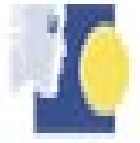


EuroValve
January 26-27, 2017



Centre Hospitalier Régional
Universitaire de Lille

Expanding indications with TAVI, what does it take?

Dr. T. Modine MD, PhD, MBA

Heart team

CHRU de Lille

www.eurovalvecongress.com



EuroValve

January 26-27, 2017

Speaker's name: Thomas Modine

☒ I have the following potential conflicts of interest to report:

Affiliation/Financial Relationship

Grant/Research Support
Consulting Fees / Honoraria
Major Stock Shareholder/Equity
Royalty Income
Ownership/Founder
Intellectual Property Rights
Other Financial Benefit

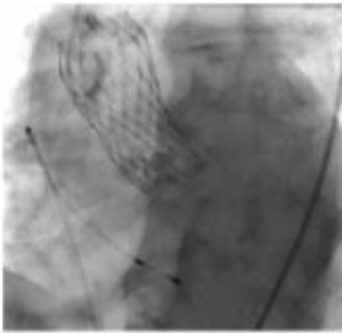
Company

- Edwards
- Abbott, Boston Scientific, Medtronic, Edwards, Cephea, Microport, GE
- Nanosurg
- Microport
- Valmy Ltd
- Yes
- Nil

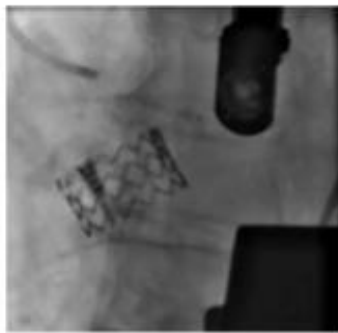
TAVI in the last years
Huge improvements, but...

TAVI Complications

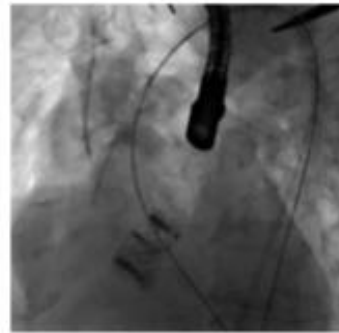
- Complications are **PROCEDURE + DEVICE** related



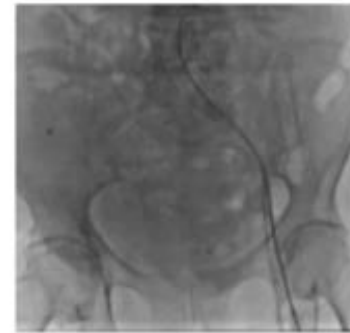
PVL



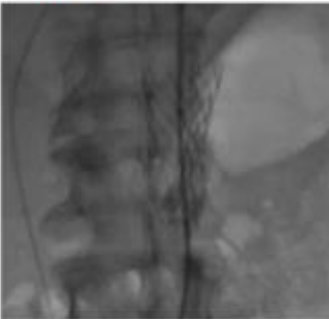
Annular rupture



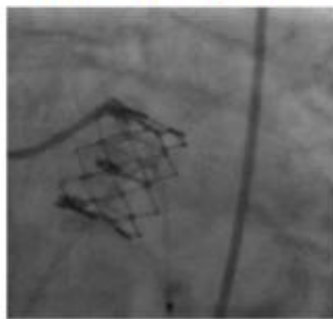
Aortic dissection



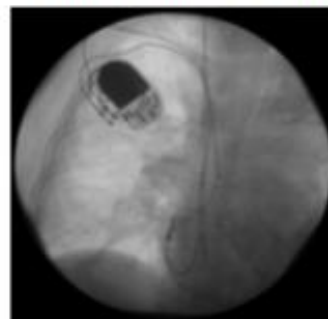
Vascular complications



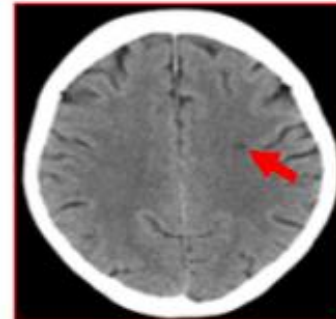
Device embolization



Coronary Occlusion



AV-Block



Stroke

Weighing complications and outcomes

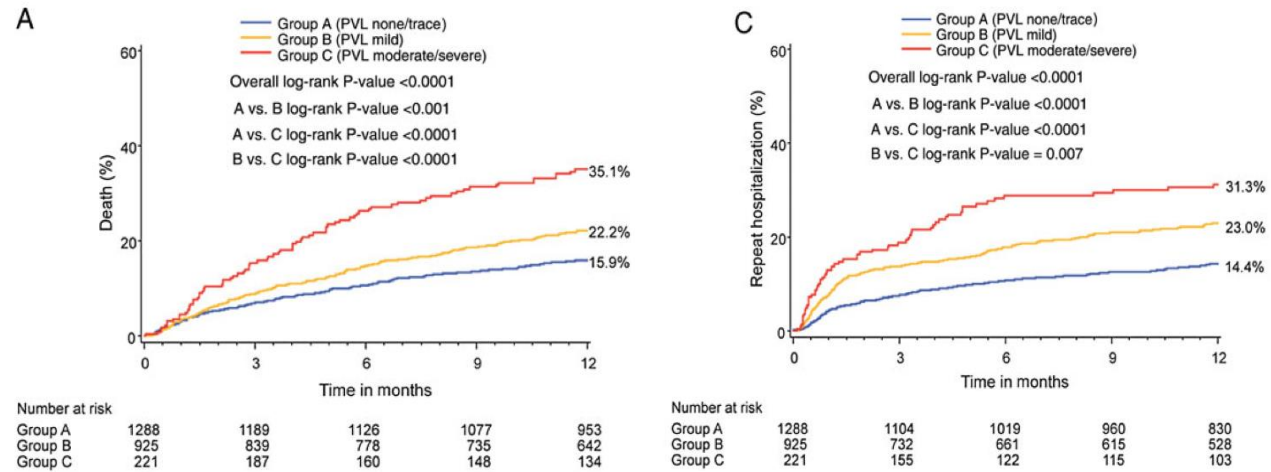
- Pro TAVI:
 - early (up to 2 years) survival benefit in high risk and possibly intermediate risk (STS < 4-8) groups
 - favorable hemodynamics (lower gradients, larger EOA)
- CON TAVI:
 - higher rate of AVB and LBBB -> PM
 - higher rate of PVL
 - higher rate of vascular complications

TAVI in the last years

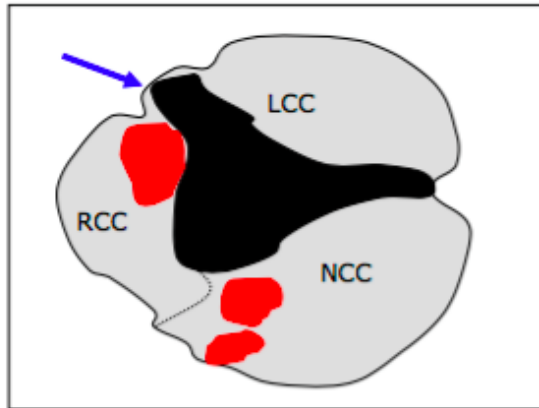
Huge improvements, but...

- PVL
- PCM
- Coronary obstruction
- Annulus rupture
- Stroke
- durability

Paravalvular regurgitation in the PARTNER trial
Kodali et al. Eur Heart J 2015;36:449-56

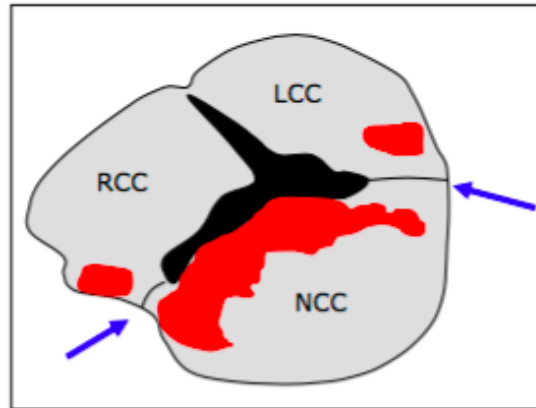


Predictors of Leakage (balloon-expandable valves)



