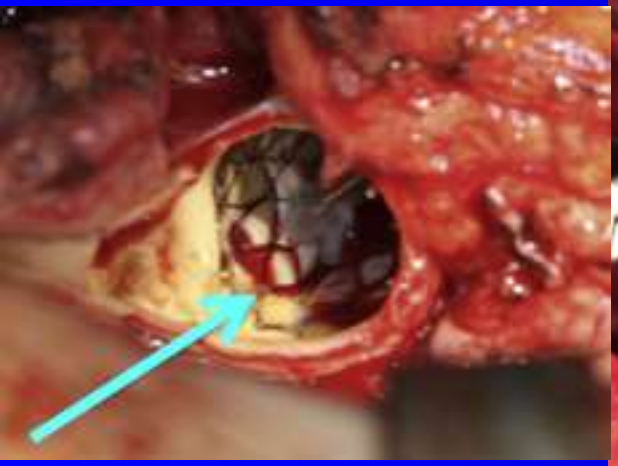
Mean age 79.3 ± 7.5 years

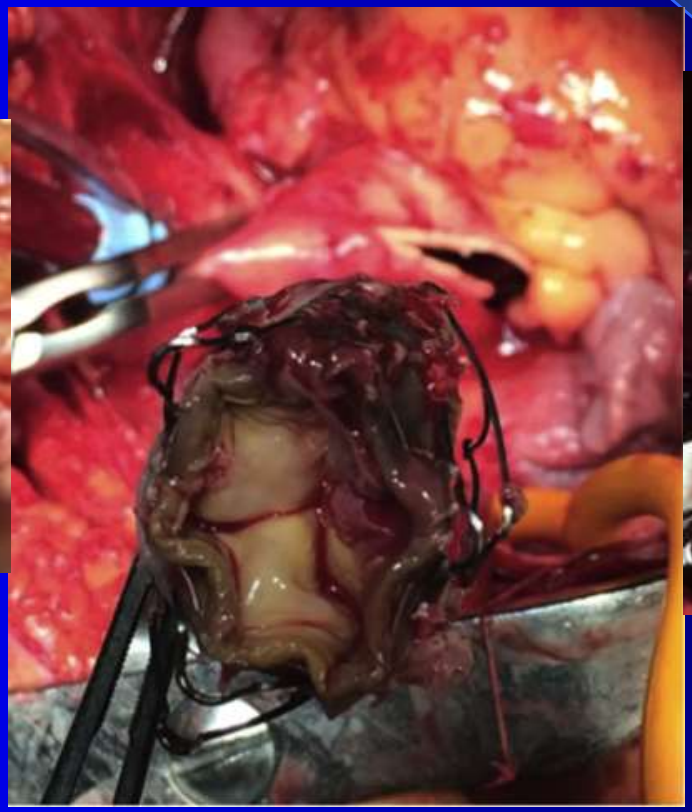
Better survival with mechanical valve in young patients (<60 y/o)

