TAVI

Transcatheter Aortic Valve Implantation for aortic stenosis

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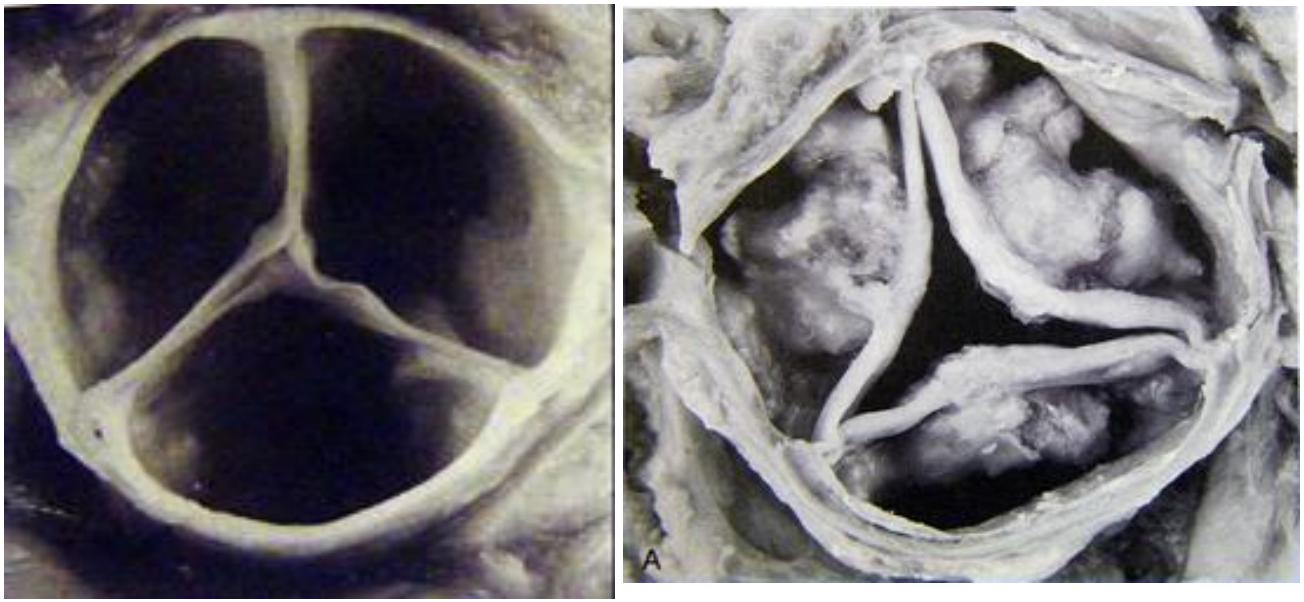
Severe Aortic Stenosis: A Significant Unmet Need