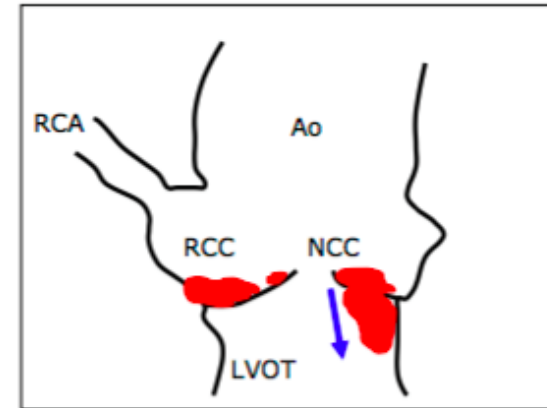
Annular eccentricity

Odds ratio 9.16 $p = 0.005$



Asymmetric cusp calcification

Odds ratio 5.65 $p = 0.009$

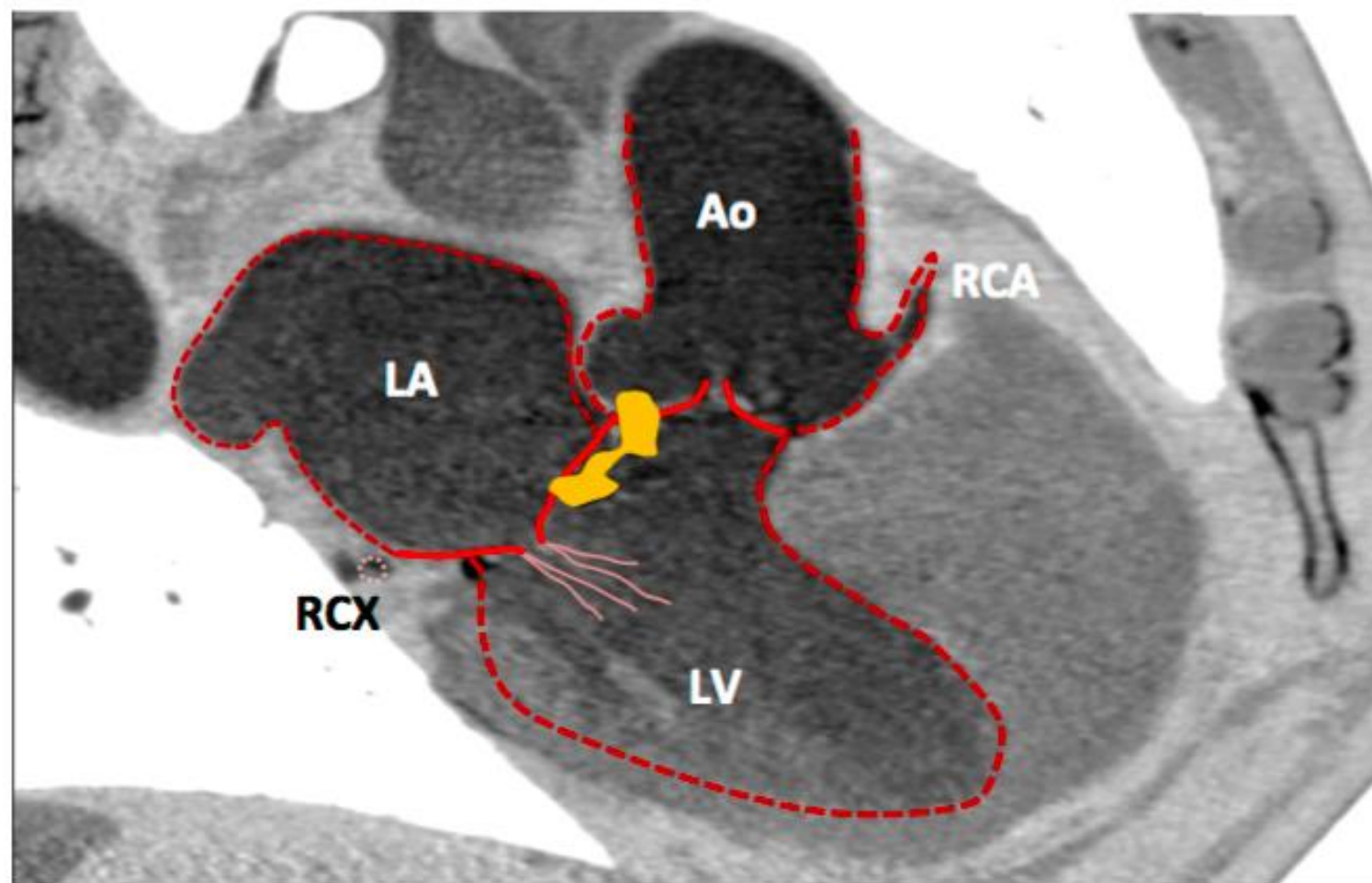


Device landing zone calcification

Odds ratio 9.16 $p = 0.005$

Unbehaun et al. Transapical aortic valve implantation: Incidence and predictors of paravalvular leakage and transvalvular regurgitation in a series of 358 patients. J Am Coll Cardiol 2012

Recognition of “Hostile” Anatomy



PVL in SAVR

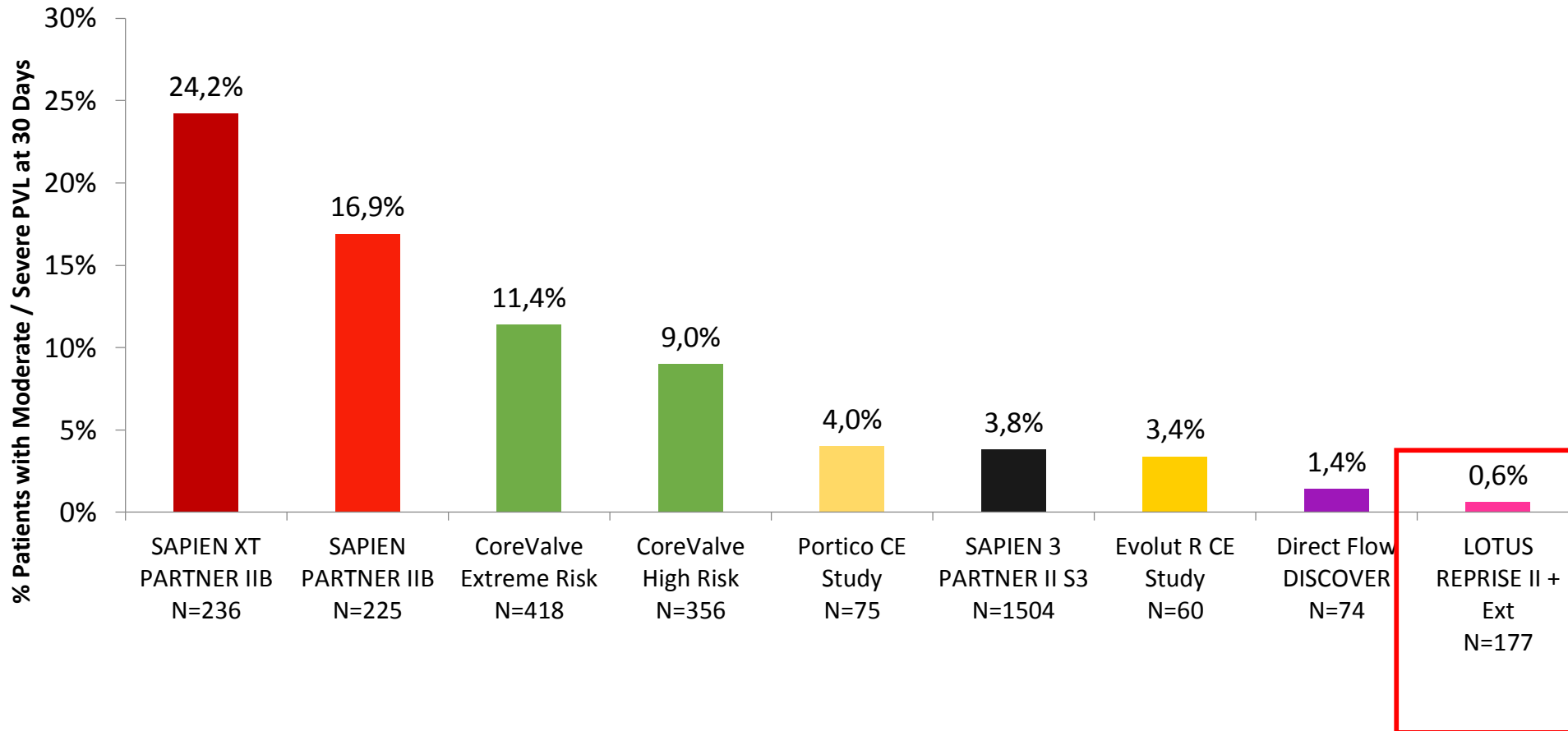
- PVL PAR after SAVR is an infrequent event and occurs in less than 1% (0.9%) of patients ¹⁾
- In contemporary trials the incidence of mild or moderate/severe PVL in the surgical arms was
 - 2.8 and 0.5% in the PARTNER 2A trial ²⁾
 - 1.9 and 1.3% in the CoreValve Trial ³⁾

