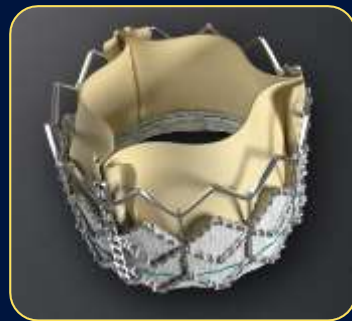


TCT-AP 2015
Seoul, April 30th, 2015

Why I select a Self-Expanding Valve

(inspired by J. Hermiller MD FACC)



Eberhard Grube, MD, FACC, FSCAI, FAPSCIC
University Hospital Bonn, Germany
Stanford University, Palo Alto, USA

Eberhard Grube, MD

Financial Disclosure

Physician Name

Eberhard Grube, MD

Company/Relationship

Medtronic, CoreValve: C, SB, AB, OF
Direct Flow: C, SB, AB
Mitralign: AB, SB, E
Boston Scientific: C, SB, AB
Cordis: AB
Abbott Vascular: AB
Valtech: E, SB,
In Seal Medical: SB, E
Claret: SB
Keystone, SB
Shockwave: E, SB

Key

G - Grant and or Research Support E - Equity Interests

C - Consulting fees, Honoraria R - Royalty Income

SB - Speaker's Bureau

O - Ownership OF - Other Financial Benefits

S - Salary, AB - Advisory Board

I - Intellectual Property Rights

TAVI has Arrived....

Current Generation Devices

***>200,000 patients treated in >750
interventional centers
around the globe!***

Edwards Lifesciences

Medtronic CoreValve

Anatomic “Footprint” of Edwards Sapien Valve vs. MDT CoreValve



Design, Frame, Metal, Leaflets, Delivery

Advantages of BE Edwards Sapien

- Short frame design – less interference with peri-valve anatomy (conduction system, CAs)
- Precise positioning in the sub-annular zone (but requires RV pacing for deployment)
- Deflectable delivery system to negotiate arch anatomy and vessel tortuosity
- Circular frame/valve deployment in annular zone
- Full thickness bovine pericardium – good durability (?)
- Access site versatility (TF, TA, TAO)

Advantages of SE MDT CoreValve

- More valve sizes to accommodate full range of annular dimensions (esp. large sizes)
- Slow controlled valve deployment without need for rapid RV pacing
- Partial repositioning features during deployment
- Less trauma to annulus and aorta – reduced risk of rupture
- Circular frame/valve in supra-annular zone (better for small annulus and small V-in-V)
- Access site versatility (TF, SC, T Ao)
- LMA distance from annulus less important

The Data and.....



Personal Preference and Experience

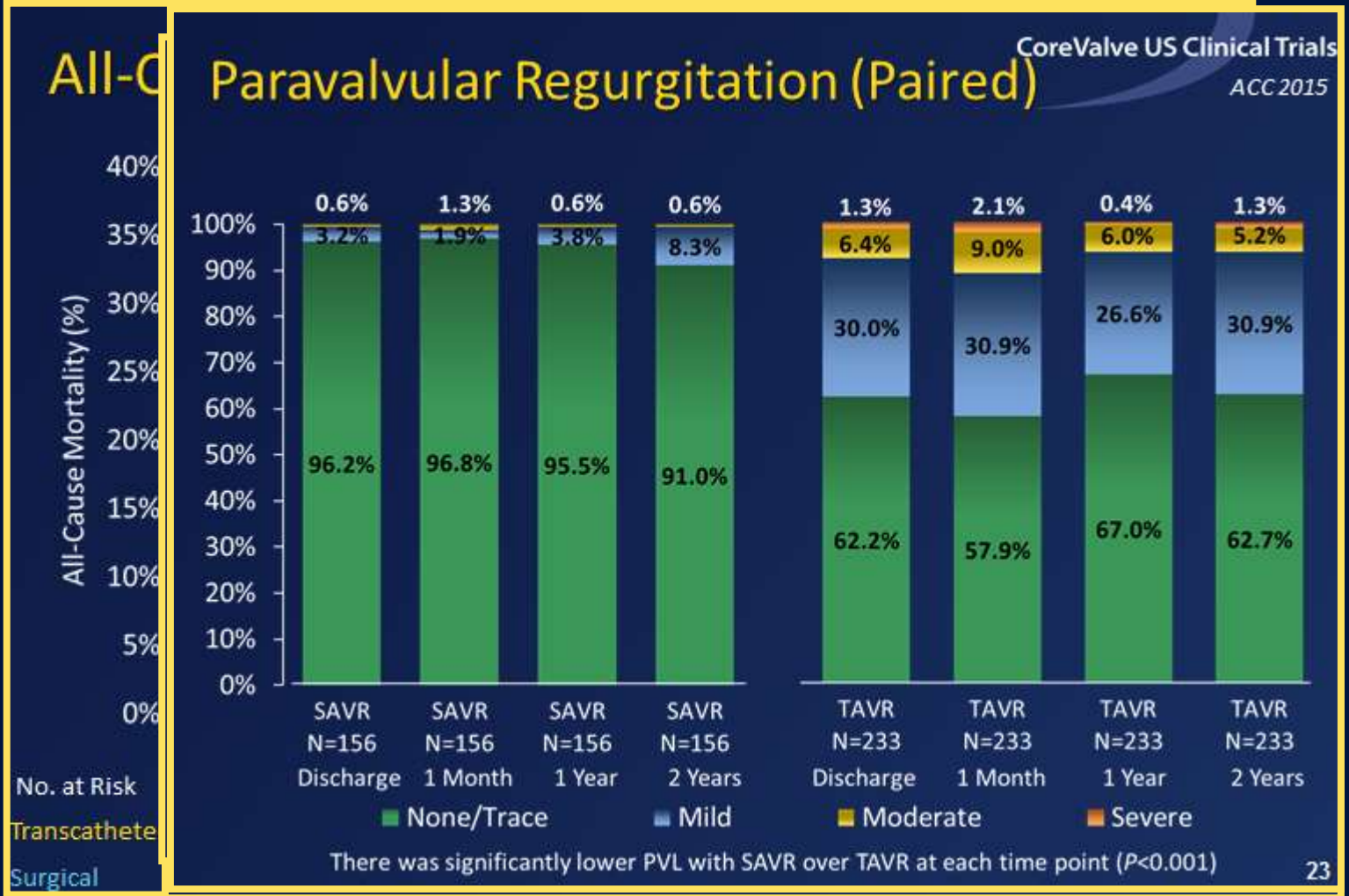
Ideal Transcatheter Heart Valve

- Valve Performance: Large EOA and Durable
- No/Minimum PVL
- Deliverable: Low Profile, Easy Positioning
- R³ = Retrievable, Repositionable, and Resheathable
- Minimize Complications:
 - Conduction Disturbances, Coronary Obstruction and Annular Perforation