Healthy Aortic Valve

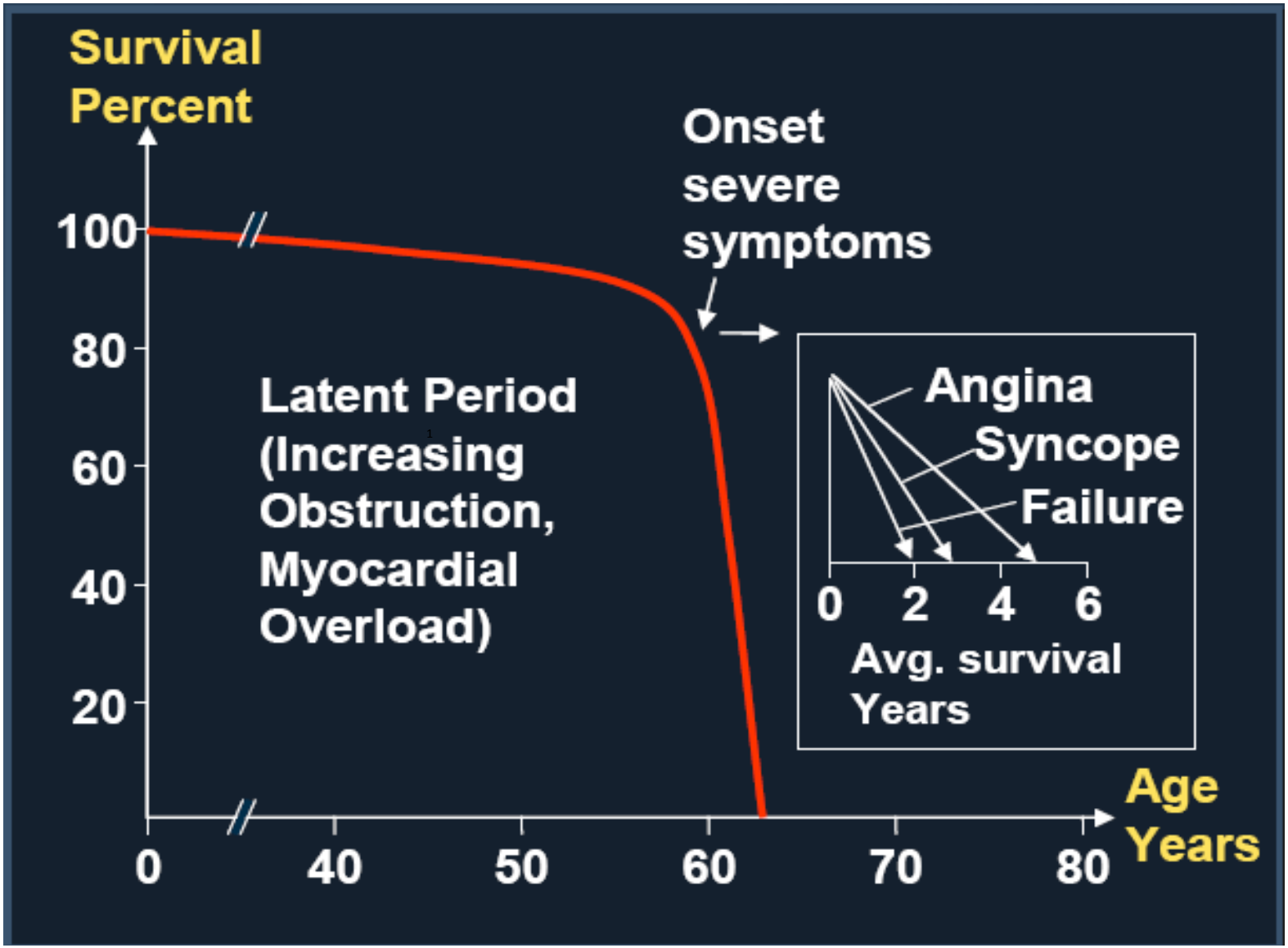
Stenosed Aortic Valve



"In adults with severe, symptomatic, calcific AS, AVR is the only effective treatment." *2006 ACC/AHA Practice Guidelines*

[1] Grube, et al. Percutaneous Aortic Valve Replacement for Severe Aortic Stenosis in High-Risk Patients Using the Second- and Current Third- Generation Self-Expanding CoreValve Prosthesis. American College of Cardiology J. 2007; 69–76.
[2] Iung B, et al. A prospective survey of patients with valvular HD in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J*. 2003;24(13):1231-43.
[3] Charlson E, Decision-making and outcomes in severe symptomatic AS. Journal of heart valve dis 15(3):312-21, 2006.

Severe Aortic Stenosis: Untreated Risks



[1] Varadarajan et al. *European Journal of Cardio-thoracic Surgery* 2006;30;722—727. Charlson E, Decision-making and outcomes in severe symptomatic AS. *Journal of heart valve dis* 15(3):312-21, 2006. PA Pellikka,The natural history of adults with asymptomatic AS. *J Am Coll Cardiol*, 1990; 15:1012-1017. B J Bouma; To operate or not on elderly patients with aortic stenosis: the decision and its consequences *Heart* 1999;82:143.

[2] Chart (lower left):Otto et al. Heart 2000;84:211-218.Lester et al. Chest 1998;113;1109-1114. Ross, Braunwald. Circulation 1968;38 (Suppl 1):61-7.