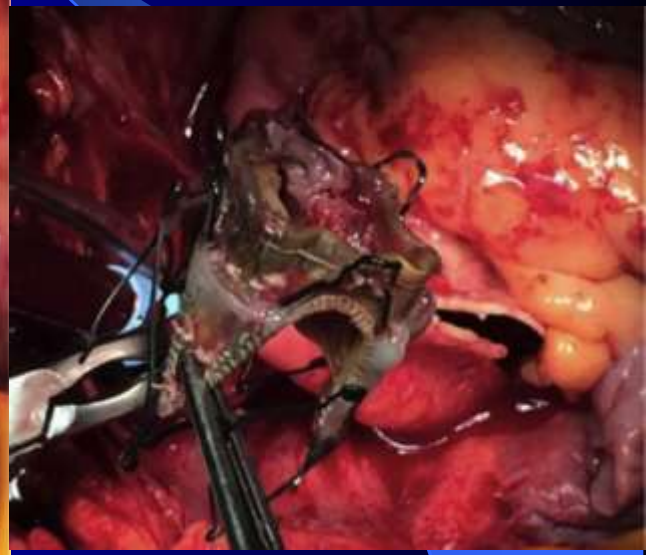


J Thorac Cardiovasc Surg 2012;144:1075-83

Re-do AVR for failed TAVI is more difficult and complicated



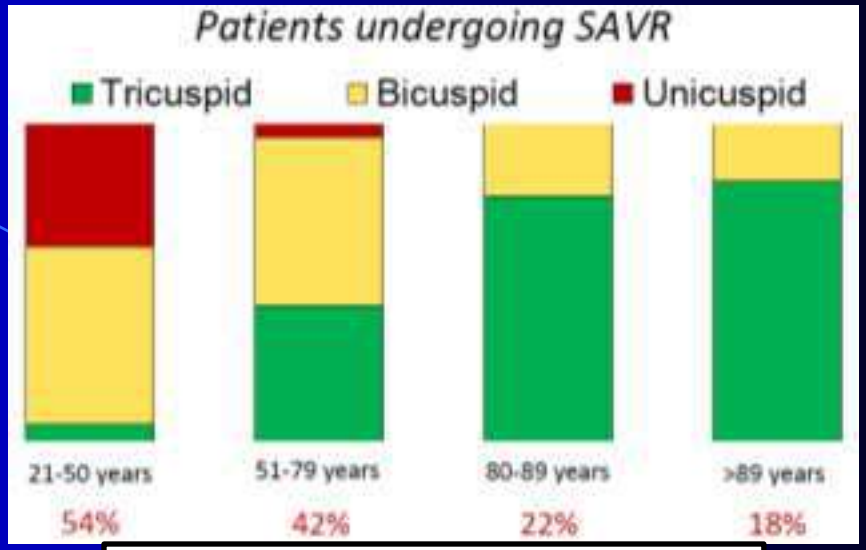




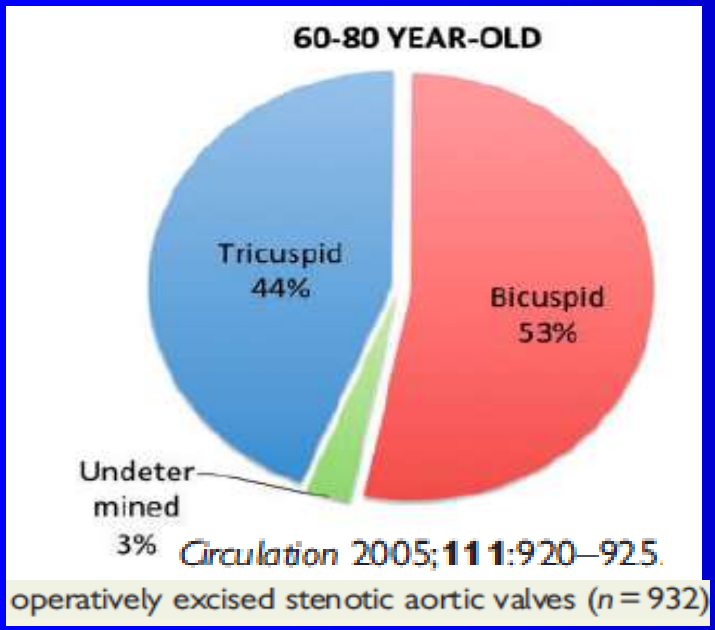
Anatomical Concerns

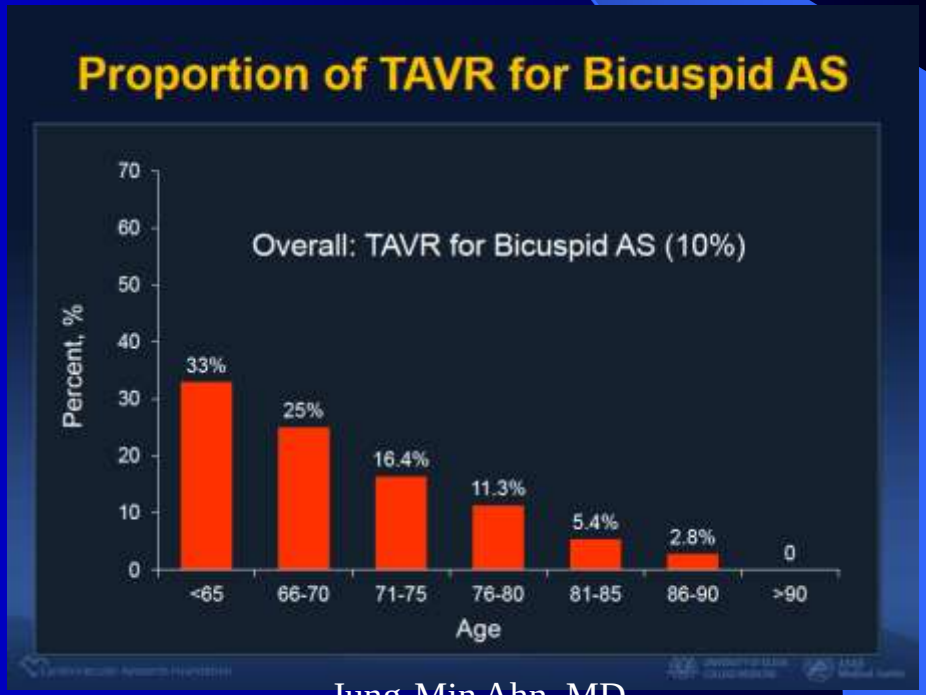