Outline

- Introduction
- Self Expanding Results
- Next Generation Self-Expanding Platforms
- Extended Applications
- Summary

Results: Self-Expanding



Results: Self-Expanding

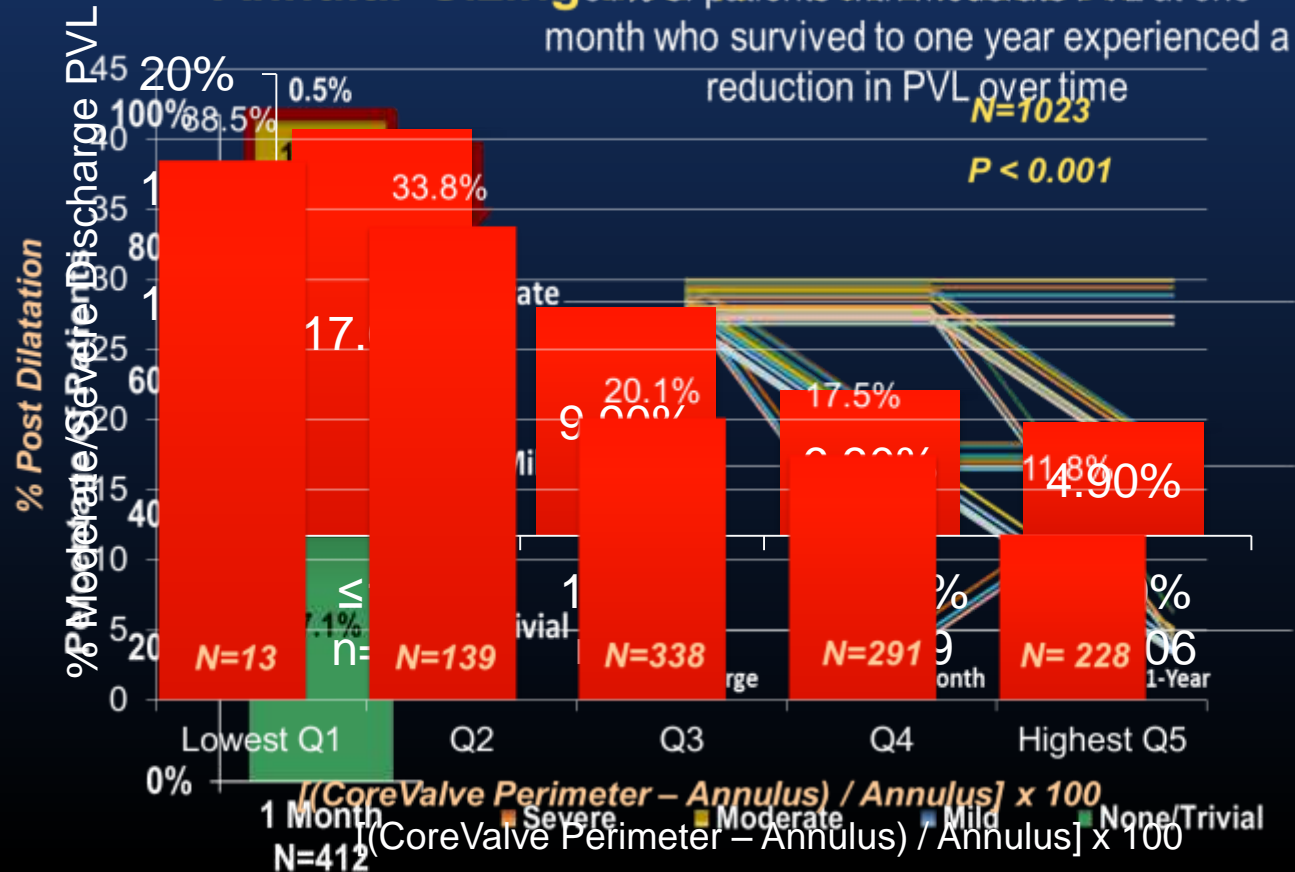
Paravalvular Regurgitation

Sizing Ratio and Mod/Severe PVL

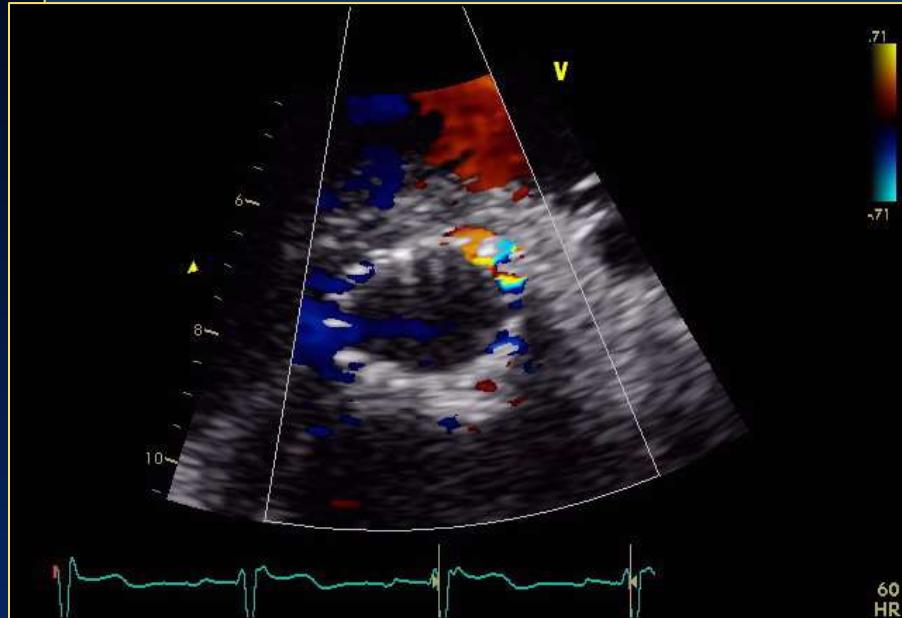
Annular Sizing and Post-Dilatation at one month who survived to one year experienced a reduction in PVL over time