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Aortic Stenosis Background

- Aortic stenosis (AS) is the most prevalent native valve disease[1]
- Over 300,000 patients have severe AS worldwide
- Prevalence of AS and comorbidities that increase the risk of surgical valve replacement increase with age[1]

1. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J*. 2003;24:1231-1243.

Treatment of Severe Aortic Stenosis

- **Surgical aortic valve replacement (sAVR) is the gold standard for treatment of severe aortic stenosis (AS)[1]**
- **However, 33% of all patients ≥ 75 with severe AS are declined for surgery[2]**
  - **Primary reasons for not undergoing surgery are age and co-morbidities**
  - **Mortality for untreated symptomatic severe AS is up to 50-60% at 2 years in high-risk patients**

1. 2006 ACC/AHA Practice Guidelines.
2. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J.* 2003;26:2714-2720.

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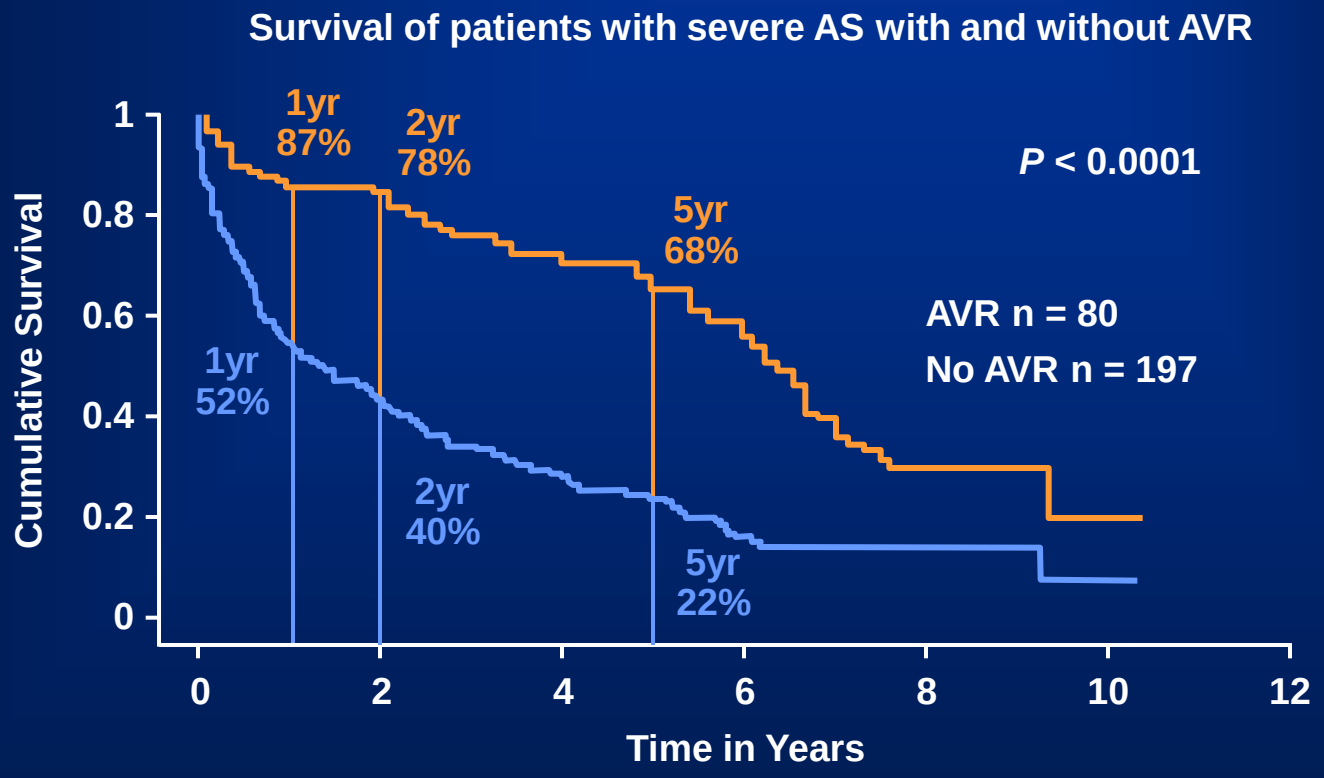
Severe AS Patients Not Undergoing AVR Have a Shorter Life Expectancy Than Those Receiving AVR