- Bicuspid AV
- Risk of coronary obstruction
- Small annulus and sinus of Valsalva
- Severe annular or subannular calcification

Incidence of bicuspid valve



Roberts et al. AJC 2012;109:1632-6

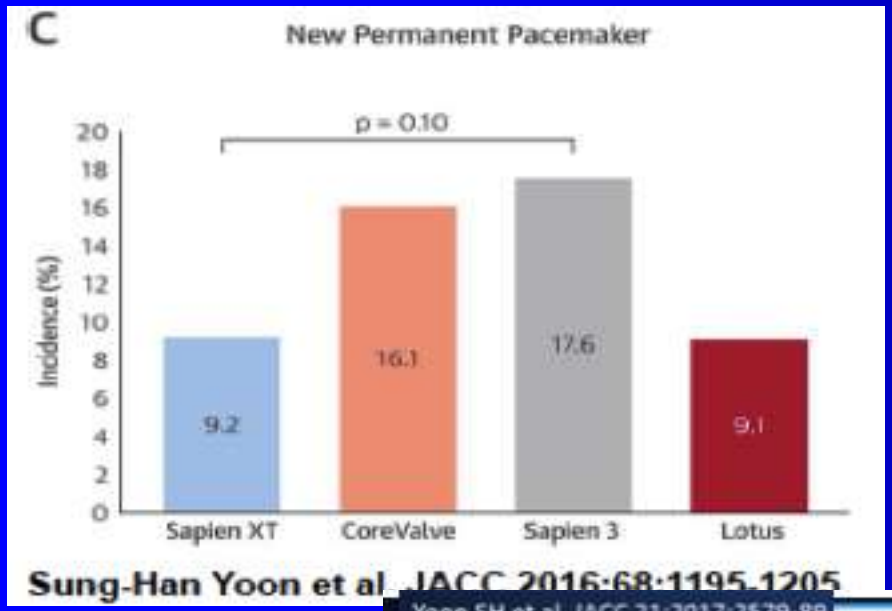




Jung-Min Ahn, MD.