N=1023

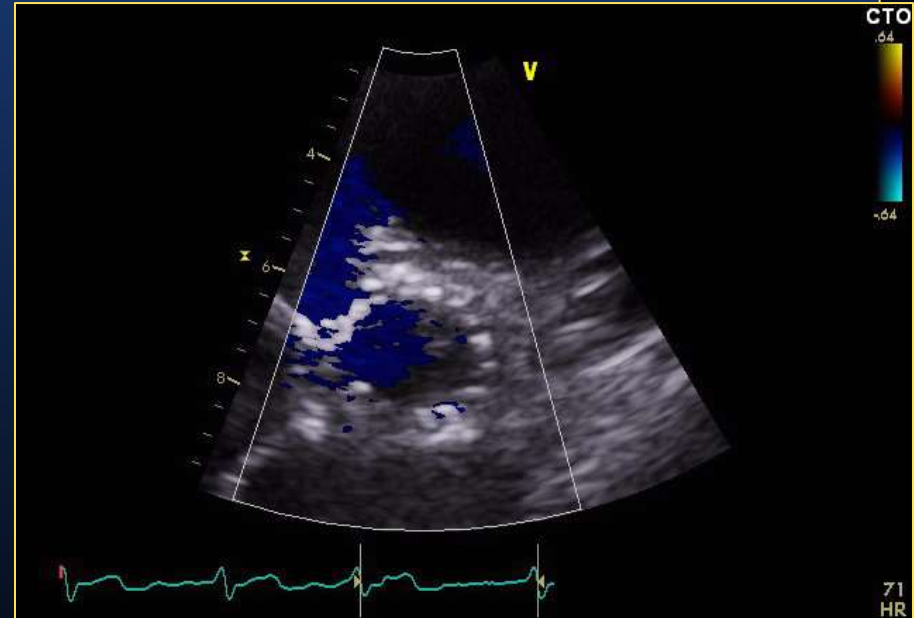
P < 0.001



PVL Regresses Over Time



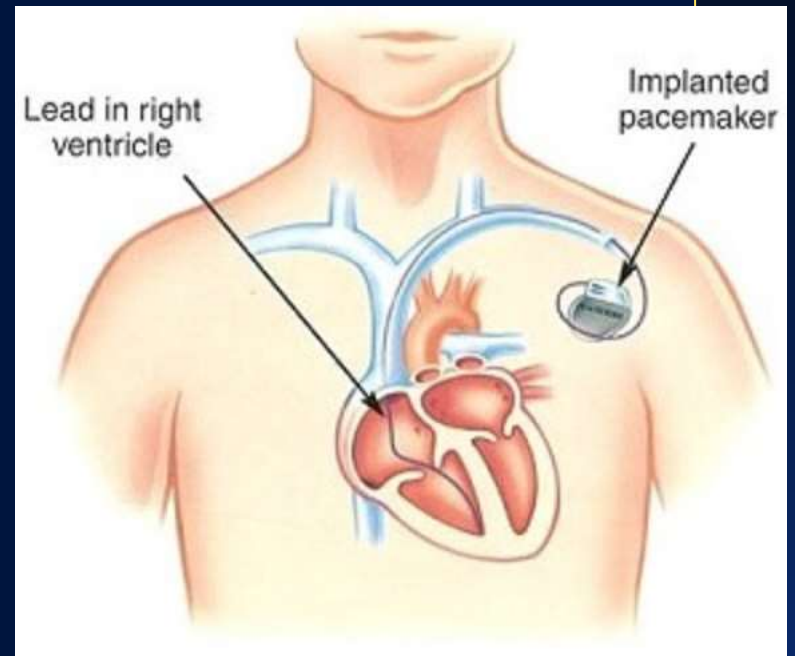
*Discharge
Moderate PVL*



1-year follow-up

Conduction Abnormalities

Self Expanding platforms

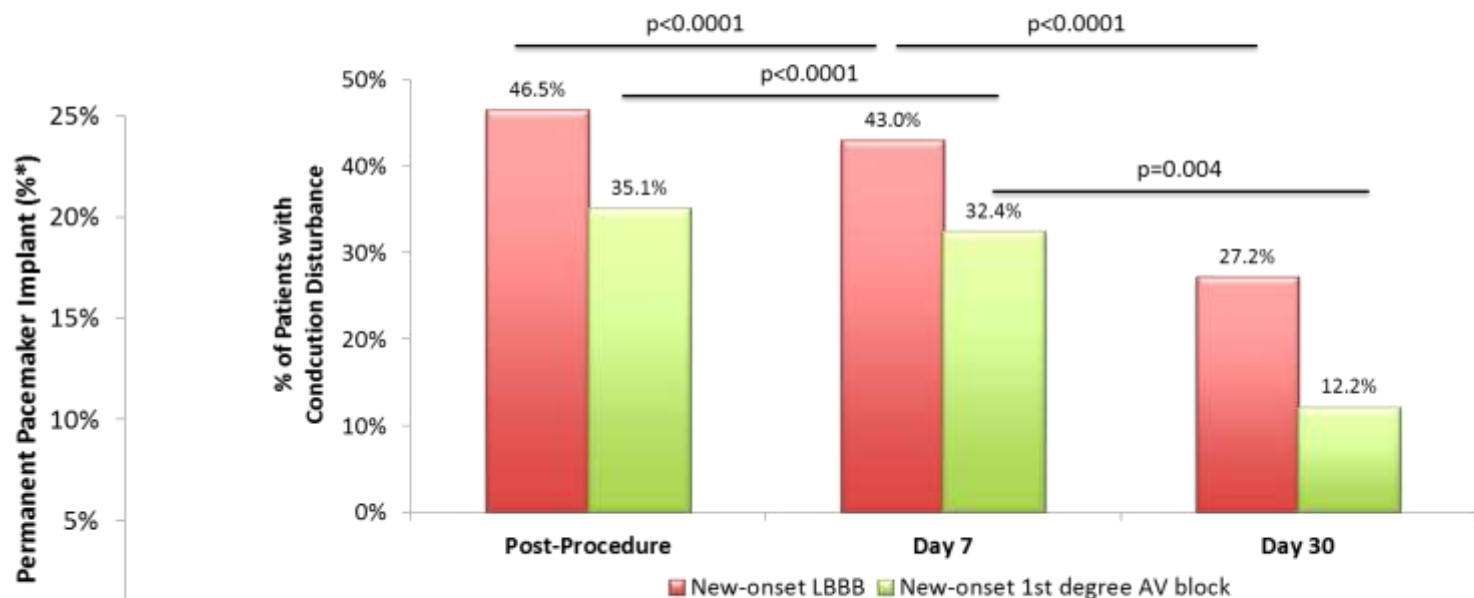


Conduction Disturbances and PPM

- The p
- depl
- 34 /

- Paired data demonstrated how new-onset conduction disturbances resolved over time
- 42% of new LBBB and 65% of new 1st degree AV block resolved spontaneously by day 30

Conduction Disturbance Resolution



Patients with normal baseline AV conduction were considered for new-onset AV block. Patients with normal baseline IV conduction were considered for new-onset LBBB. New-onset is defined as a new conduction disturbance which initiates within 48 hours of TAVI.

Patients receiving new permanent pacemakers were excluded.