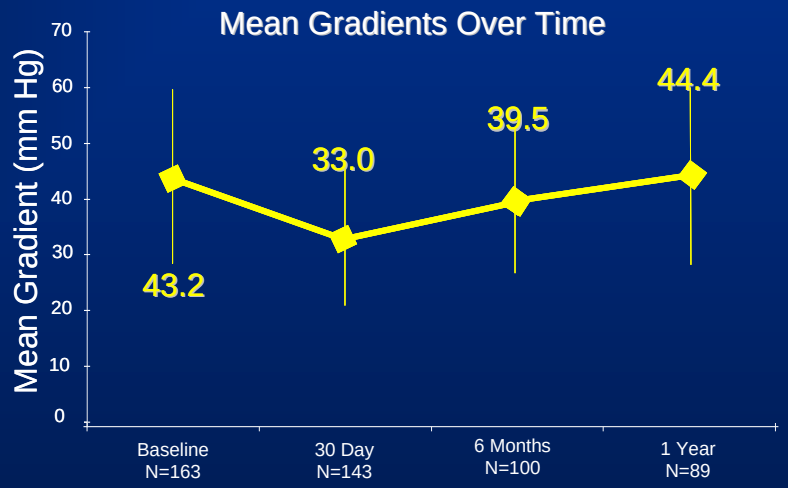


Number at risk											
	80	63	54	41	33	26	16	8	4	3	2	AVR group
	197	97	67	48	37	29	17	9	6	4	1	No AVR group

1. Varadarajan P, Kapoor N, Bansal RC, Pai RG. Survival in elderly patients with severe aortic stenosis is dramatically improved by aortic valve replacement: results from a cohort of 277 patients aged ≥ 80 years. *Euro J Cardiothorac Surg*. 2006;30:722-727.

BAV has little to no clinically benefit

- BAV had little impact on overall survival
- Any acute improvements in hemodynamics were short-lived
  - 26% needed a repeat BAV after 30 days



- Little to no symptomatic improvement
  - Only 21% of patients were in NYHA II or less at 1-year
  - Only 28% of patients survived without a rehospitalization

Tuzcu, E.M. Clinical Outcomes from "Standard Therapy" in the PARTNER Inoperable Patients. TCT 2010, Washington D.C.