1) Weisenberg JHVD 2011

2) Leon MB NEJM 2016

3) Reardon MJ US CorValve Trial JACC 2015

PVL



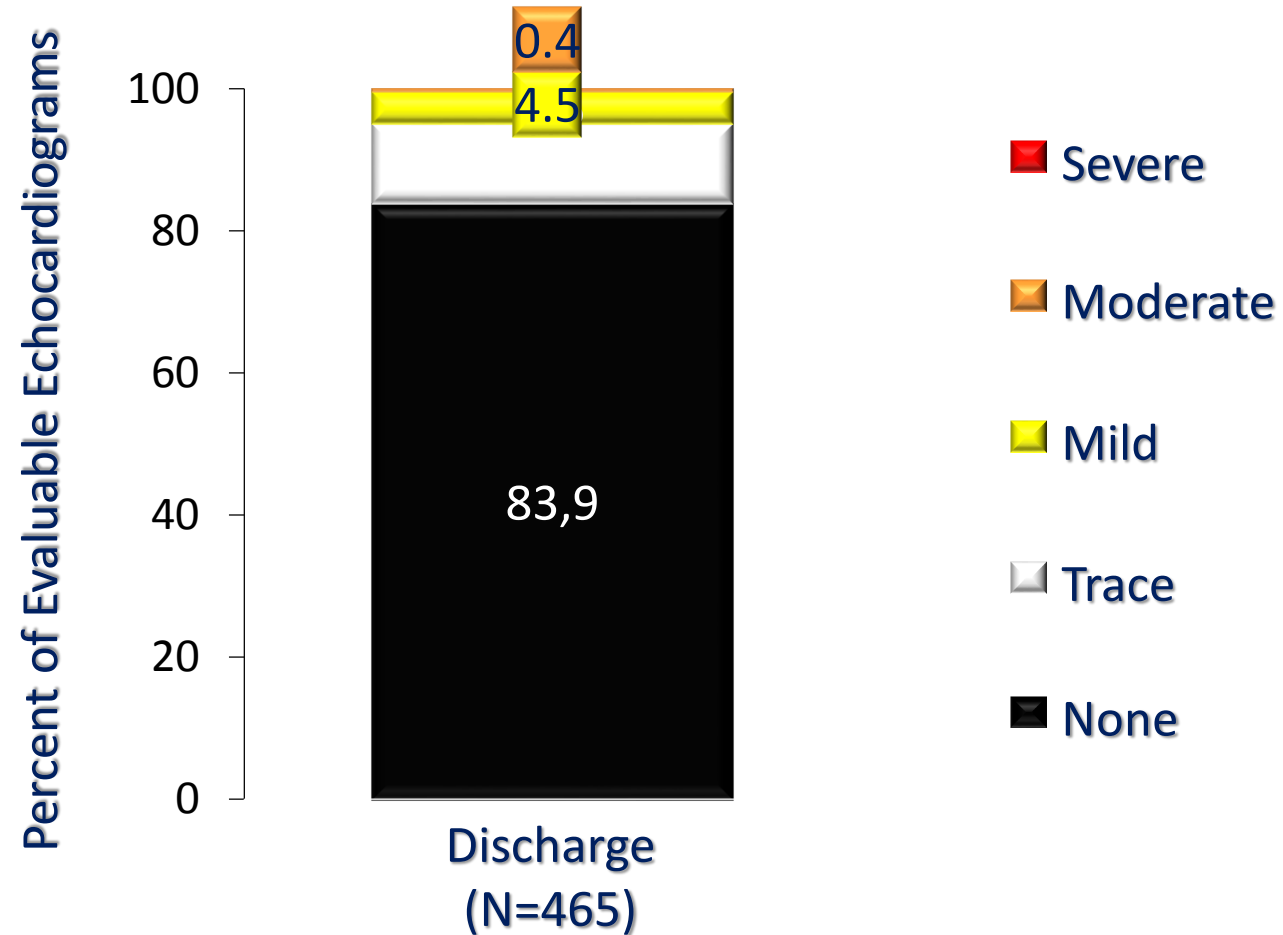
¹Leon, et. al. presented at ACC 2013; ²Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ³Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ⁴Manoharan, et al., et. al. presented at TCT 2014; ⁵Kodali, et al., presented at ACC 2015; ⁶Meredith, et al., presented at ACC 2015; ⁷Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; ⁸Meredith, et al., presented at PCR London Valves 2014

CLINICAL FOCUS, INNOVATION, AND PROGRESS: EVOLUTE R

Paravalvular Aortic Regurgitation

500-Patients Interim Analysis

Core-Lab Adjudicated Data



TAVI in the last years

Huge improvements, but...

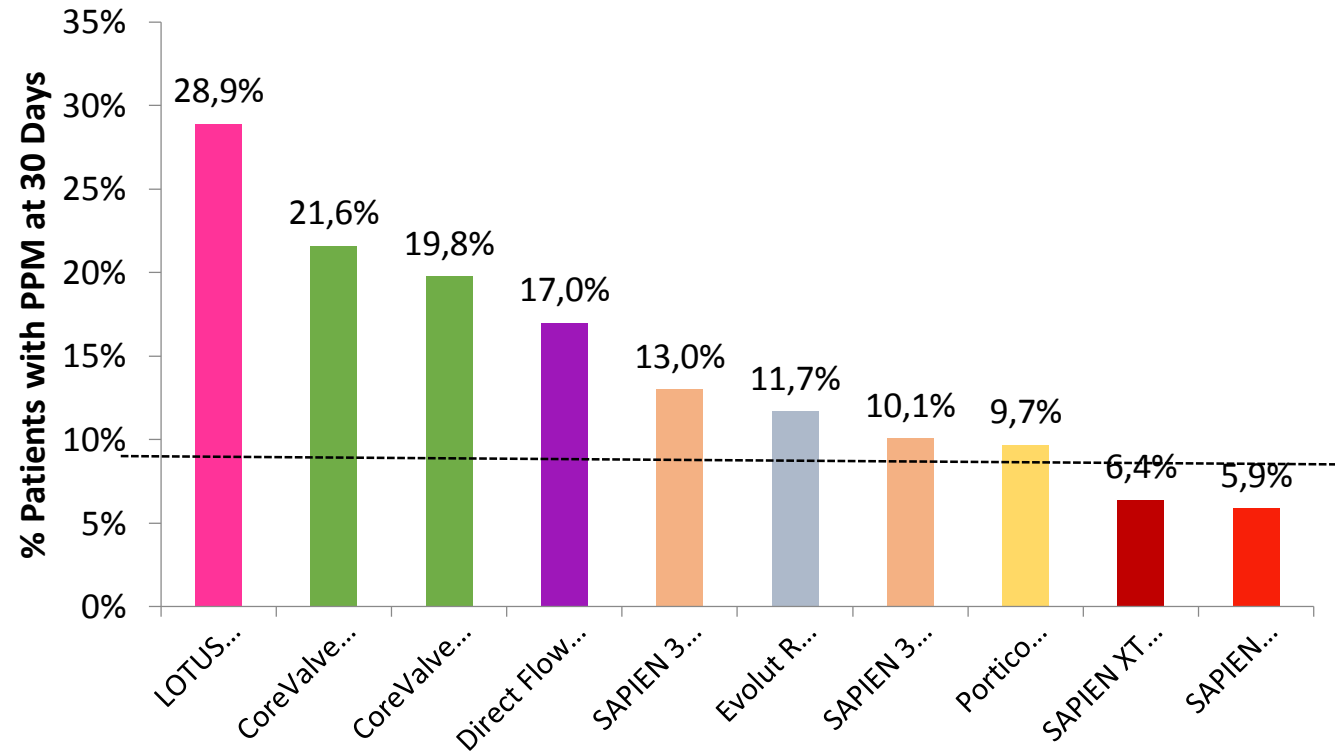
- PVL
- PCM
- Coronary obstruction
- Annulus rupture
- Stroke
- durability

PM related problems

Chronic RV pacing is known to be associated with:

- (1) LA remodeling, reduced atrial function and higher incidence of AF
- (2) LV dyssynchrony
- (3) impaired LVF
- (4) limited exercise capacity
- (5) progressive LV remodeling
- (6) can finally lead to heart failure esp. in pats. with impaired LVF
- (7) Lead/Surgical site Infection

30-day Permanent Pacemaker



¹Meredith, et al., presented at PCR London Valves 2014; ²Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ³Adams, et al., *N Engl J Med* 2014; 370: 1790-8;

⁴Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; ⁵Kodali, et al., presented at ACC 2015; ⁶Meredith, et al., presented at ACC 2015; ⁷Manoharan, et al., et. al. presented at TCT 2014; ⁸Leon, et. al. presented at ACC 2013

TAVI in the last years

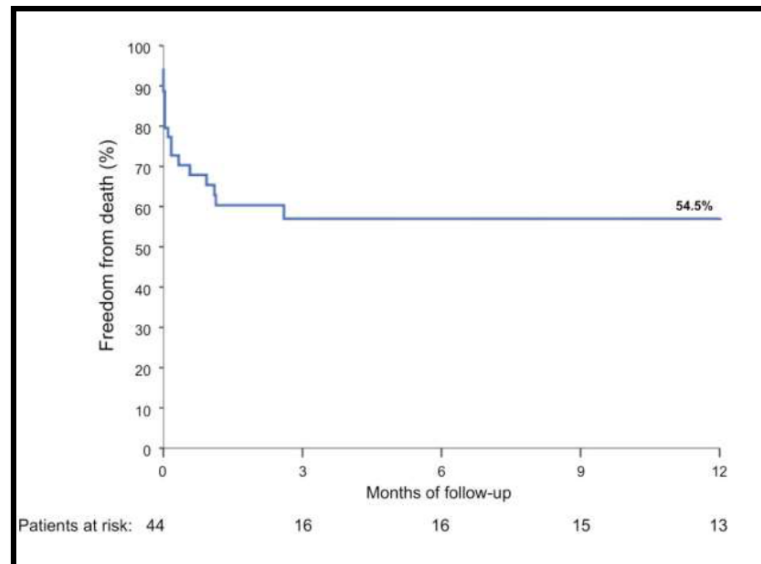
Huge improvements, but...