Paired data for each type of conduction disturbance. LBBB n=114, 1st degree block n=74

Implant depth defined as the distance from the lower edge of the non-coronary leaflet to the ventricular edge of the frame

CoreValve ADVANCE II Study

*Kaplan-Meier rate
*Z-test

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Nitinol platforms - R³

Recapture – Reposition - Retrieve

Operator
confidence

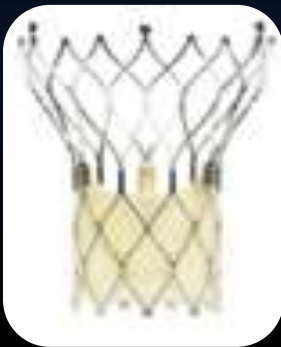
Learning curve

Malplacement

Valve embolization

Paravalvular aortic
regurgitation

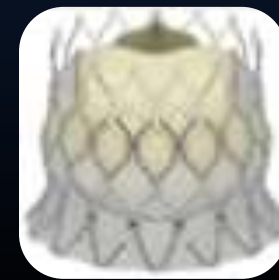
Conduction
abnormalities



***St. Jude
Portico***



***Medtronic CoreValve
Evolut R***



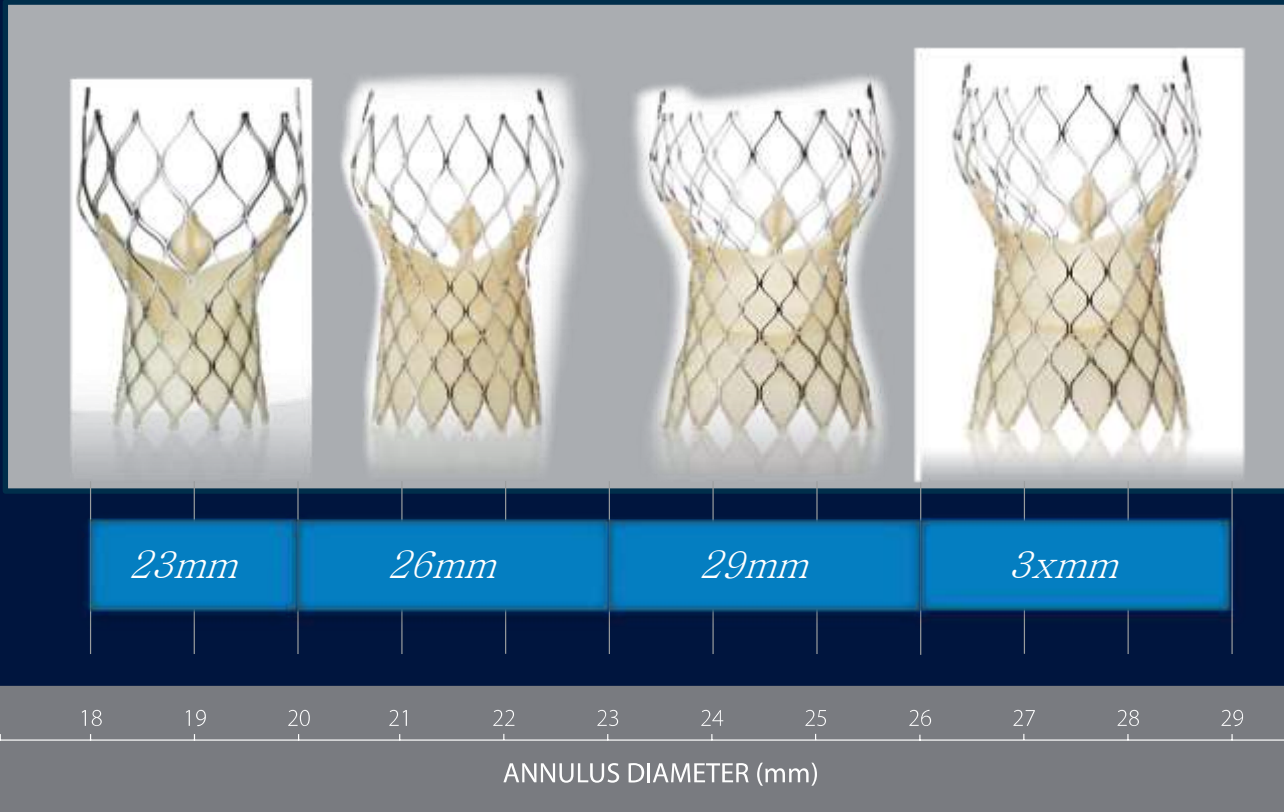
***Edwards
Sapien***

Future Platforms....



CoreValve Evolut System

Fully Resheathable, Repositionable, Recapturable



- *Annulus range (18 – 29mm)*
- *Radial force throughout expansion uniform*
- *Shorter prosthesis length*

CoreValve Evolut System

[2101-295] Early Results From the CoreValve Evolut R CE Study

Ian T. Meredith, MBBS, PhD, FACC¹; Antony Walton, MBBS²; Stephen Brecker, MD³; Sanjeevan Pasupati, MBChB⁴; Daniel Blackman, MD⁵; Ganesh Manoharan, MBBCh, MD⁶
¹MonashHEART and Monash University, Melbourne, Australia; ²Epworth Hospital, Melbourne, Australia; ³St. George's Hospital, London, United Kingdom; ⁴Waikato Hospital, Hamilton, New Zealand; ⁵Leeds General Infirmary, United Kingdom; ⁶Royal Victoria Hospital, Belfast, United Kingdom

CoreValve Evolut R CE Study

Background	Baseline Characteristics	Procedural Outcomes	Clinical Performance
Technological advancements in transcatheter aortic valve replacement (TAVR) have improved outcomes. However, optimal positioning may be associated with less paravalvular leak (PVL) and lower pacemaker rates. We evaluated 30-day outcomes following TAVR with the fully repositionable CoreValve Evolut R self-expanding TAV.	Characteristic, % or mean ± SD N=80	Characteristic, % N=80	Event, % N=80
	Age, years 82.8 ± 6.1	General anesthesia 63.3	Absence of procedural mortality 100.0 (60/60)
	Weight, kg 66.7	Access approach (transfemoral) 98.3	Correct positioning of 1 valve in proper location 98.3 (59/60)
	Body surface area (m ²) 1.7 ± 0.2	Pre-TAVR balloon aortic valvuloplasty 96.7	Mean gradient < 20 mm Hg or peak velocity < 3 m/sec 98.3 (59/60)
	STS Predicted Risk of Mortality (%) 7.0 ± 3.7	Successful valve repositioning, if attempted (n=15*) 100 (22/22)†	Absence of moderate or severe PVL 93.3 (56/60)
	Logistic EuroSCORE I (%) 20.5 ± 12.5	Valve repositioning, n 10	Absence of patient prosthesis mismatch* 83.6 (46/55)
	New York Heart Association class III or IV 68.3	Valve recapture, n 12	VARC-2 device success 78.6 (44/56)
	Previous CABG 28.3	Valve size implanted	
	Any chronic lung disease 43.3	26 mm 31.7	
	Diabetes 26.3	29 mm 68.3	
	Coronary artery disease 68.3	Post-TAVR balloon dilatation 21.7	
	Atrial fibrillation / atrial flutter 36.7	Valve-related dysfunction requiring repeat procedure 0.0	
	Frailty 68.3		
	Pre-existing permanent pacemaker 11.7		

Procedural Result

Event, %

Study Design & Methods

The CoreValve Evolut R CE Clinical Study evaluated the safety and clinical performance of the CoreValve Evolut R System (26-32 mm) in 80 patients with aortic stenosis. The study was a prospective, non-randomized, single-center study conducted in Australia, New Zealand, and the United Kingdom. The primary safety endpoints were the rate of all-cause mortality and the rate of stroke at 30 days. The primary clinical performance endpoints were the rate of moderate or severe PVL, the rate of moderate or severe PVL, and the rate of permanent pacemaker implantation at 30 days. All patients underwent a multidisciplinary team assessment. Multislice CT of the peripheral aortic and aortic annulus was performed. A central core laboratory (Mayo Clinic, Rochester, Minnesota) assessed all echocardiographic results. All patients were followed up for 30 days post-procedure.