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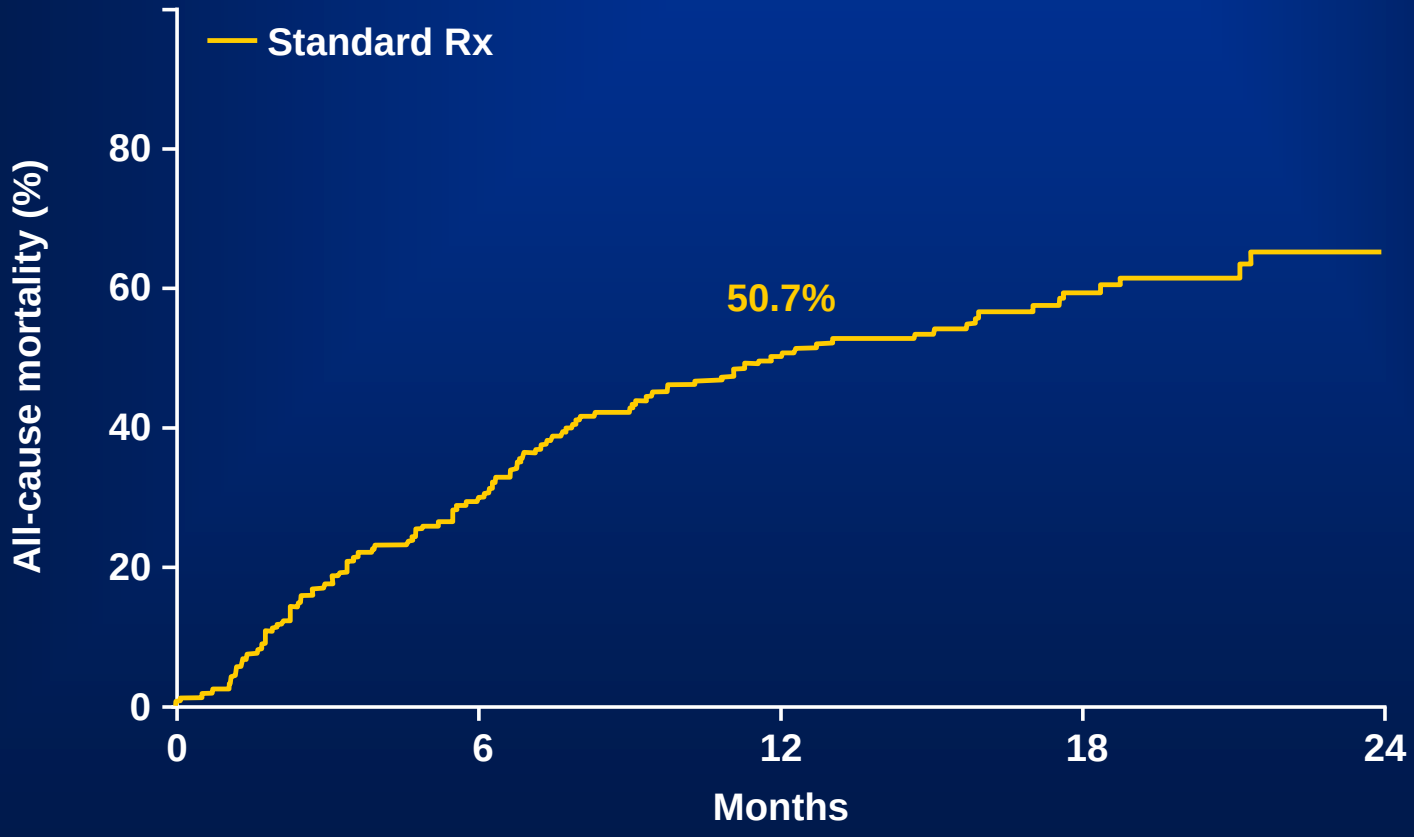
Patients treated with medical tx or BAV have dismal outcomes

- More than ½ are dead at 1-year



1. Presented by Leon, M. Transcatheter Aortic Valve Implantation in Inoperable Patients with Severe Aortic Stenosis. TCT, September 2010.

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Outcomes of Inoperable Patients that underwent SAVR

1. Presented by Leon, M. Transcatheter Aortic Valve Implantation in Inoperable Patients with Severe Aortic Stenosis. TCT, September 2010.

- Despite inoperable status:
  - 17 patients underwent SAVR
    - 12 AVR
    - 5 AVR + conduit
- 1-year mortality of pts receiving SAVR was 47%
  - AVR – 33%
  - AVR + conduit – 80%