- PVL
- PCM
- Coronary obstruction
- Annulus rupture
- Stroke
- durability

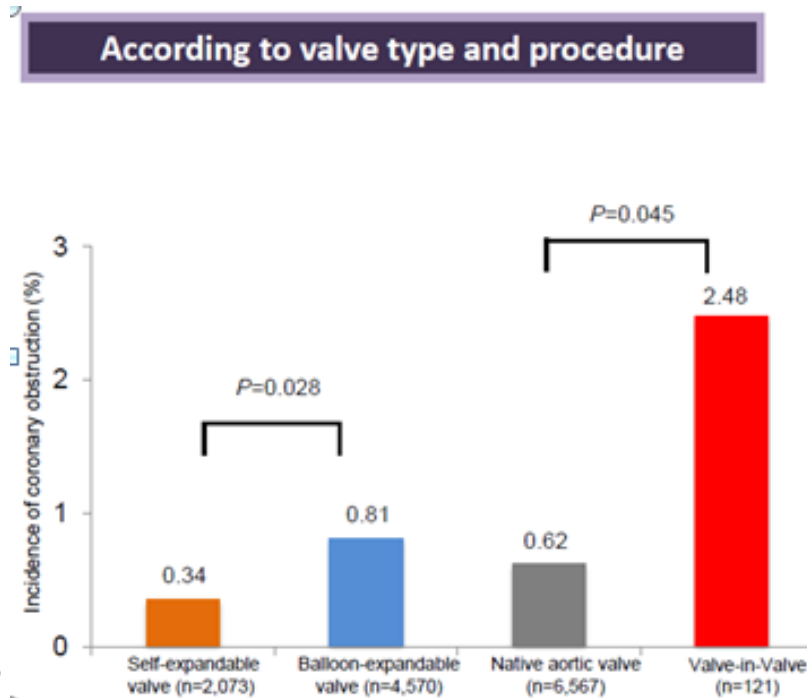
Coronary Occlusions

Rare but Catastrophic

- Coronary occlusions lead to 41% in-hospital mortality
- Significantly more common with balloon expandable than self expandable valves (0.81% vs. 0.34%, $p=0.028$)^{1,2}



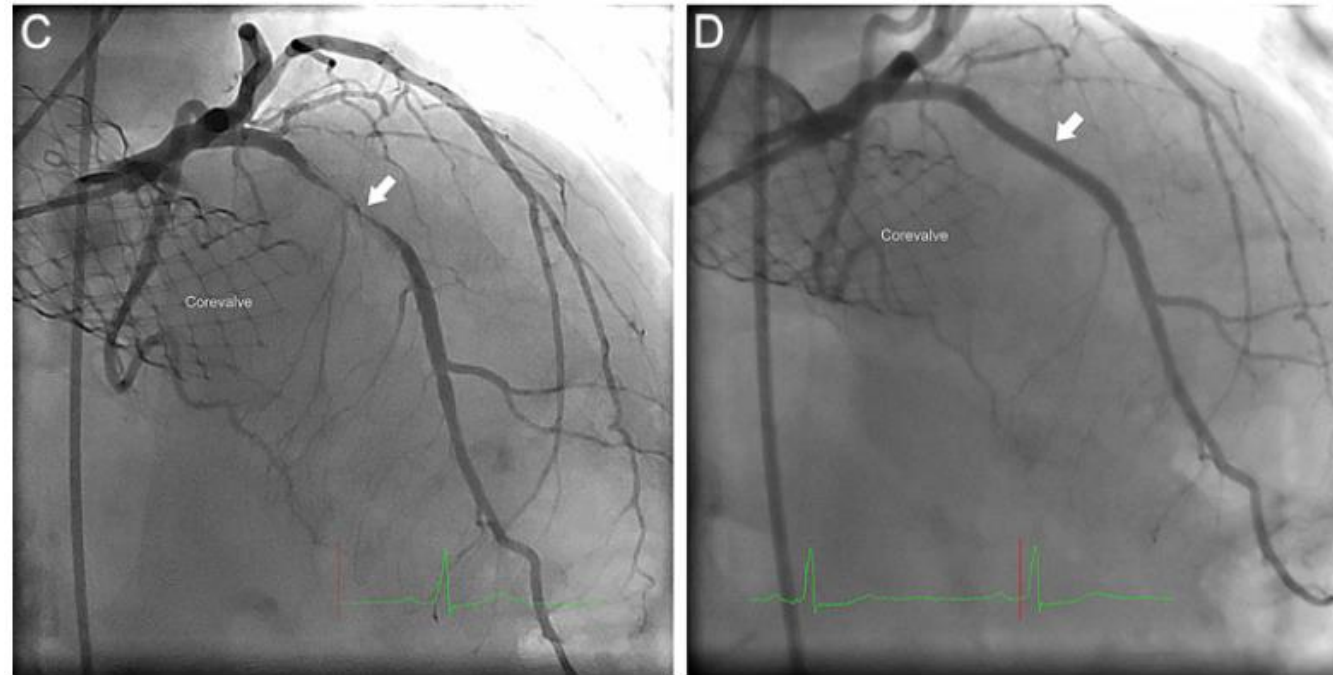
¹Ribeiro, et. al. presented at EuroPCR 2013; ²Ribeiro, et. al., *J Am Coll Cardiol* 2013; epub



Coronary Occlusions

Emergency Treatment

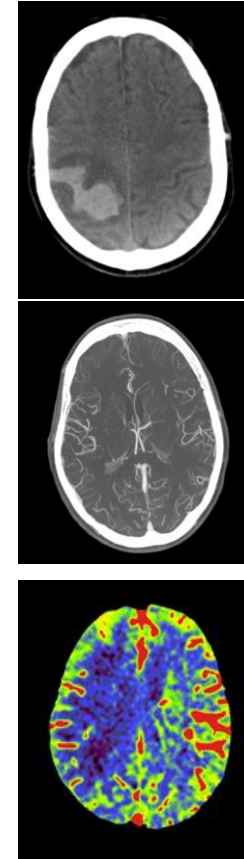
- The clinical feasibility of PCI in CoreValve patients, both as an emergency bailout maneuver and as treatment for in-stent restenosis, has been demonstrated.



TAVI in the last years

Huge improvements, but...

- PVL
- PCM
- Coronary obstruction
- Annulus rupture
- **Stroke**
- durability



Risk of stroke after transcatheter aortic valve implantation (TAVI): a meta-analysis of 10,037 published patients

53 studies, 10,037 patients

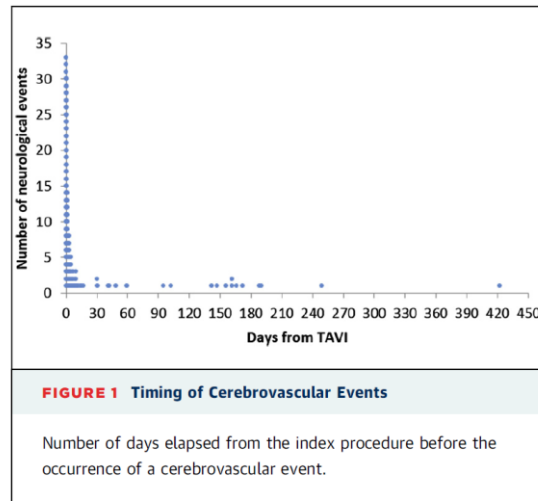
TF CoreValve (1.4±1.5%);
TF Edwards (2.1±3.0%)

	Medtronic/CoreValve transarterial			Edwards SAPIEN transarterial		
	Number of publications with available data (n)	Overall number of patients with available data (n)	Weighted mean±SD	Number of publications with available data (n)	Overall number of patients with available data (n)	Weighted mean±SD
Patient age (years)	18	3236	81.1±1.3	23	1733	82.3±2.6
Female gender	16	2798	52.7±6.4%	22	1634	50.2±3.5%
Logistic EuroSCORE (%)	18	3236	22.09±3.66	20	1530	25.61±4.16
Procedural stroke (<24h)	9	1872	1.4±1.5%	11	571	2.1±3.0%
30-day stroke/TIA	18	3236	3.1±2.2%	24	1861	4.2±2.2%
30-day major stroke	14	1795	2.5±1.8%	20	1190	3.0±2.0%
30-day minor stroke/TIA	14	1795	0.7±1.4%	19	1091	1.7±1.8%
30-day overall mortality	18	3236	6.4±5.1%	22	1829	6.9±3.8%

Procedural stroke (<24 hr.) 1.5±1.4%				
30-day stroke/TIA 3.3±1.8%				
1-year stroke/TIA 5.2±3.4%				
	Number of publications with available data (n)	Overall number of patients with available data (n)	Number of events (n)	Weighted mean±SD
Procedural stroke (<24h)	24	3041	47	1.5±1.4%
30-day stroke/TIA	53	10037	334	3.3±1.8%
30-day major stroke	42	5514	158	2.9±1.8%
30-day minor stroke/TIA	42	5514	53	1.0±1.3%
30-day overall mortality	52	10022	812	8.1±3.9%
30-day mortality in patients suffering stroke	29	4430	41	25.5±21.9%
30-day mortality in patients without stroke	29	4430	312	6.9±4.2%
6-month stroke	9	669	29	4.3±1.6%
12-month stroke	7	1507	78	5.2±3.4%

Eggebrecht et al. EuroIntervention 2012

Stroke Timing post TAVI



Timing of Cerebrovascular Events (CVE) in FRANCE-2 Registry (n=3,191)

- CVE most frequently occur day 0-1
- >50% are major strokes
- Median time to major stroke is 1 day

D. Tchetché et al. *JACC CV Int.* 2014;7:1138-1145

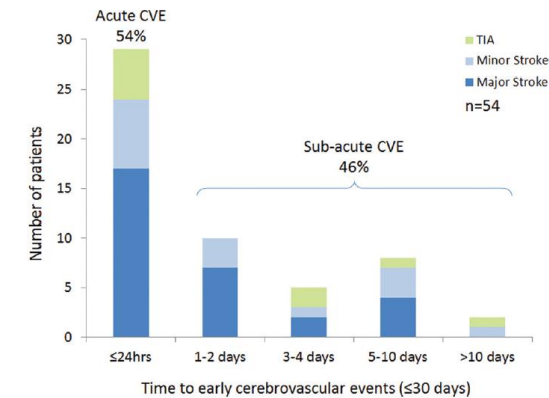


Figure 2. Timing of cerebrovascular events (CVEs) within 30 days after transcatheter aortic valve implantation. TIA indicates transient ischemic attack.