Absence of procedural mortality

Correct positioning of 1 valve in proper location

30 Day Event, %
 Mean gradient < 20 mm Hg or peak velocity < 3m/sec

N=60

100.0 (60/60)

98.3 (59/60)

98.3 (59/60)

30-Day Outcomes

Event, %	N=80
All-cause mortality	0.0
All stroke	0.0
Absence of moderate or severe PVL	96.6
Permanent pacemaker implantation	11.7

N=60

93.3 (56/60)

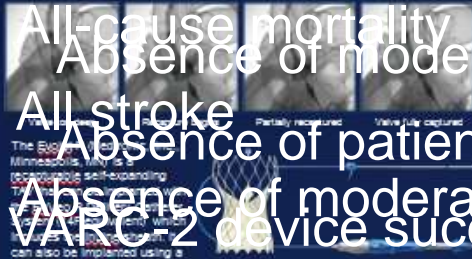
83.6 (46/55)

96.6

78.6 (44/56)

11.7

Device Description and Use



All-cause mortality

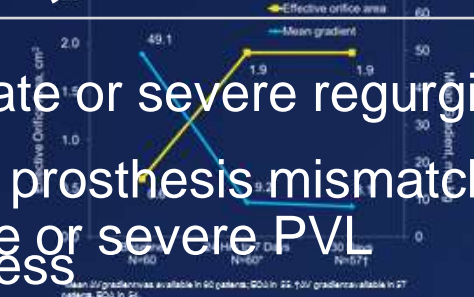
Absence of moderate or severe regurgitation

All stroke

Absence of patient prosthesis mismatch*

Absence of moderate or severe PVL

VARC-2 device success



Summary & Conclusions

All attempts at repositioning of the Evolut R TAVR were successful and resulted in a final implant depth of 1.6 ± 0.3 ± 4.1 mm, NCS = 5.9 ± 3.4 mm. The ability to achieve the target implant depth in affected the rate of moderate or severe PVL. The mean orifice area in the implanted patients who had permanent pacemakers. The mean orifice area in the implanted patients who had permanent pacemakers compared with those who did not had a mean difference of 3.1 mm, NCS: 3.3 ± 2.5 mm vs 8.1 ± 3.5 mm, both P < 0.001. In addition, the percentage of patients with mild or less paravalvular leak (PVL) was 93.3% at the early post-procedure evaluation, and 96.6% at 30 days.

The VARC-2 overall device success rate was 78.6% in patients who had permanent pacemaker implantation. There were no deaths or strokes at 30 days. The CoreValve Evolut R TAVR system is safe and effective at treating aortic stenosis. The ability to repositioning was successful in all patients when required, and resulted in low rates of moderate or severe PVL and the need for permanent pacemakers.

Smaller Profile

CoreValve Evolut System

*CoreValve w/
18 Fr Cook Sheath*

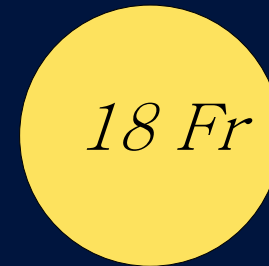


7.3 mm

4 Fr reduction

*68% cross-sectional
area reduction*

*EnVeo R w/
InLine Sheath*



6.0 mm

Minimal lumen artery diameter = 5 mm

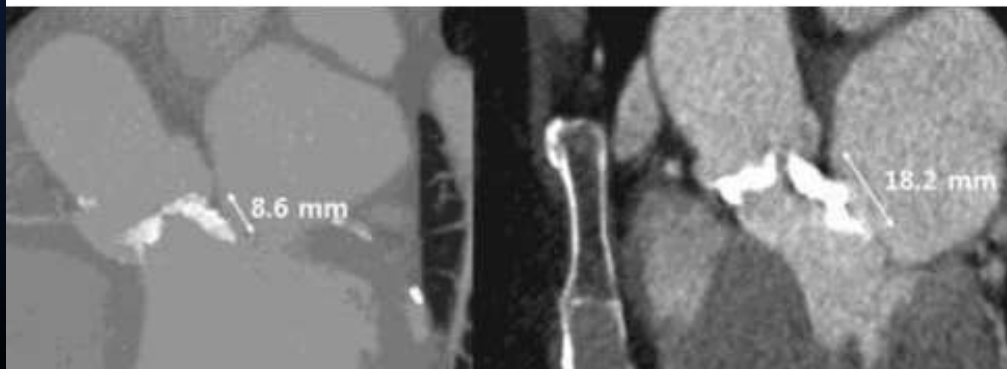
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High Risks for Annular Rupture

Anatomical and Procedural Features Associated With Aortic Root Rupture During Balloon-Expandable Transcatheter Aortic Valve Replacement