Thus we need new option

alternative to Medicine, BAV, SAVR

for the Inoperable AS Patients

Transcatheter Aortic Valve Implantation

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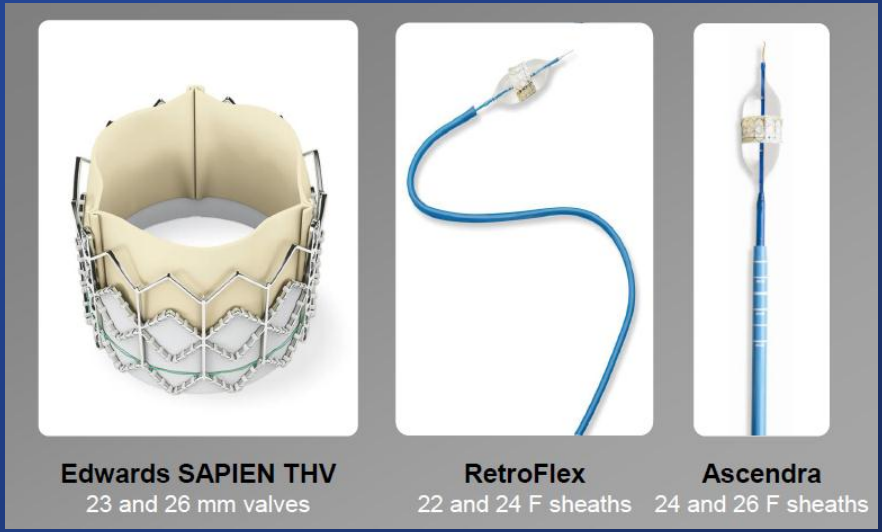
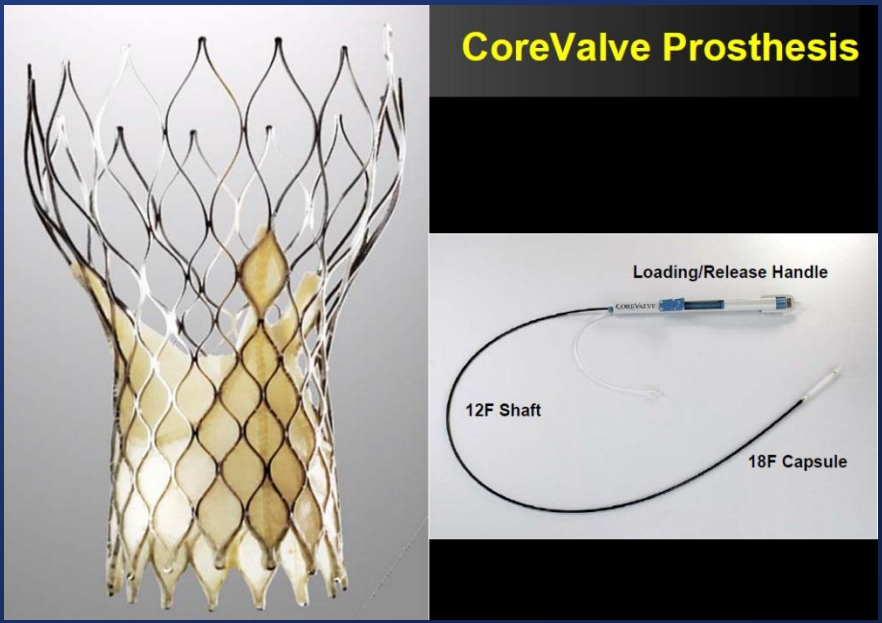
Trans-catheter Aortic Valves