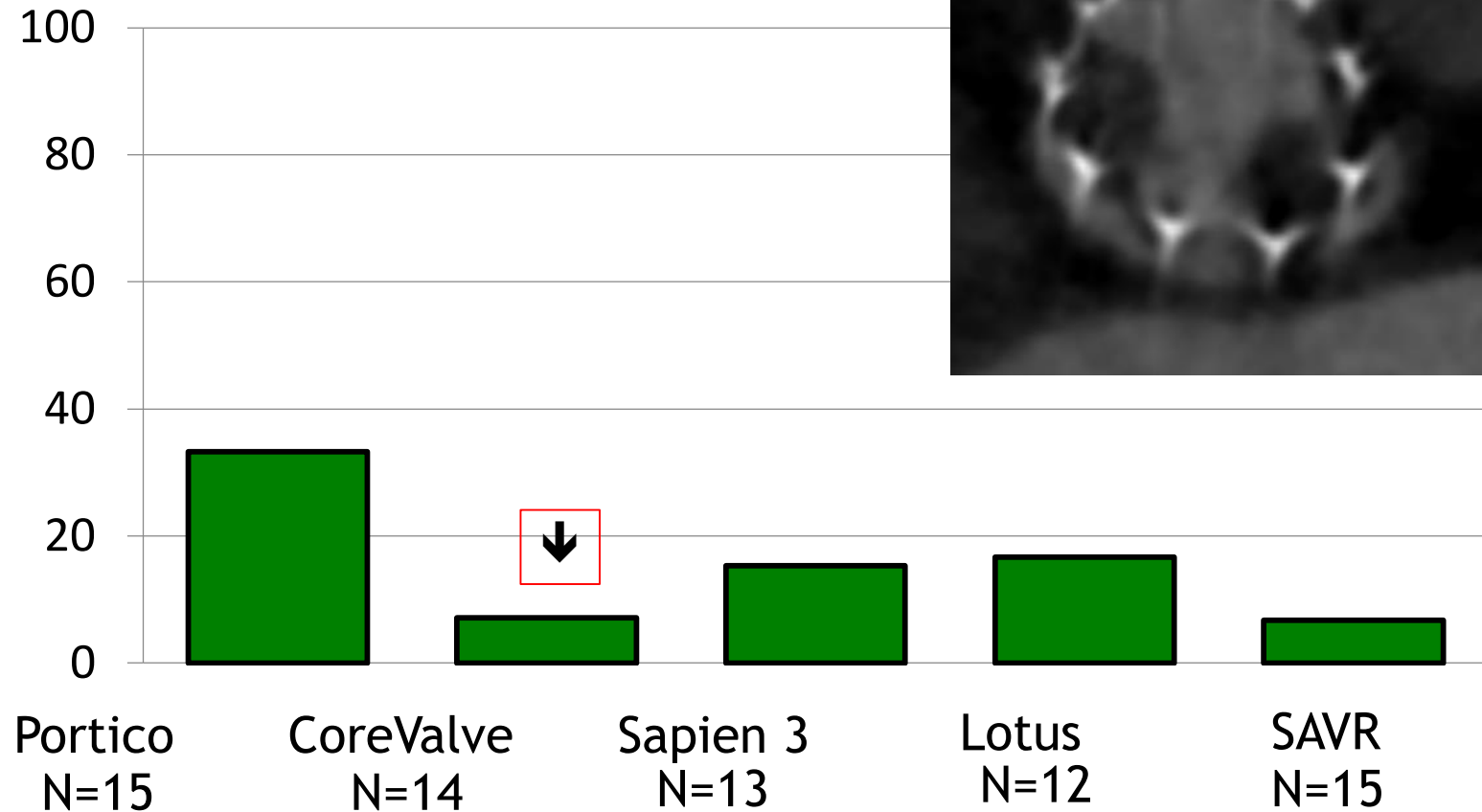
Multi-center cohort of 1,061 TAVI patients

- CVE most frequently occur day 0-1
- >50% are major strokes
- >95% of strokes are ischemic

Nombela-Franco et al., *Circulation* 2012;126:3041-53

Leaflet stress/mobility and thrombus risk

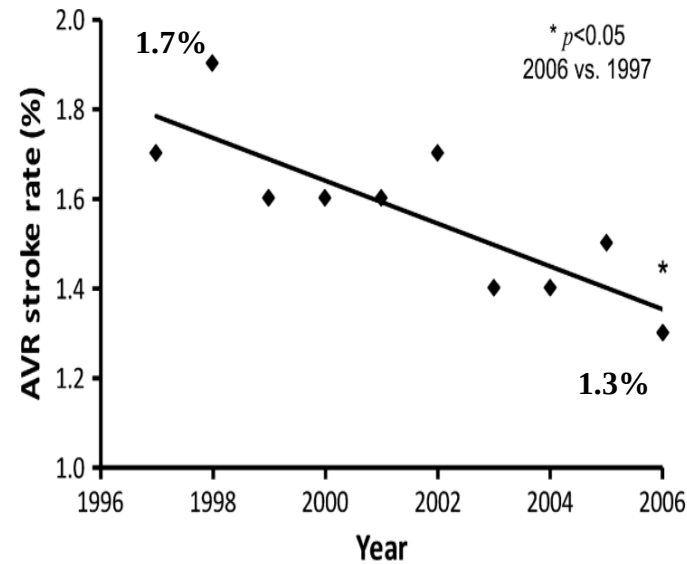
Reduced leaflet motion



P-value = 0.35 for comparing observation rates across the 5 groups

NEUROLOGIC COMPLICATIONS

STS Database. Brown et al. J Thorac
Cardiovasc Surg 2009;137:82-90

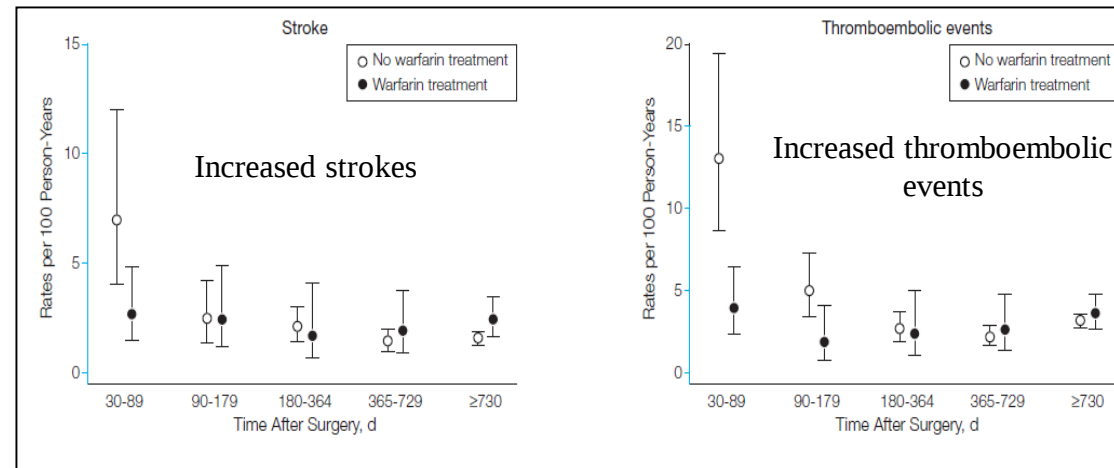


The impact of neurologic complications is controversial
Different definitions complicate the interpretation
Despite an aging and more severe population, surgical AVR shows a significant reduction in the rate of stroke over time

Association of warfarin therapy with clinical events after bioprosthetic AVR: Danish Registry

4075 patients undergoing bioprosthetic AVR in the Danish Registry

Discontinuation of warfarin treatment within 6 months after bioprosthetic AVR associated with worse outcomes



Merie C. et al. JAMA 2012

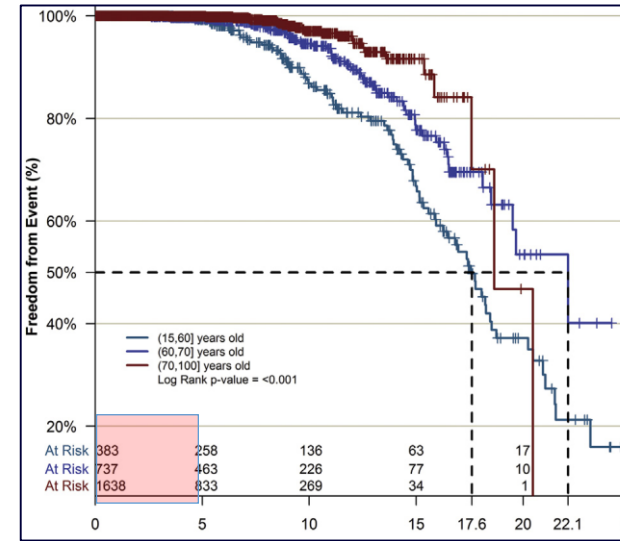
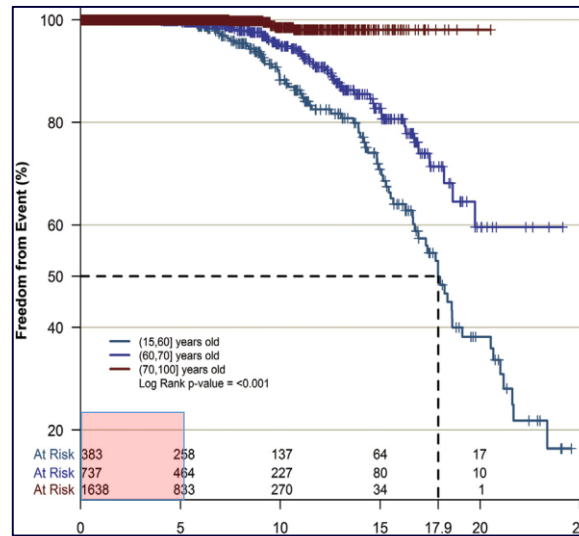
TAVI in the last years

Huge improvements, but...