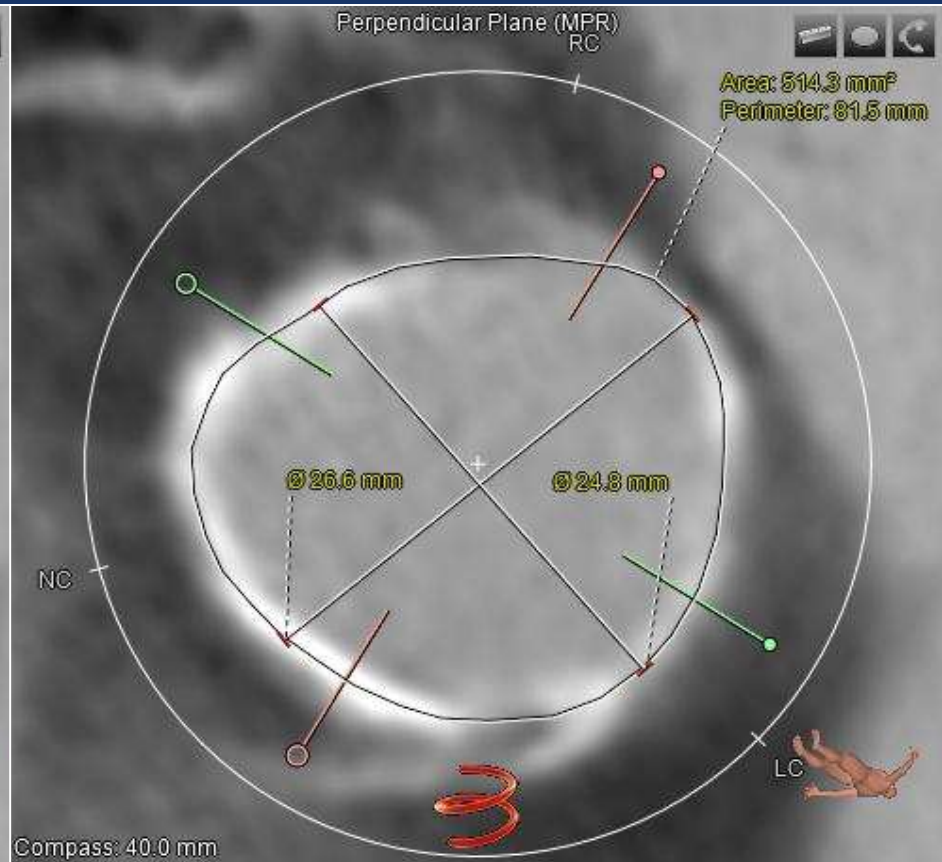
Marco Barbanti, MD; Tae-Hyun Yang, MD, Josep Rodès Cabau, MD; Corrado Tamburino, MD; David A. Wood, MD; Hasan Jilaihawi, MD; Phillip Blanke, MD; Raj R. Makkar, MD; Azeem Latib, MD; Antonio Colombo, MD; Giuseppe Tarantini, MD; Rekha Raju, MD; Ronald K. Binder, MD; Giang Nguyen, MD; Melanie Freeman, MD; Henrique B. Ribeiro, MD; Samir Kapadia, MD; James Min, MD; Gudrun Feuchtner, MD; Ronen Gurtvich, MD; Faisal Alqoofi, MD; Marc Pelletier, MD; Gian Paolo Ussia, MD; Massimo Napodano, MD; Fabio Sandoli de Brito, Jr, MD; Susheel Kodali, MD; Bjarne L. Norgaard, MD; Nicolaj C. Hansson, MD; Gregor Pache, MD; Sergio J. Canovas, MD; Hongbin Zhang, PhD; Martin B. Leon, MD; John G. Webb, MD; Jonathon Leipsic, MD



- 1) Valve oversizing >20%
- 2) Moderate/severe LVOT calcification

Barbanti et al. Circulation. 2013;128:244-253.

Heavily calcified and relatively small STJ





Conformability

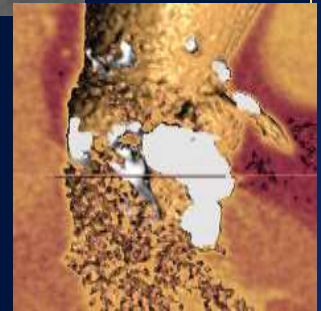
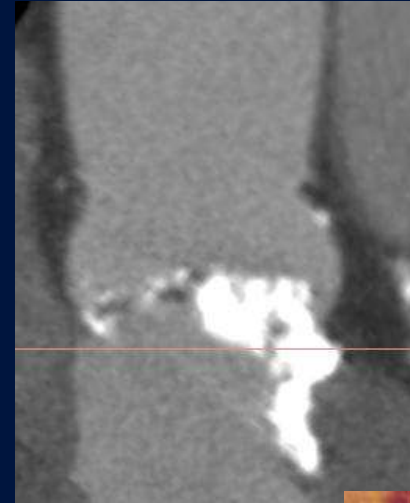
Many Important Anatomical Considerations



Calcification



Tortuosity



Other Challenges

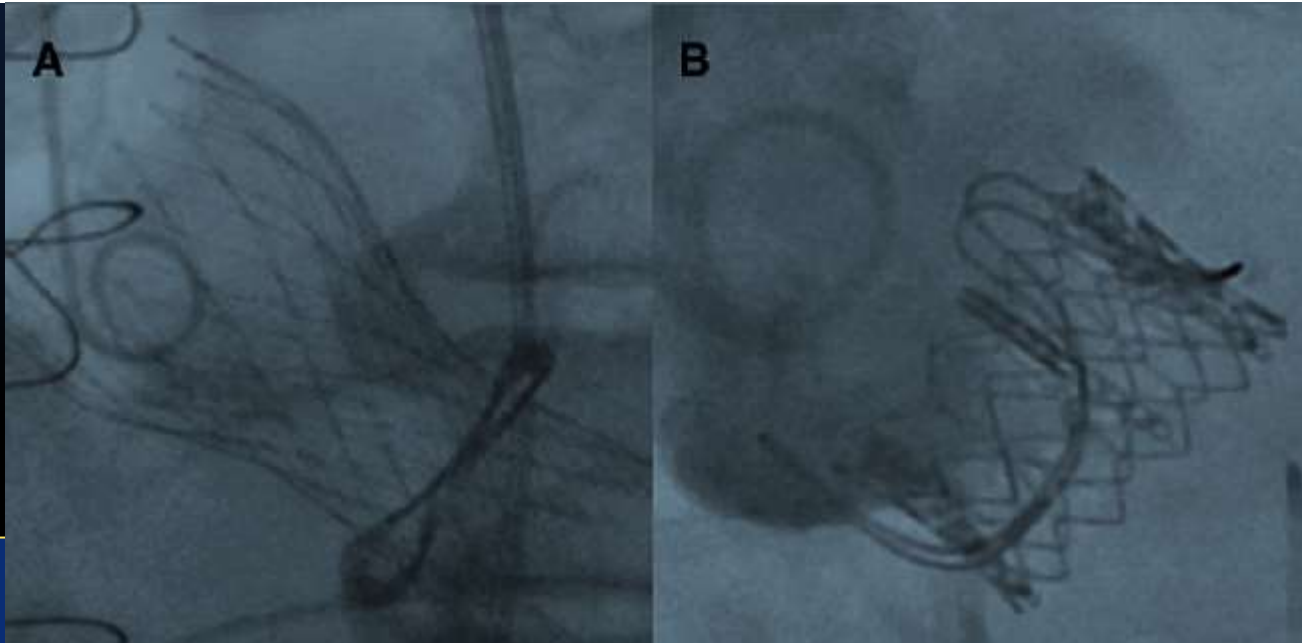
Valve in Valve

Original Investigation

Transcatheter Aortic Valve Implantation in Failed Bioprosthetic Surgical Valves

Danny Dvir, MD; John G. Webb, MD; Sabine Bleiziffer, MD; Miralem Pasic, MD, PhD; Ron Waksman, MD; Susheel Kodali, MD; Marco Barbanti, MD; Azeem Latib, MD; Ulrich Schaefer, MD; Josep Rodés-Cabau, MD; Hendrik Treede, MD; Nicolo Piazza, MD, PhD; David Hildick-Smith, MD; Dominique Himbert, MD; Thomas Walther, MD; Christian Hengstenberg, MD; Henrik Nissen, MD, PhD; Raffi Bekeredjian, MD; Patrizia Presbitero, MD; Enrico Ferrari, MD; Amit Segev, MD; Arend de Weger, MD; Stephan Windecker, MD; Neil E. Moat, FRCS; Massimo Napodano, MD; Manuel Wilbring, MD; Alfredo G. Cerillo, MD; Stephen Brecker, MD; Didier Tchetché, MD; Thierry Lefèvre, MD; Federico De Marco, MD; Claudia Fiorina, MD; Anna Sonia Petronio, MD; Rui C. Teles, MD; Luca Testa, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; Ran Kornowski, MD;
for the Valve-in-Valve International Data Registry Investigators