Edwards-Sapien™



CoreValve Revalving™

Coronary Complications & Access

Edwards SAPIEN XT valve

14 MM

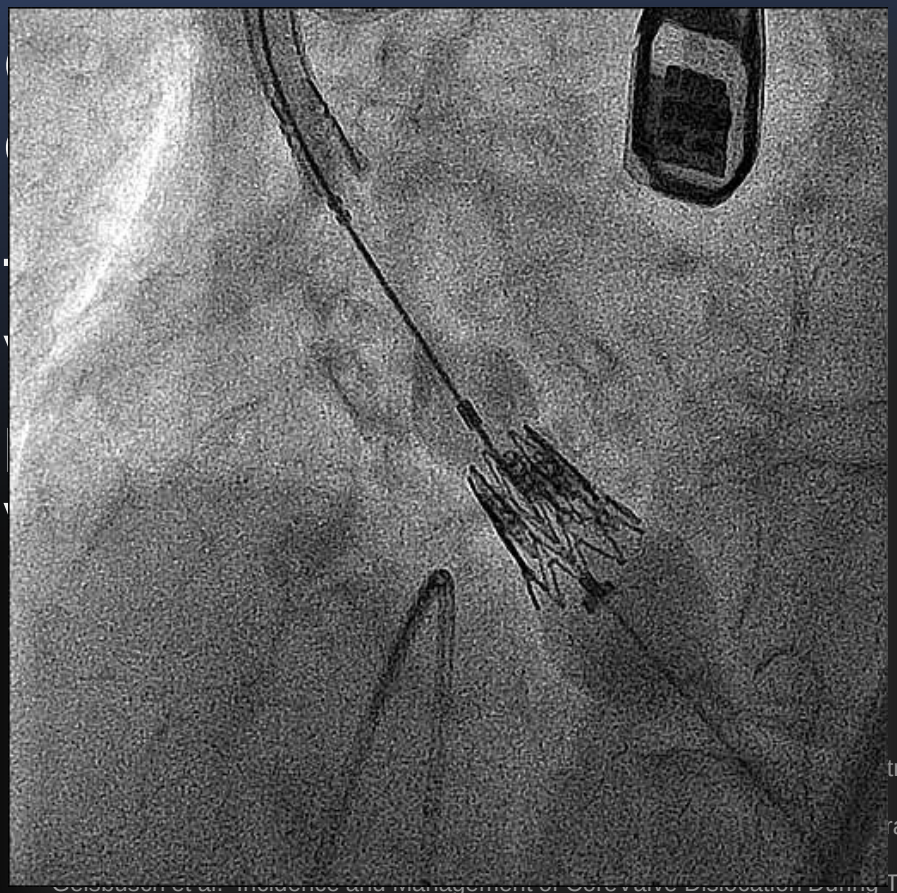
CoreValve ReValving System

55 MM

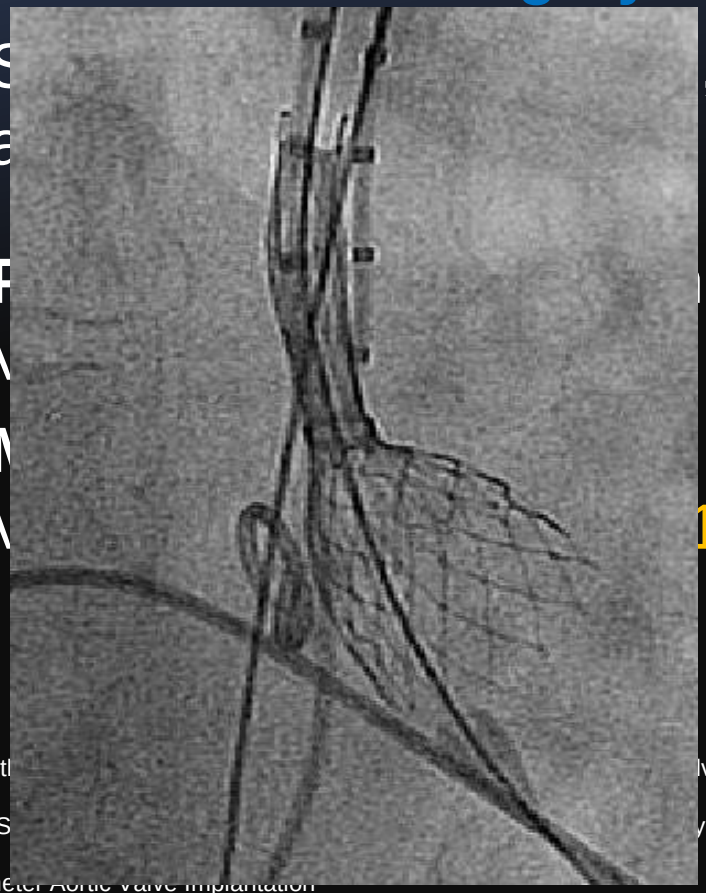
Coronary Obstruction Rates in TAVR remain very low:
0 – 2% in most series

Ease & Accuracy of Deployment

Edwards SAPIEN valve



CoreValve ReValving System



10%

try, using th lve

ration CRS year

Transcatheter Aortic Valve Implantation

Difference betweeen two valves

Edwards Valve	CoreValve
Adapted from surgical designs	Specific transcatheter design
Bovine, equine or porcine 1 or 3 pieces of pericardium 1 pinched tube or 3 leaflets joined in annulus	Porcine 6 pieces of pericardium 3 leaflets + 3 skirt parts for optimal folding
Single radial force stents	Multi-level frame = Three different radial & hoop forces
Flexing struts designs	Static frame design
Intra-annular anchoring + function	Supra-annular function Intra-annular anchoring