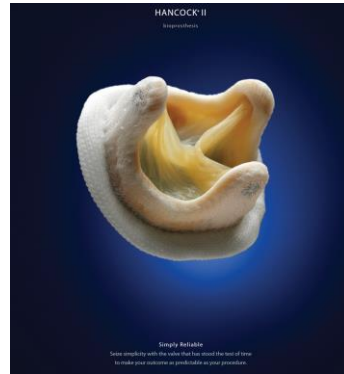
- PVL
- PCM
- Coronary obstruction
- Annulus rupture
- Stroke
- **durability**

LONGEVITY OF BIOLOGICAL PROSTHESES

Outcomes of the Carpentier-Edwards Perimount in Ao.
Bourguignon et al. Ann Thorac Surg 2015;99:831-7



Structural valve deterioration is the **Achille's heel** of bioprostheses



European Journal of Cardio-thoracic Surgery xxx (2010) xxx–xxx

EUROPEAN JOURNAL OF
CARDIO-THORACIC
SURGERY

www.elsevier.com/locate/ejcts

The fate of Hancock II porcine valve recipients 25 years after implant[☆]

Carlo Valfrè^{a,*}, Paolo Ius^a, Giuseppe Minniti^a, Loris Salvador^a, Tomaso Bottio^b,
Francesco Cesari^a, Giulio Rizzoli^b, Gino Gerosa^b

^a Cardiovascular Surgery Department, Cà Foncello Hospital, Treviso, Italy

^b Department of Cardiothoracic and Vascular Surgery, University Hospital, Padova, Italy

Received 30 September 2009; received in revised form 11 January 2010; accepted 14 January 2010

Abstract

Objective: The Hancock II (HII) is a second-generation porcine bioprosthesis introduced into clinical use in 1982. This study aimed to evaluate very long-term outcomes for the HII valve in a large patient population. **Methods:** Between May 1983 and November 1993, 517 consecutive patients (pts) (309 male, mean age: 64 ± 9 years) underwent valve replacement (VR) surgery with HII, with 302 (58.4%) in the aortic VR (AVR) and 215 (41.6%) in the mitral VR (MVR) position, respectively. At implant, 106 pts (20.5%) were <60 years of age (G1), while 411 (79.5%) were ≥ 60 years of age (G2). The 25-year follow-up was complete for all pts at a median of 12 years (range: 0–25). **Results:** Long-term death occurred in 208 AVR and in 165 MVR pts. Survival at 15 and 20 years was 39.5% and 23.3% in AVR pts and 39.0% and 15.8% in MVR pts. At 25 years the survival of MVR pts was 13.7% (four pts at risk). Late freedom from re-operation was 85.5% and 79.3% at 15 and 20 years in the AVR pts and 73.3% and 52.8% in the MVR pts, respectively. In the AVR population, 20-year freedom from re-operation was 52.2% in G1 pts and 86.8% in G2 pts ($p < 0.0001$), while in the MVR population it was 41.4% in G1 pts and 61.9% in G2 pts ($p = 0.201$), respectively. **Conclusions:** These results confirm the excellent long-term performance of the HII bioprosthesis.

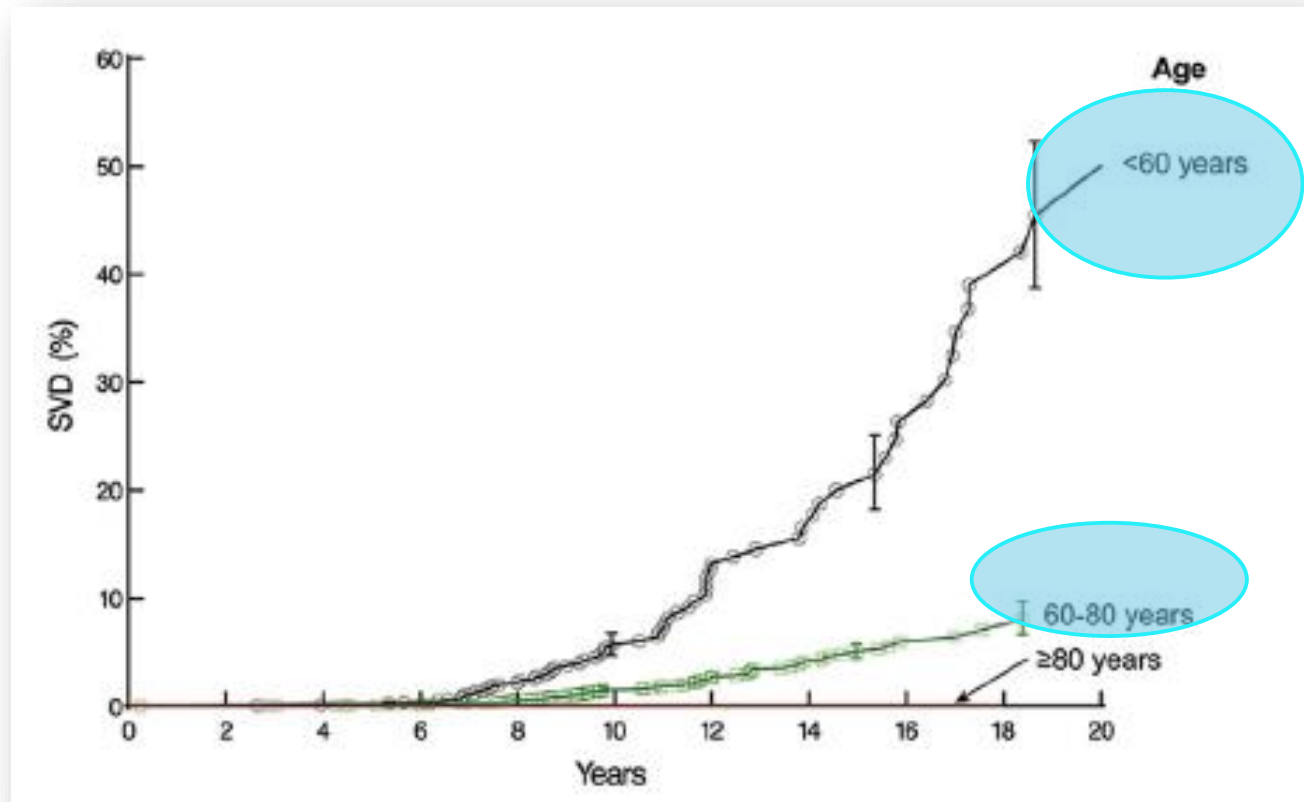
© 2010 Published by Elsevier B.V. on behalf of European Association for Cardio-Thoracic Surgery.

Keywords: Bioprosthesis; Hancock valve; Long-term outcome

Long-Term Durability of Bioprosthetic Aortic Valves: Implications From 12,569 Implants

Douglas R. Johnston, MD, Edward G. Soltesz, MD, Nakul Vakil, MD, Jeevanantham Rajeswaran, PhD, Eric E. Roselli, MD, Joseph F. Sabik, III, MD, Nicholas G. Smedira, MD, Lars G. Svensson, MD, PhD, Bruce W. Lytle, MD, and Eugene H. Blackstone, MD

Department of Thoracic and Cardiovascular Surgery, Heart and Vascular Institute, and Department of Quantitative Health Sciences, Research Institute, Cleveland Clinic, Cleveland, Ohio