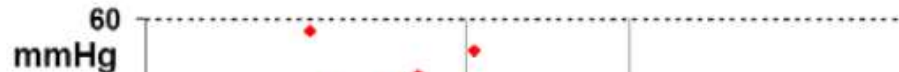
JAMA 2014 312(12):162-170



Analysis of Post-procedural Gradients After Valve-in-Valve (VinV) Procedures According to Surgical Bioprosthesis Size: Small (Internal Diameter <20 mm), Intermediate (≥ 20 and <23) and Large (≥ 23 mm)

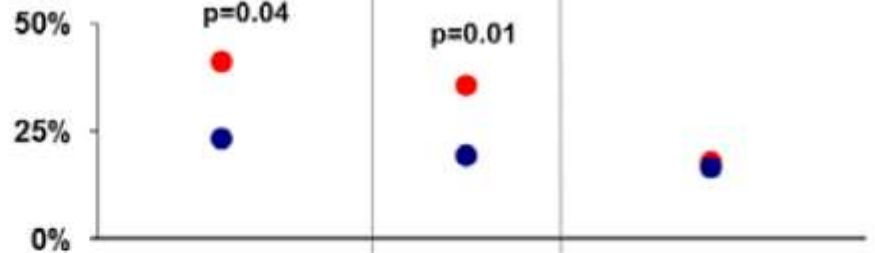
Dvir D, et al. JAMA 2014 312(12):162-170

A



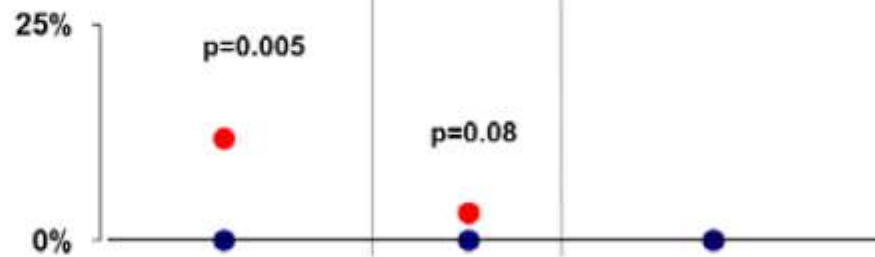
C

Rate of Post-procedural mean gradients ≥ 20 mmHg



D

Rate of Post-procedural mean gradients ≥ 40 mmHg



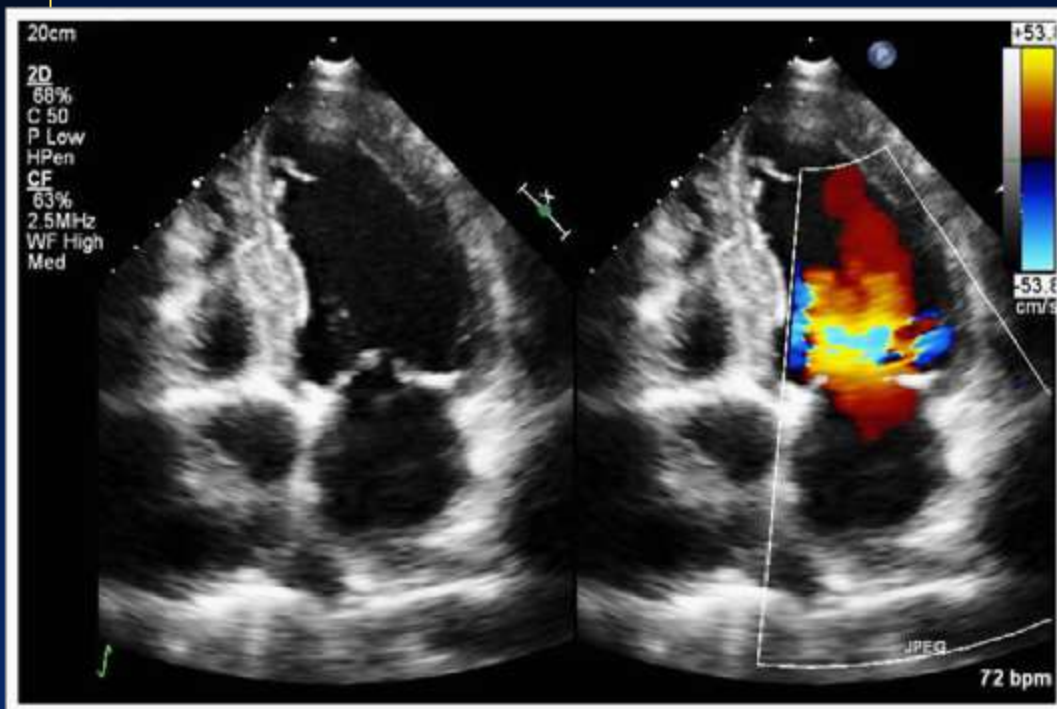
● Edwards valve

● CoreValve

Small < 20	Intermediate ≥ 20 & < 23	Large ≥ 23
SAPIEN, n=51 CoreValve, n=64	SAPIEN, n=123 CoreValve, n=93	SAPIEN, n=56 CoreValve, n=42

Surgical valve internal diameter (mm)

Avoid Rapid Pacing



- Severe LVD
- Bad MR
- CAD - Diffuse

Outline

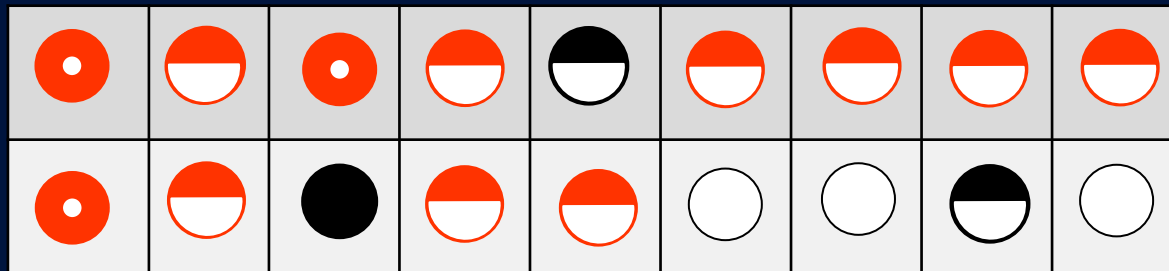
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2016 THV Landscape