Issues with Bicuspid AV

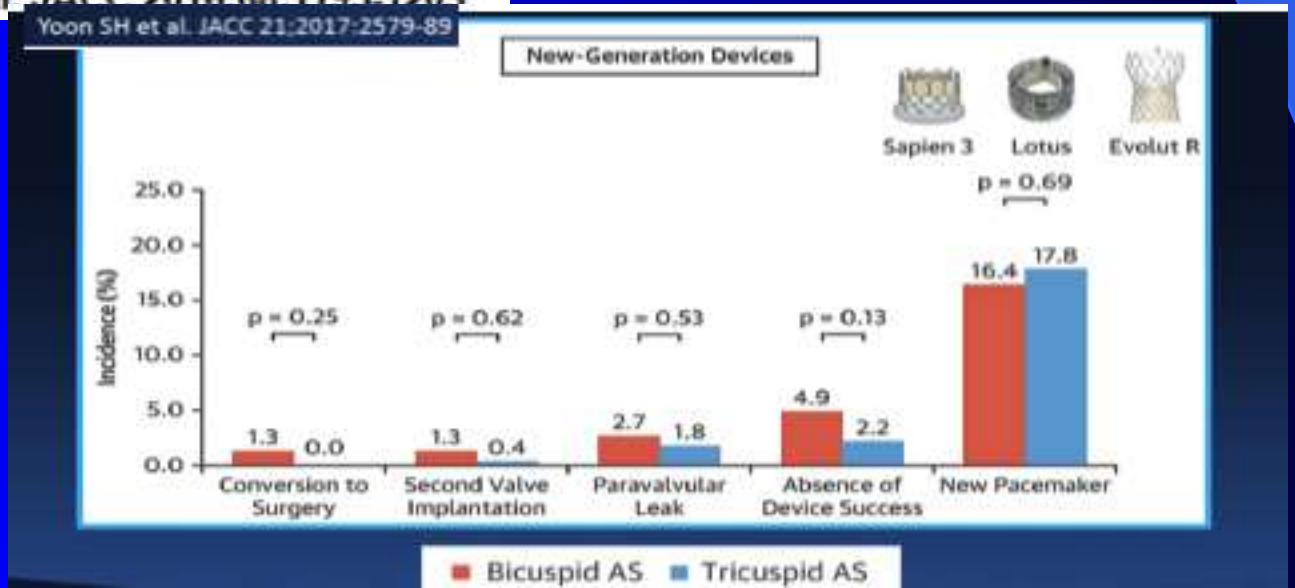
Higher stroke rate



30-day Outcomes – Matched

KM estimate %	Bicuspid	Tricuspid AS	p-value
All-cause mortality	2.9	2.1	0.11
All stroke	2.5	0.9	0.0001
Life-threatening bleeding	0.1	0.1	0.98
Major vascular complication	1.0	0.7	0.35
New pacemaker	9.3	8.4	0.42
Aortic valve reintervention	0.2	0.2	0.71

Makkar R, presented at EuroPCR 2018

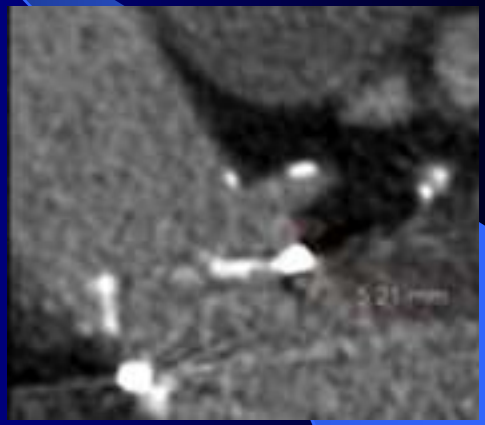


Other Anatomical Concerns

Potential risk of aortic/annulus rupture

- **Potential PPM**
- **No VinV option for failed TAVI**
- **Difficulty in coronary access**

Risk of Coronary obstruction



My Answer

Yes

It is Early to Tell TAVR in All Patients with Aortic Stenosis!

Too early to recommend TAVI in following patients

- Healthy young patients <65 y/o
- Low risk patients with bicuspid aortic valve
- Low and intermediate risk patients with suboptimal anatomy for TAVI
- Low and intermediate risk patients with small aortic annulus and root (PPM is expected), requiring root enlargement
- Associated with other heart disease that is better treated by OHS