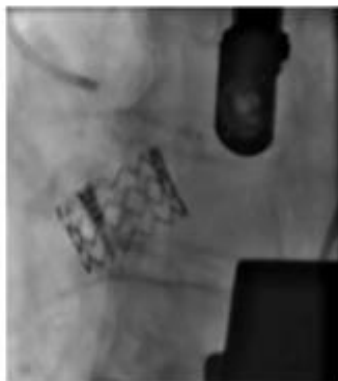


TAVI Complications

- Complications are **PROCEDURE + DEVICE** related



PVL



Annular rupture



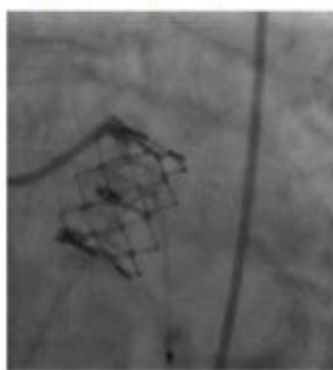
Aortic dissection



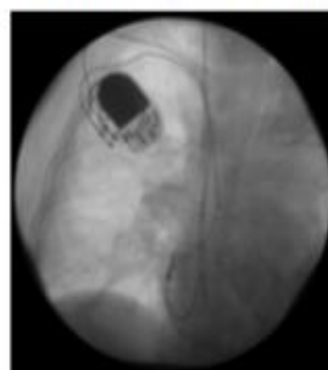
Vascular complications



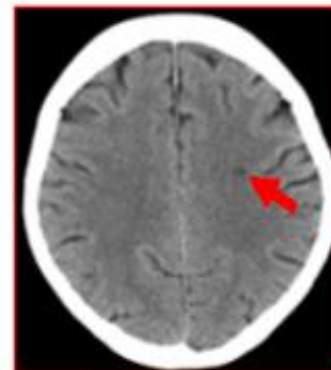
Device embolization



Coronary Occlusion



AV-Block



Stroke

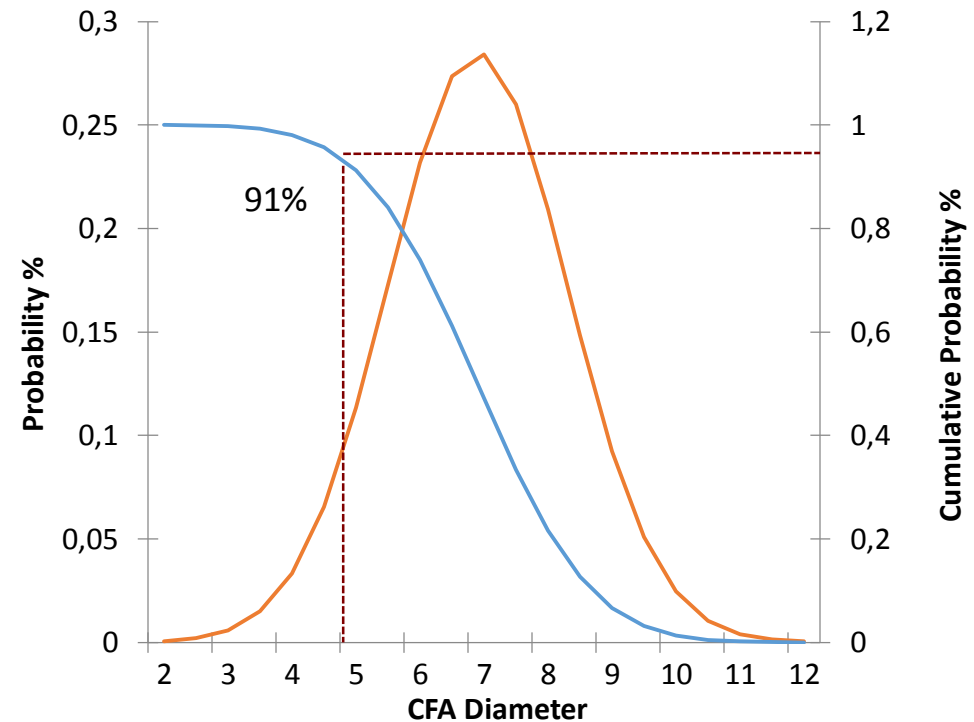
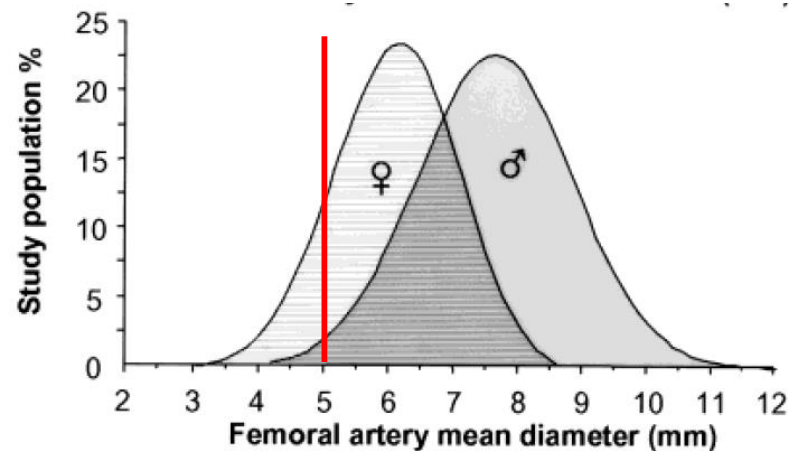
Minimal Femoral Artery Diameter

How Many Patients Can We Treat Transfemorally?

Common Femoral Artery was measured by angiography in 200 patients

Mean Lumen Diameter (mm)	6.9 ± 1.4	5.1 ± 1.1	6.3 ± 1.2
--------------------------	-----------	-----------	-----------

- ~74% of patients have CFA ≥6 mm
- ~91% of patients have CFA ≥5 mm



Contemporary Delivery Systems

Indicated Vessel Size

Evolut R has the potential to reach 17% more patients due to it's low profile

	 SAPIEN XT			 SAPIEN 3		 Lotus	 CoreValve	 Evolut R
Valve Size (mm)	20, 23	26	29	20, 23, 26	29	23, 25, 27	23, 26, 29, 31	23, 26, 29
Indicated Vessel Diameter (mm)	6.0	6.5	7.0	5.5	6.0	6.0	6.0	5.0

- Clinical expertise → overcome gaps from access to deployment by tips and tricks skills
- Engineering → Reliability, Reproducibility, Durability

Time for a make over?



All lights are green for extension?

- ✓ Screening is more simple and well defined
- ✓ We have learned how to avoid futile cases
- ✓ The procedure is well standardised and the outcome predictable
- ✓ Femoral approach/ alternatives are safe and less invasive
- ✓ The risk of stroke is lower compared to surgery
- ✓ We have learned how to avoid and manage complications

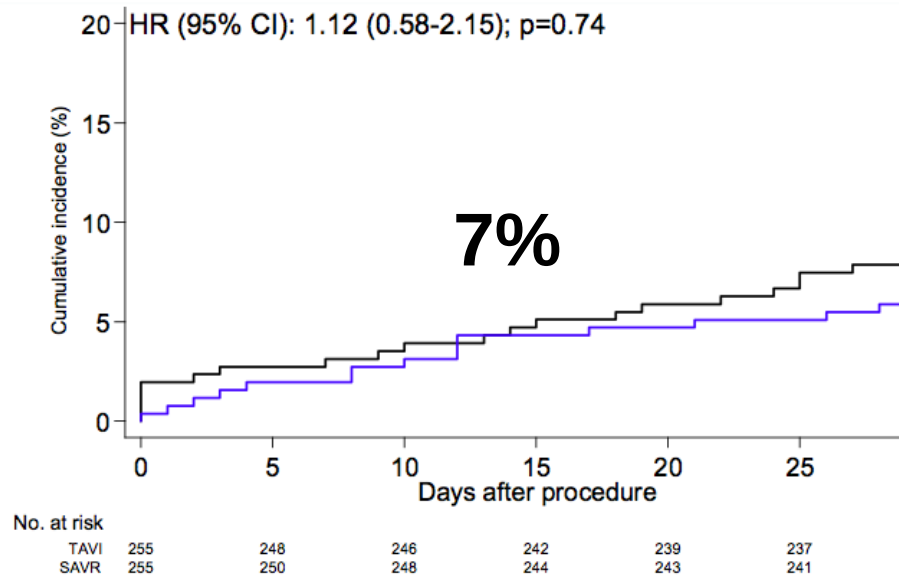
A 3-Center Comparison of 1-Year Mortality Outcomes Between Transcatheter Aortic Valve Implantation and Surgical Aortic Valve Replacement on the Basis of Propensity Score Matching Among Intermediate-Risk Surgical Patients

Nicolo Piazza, MD, PhD,*† Bindu Kalesan, PhD,‡ Nicolas van Mieghem, MD,§
Stuart Head, MSc,|| Peter Wenaweser, MD,¶ Thierry P. Carrel, MD,# Sabine Bleiziffer, MD,*†
Peter P. de Jaegere, MD, PhD,§ Brigitta Gahl,# Robert H. Anderson, MD, PhD,**
Arie-Pieter Kappetein, MD, PhD,|| Ruediger Lange, MD, PhD,*†
Patrick W. Serruys, MD, PhD,§ Stephan Windecker, MD,¶ Peter Jüni, MD‡

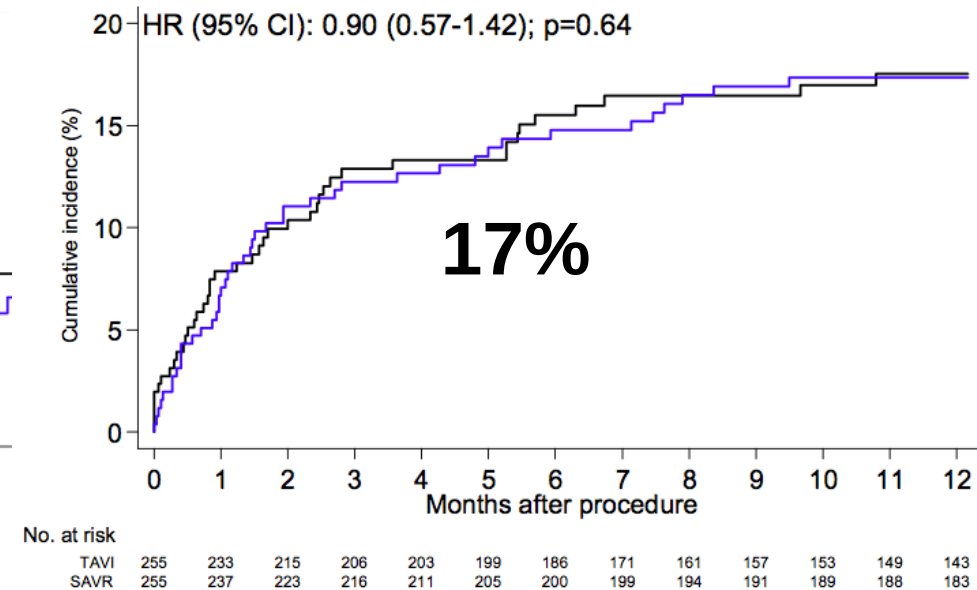
Matched TAVI vs. SAVR

STS 3-8%

30-day All-cause mortality



1-year All-cause mortality



— TAVI — SAVR

Similar outcomes between TAVI & SAVR in “matched” intermediate risk . . .