EOA and Durability
 PVL Early
 Reposition/Retrieve
 Delivery Profile
 Need for PPM/RBBB
 Annular Rupture
 ViV (<23 valve)
 Subclavian Access
 LVD/Untreated CAD

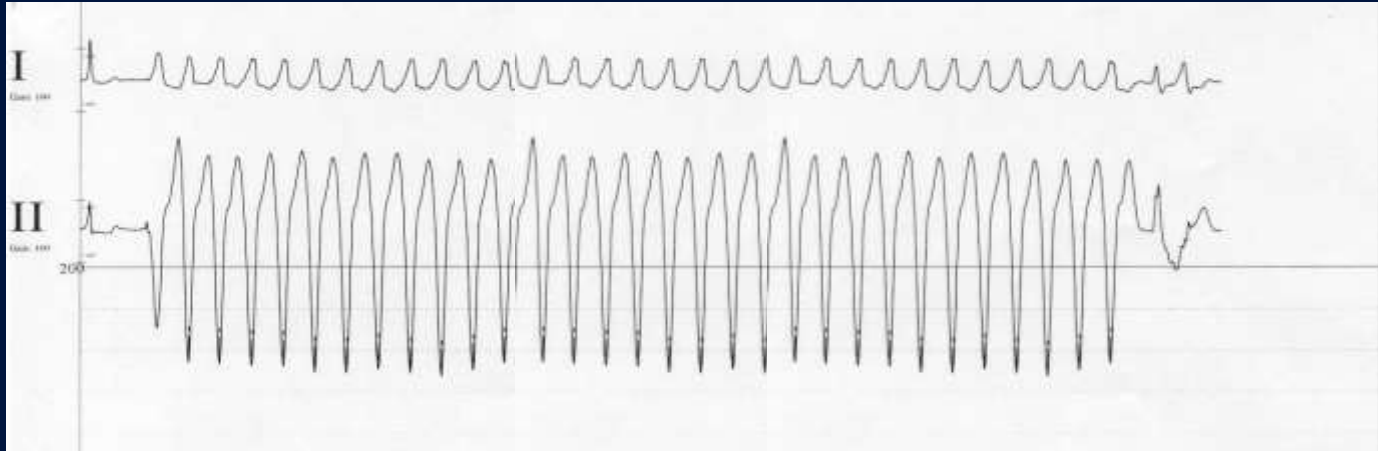
Self Expanding

Balloon Expandable

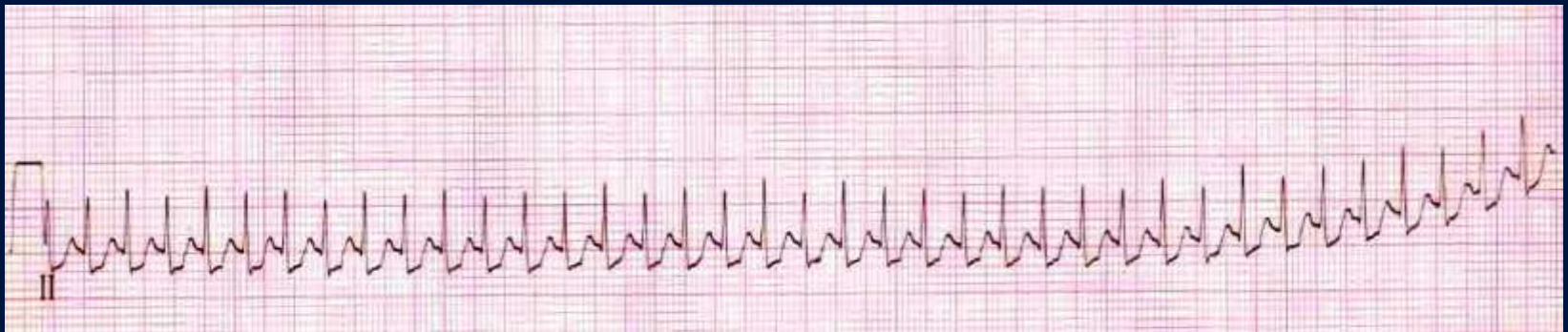


Final Thought: Procedural Differences

Patient During Balloon-Expandable THC Deployment



Doctor During Balloon-Expandable THC Deployment



Final Thought: Procedural Differences

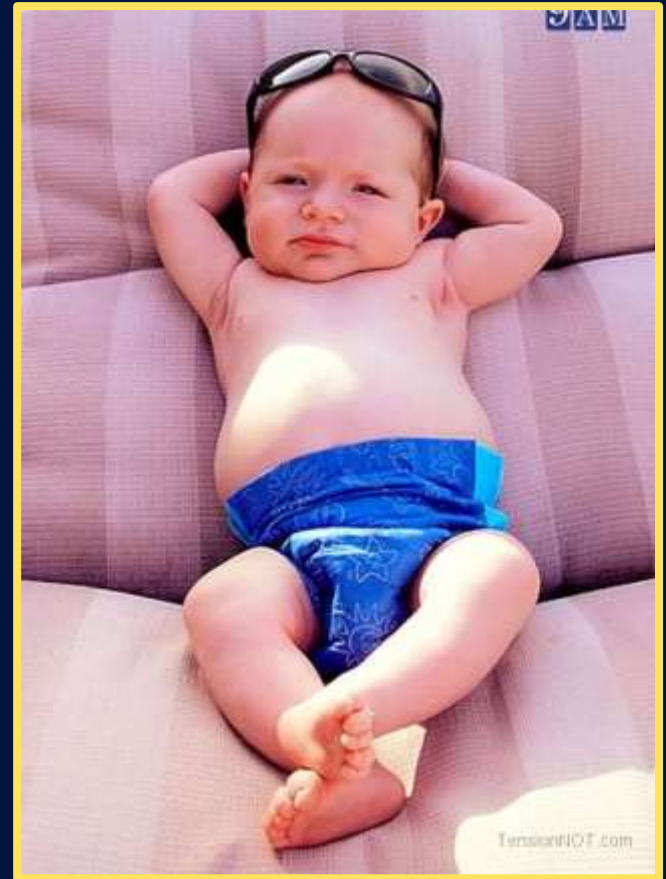
Patient During Resheathable Self-Expanding THC Deployment



Doctor During Resheathable Self-Expanding THC Deployment



Controlled Resheathable Self-Expanding Deployment



Conclusion

We and Our Patients are Lucky:
Two Great THV Platforms in 2016



Conclusion

The biggest issue is not which valve to use, but getting patients who can benefit from TAVR, the therapy they deserve