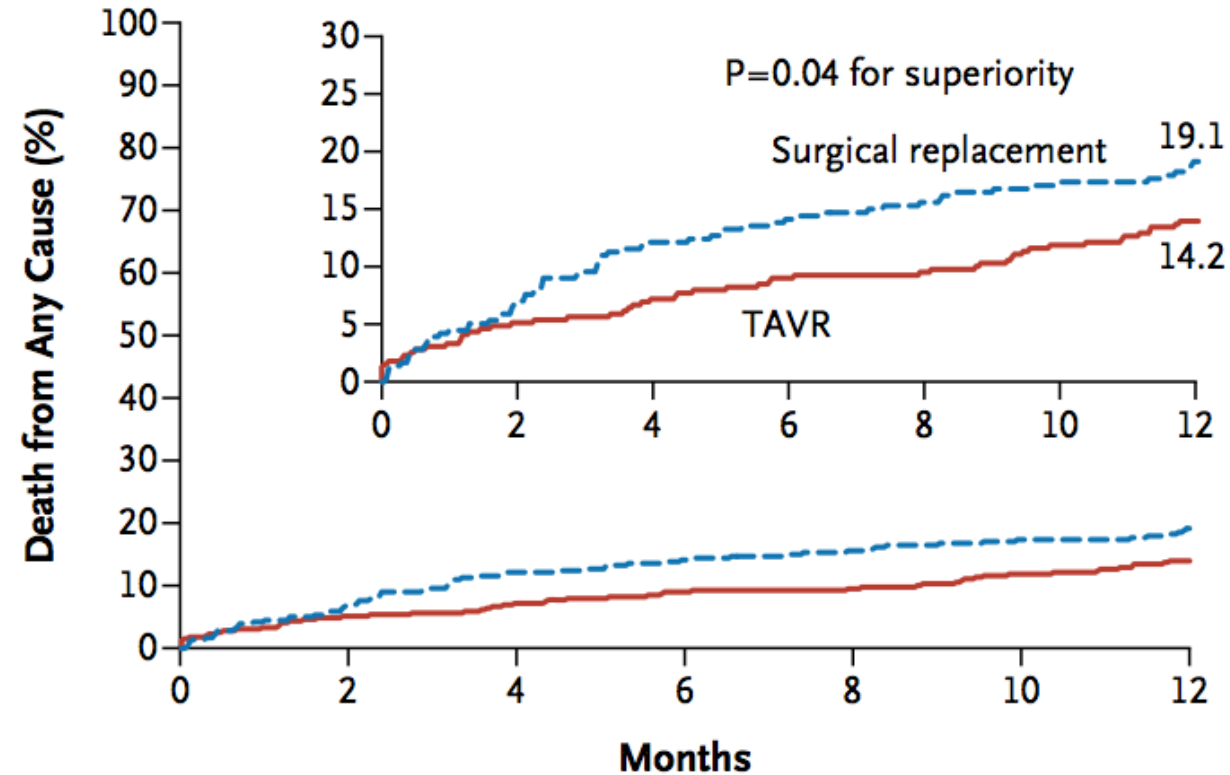
	Piazza ¹			OBSERVANT ²			Latib ³		
	TAVI (n=255)	SAVR (n=255)	p	TAVI (n=133)	SAVR (n=133)	p	TAVI (n=111)	SAVR (n=111)	p
STS (%, mean)	3-8	3-8		na	na		4.6	4.6	
Log EuroSCORE (%, mean)	17.3	17.6		8.9	9.4		23.2	24.4	
30 Day Mortality (%)	7.8	7.1	0.74	3.8	3.8	1.0	1.8	1.8	1.0

¹Piazza, et al. J Am Coll Cardiol Interv 2013; 6:443-51

²D’Errigo, et al. Int J Cardiol 2013; 167:1945-52

³Latib, et al. Am Heart J 2012; 164:910-7

US Pivotal Corevalve High-Risk SAVR vs. TAVI



No. at Risk

TAVR	390	377	353	329
Surgical replacement	357	341	297	274

High Risk



Morbidities

Intrinsic Co-Morbidities

- ✓ **Diabetes**
- ✓ **COPD**
- ✓ **CKD**
- ✓ **LV dysfunction**
- ✓ **Frailty**
- ✓ **...**

Procedure Morbidities

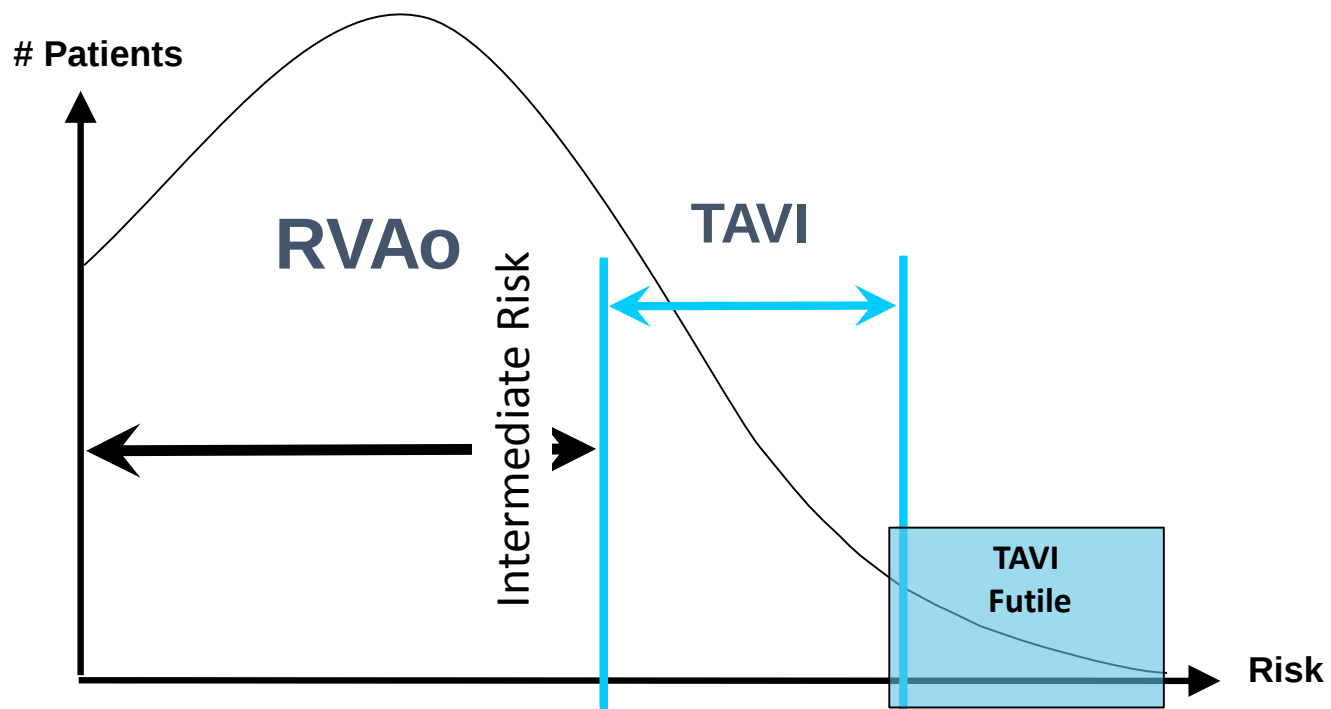
- ✓ **SAVR**
- ✓ **Alternative access**
- ✓ **Need for general anesthesia**
 - ✓ **Delirium**
 - ✓ **Pain**
 - ✓ **Recovery time**
 - ✓ **QOL**

**15 years after the first compassionate
case performed by Alain Cribier**

What conditions should be fulfilled to extend TAVI

- ✓ Safety at least similar to surgery
- ✓ Outcome at least similar to surgery
- ✓ Hospital stay shorter
- ✓ Recovery quicker
- ✓ Cost lower
- ✓ Valve performance at least similar
- ✓ Durability at least similar

...Intermediate Risk...

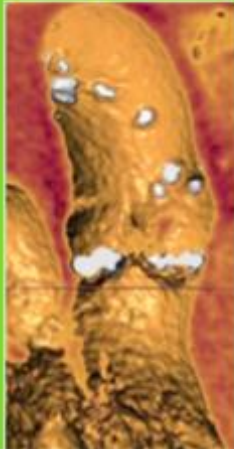


Tailored indications

Easy

almost all devices will work

- No PVL
- No PPM
- No DLZ rupture
- No coronary occlusion



Intermediate

might favor one specific device or strategy to avoid

- PVL
- PPM
- DLZ rupture
- coronary occlusion

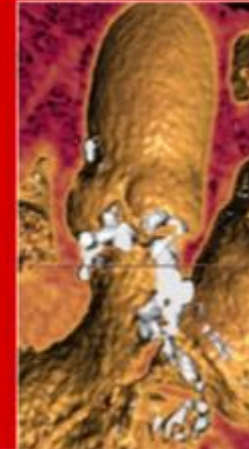


Hostile

TAVI might not be the best option

Risk for

- PVL
- PPM
- coronary occlusion
- DLZ rupture



Conclusion

- SAVR also has limits
- TAVR would be a better option:
- If performed within the confines of a Heart Team
- If outcomes with newer generation valves and technical improvements address common technical limitations
- RCT

Innovation is inevitable...
Do you want to part of it?

*It is not the strongest species that survives, nor the most intelligent, but rather the one most **adaptable to change**.*

----- Charles Darwin

All for ONE and ONE for All



“ONE Heart Center”

“ONE Heart Team”

**“ONE Disease with multiple
treatment options”**