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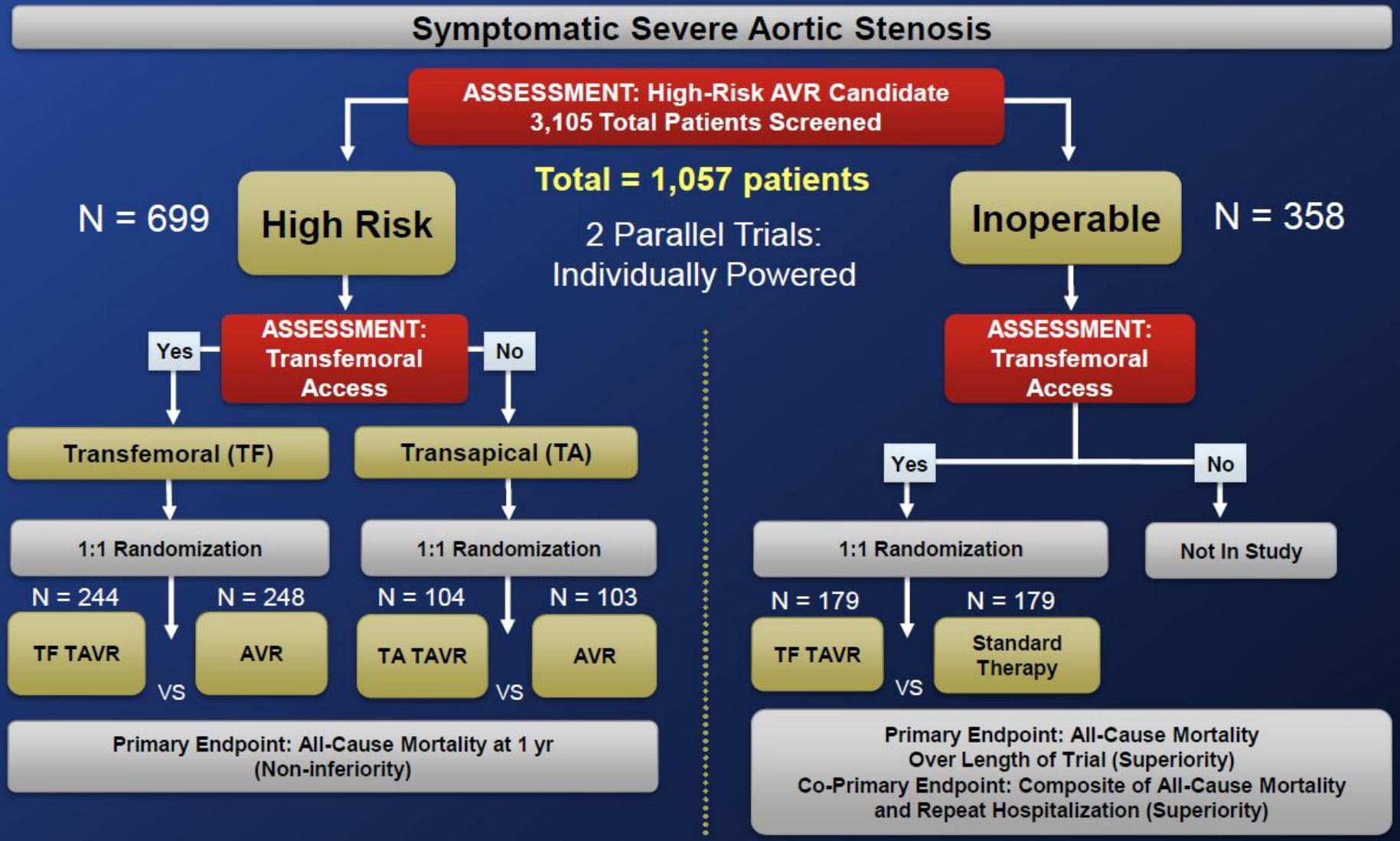
PARTNER trial: Study Design



Inoperable PARTNER Cohort B: Result

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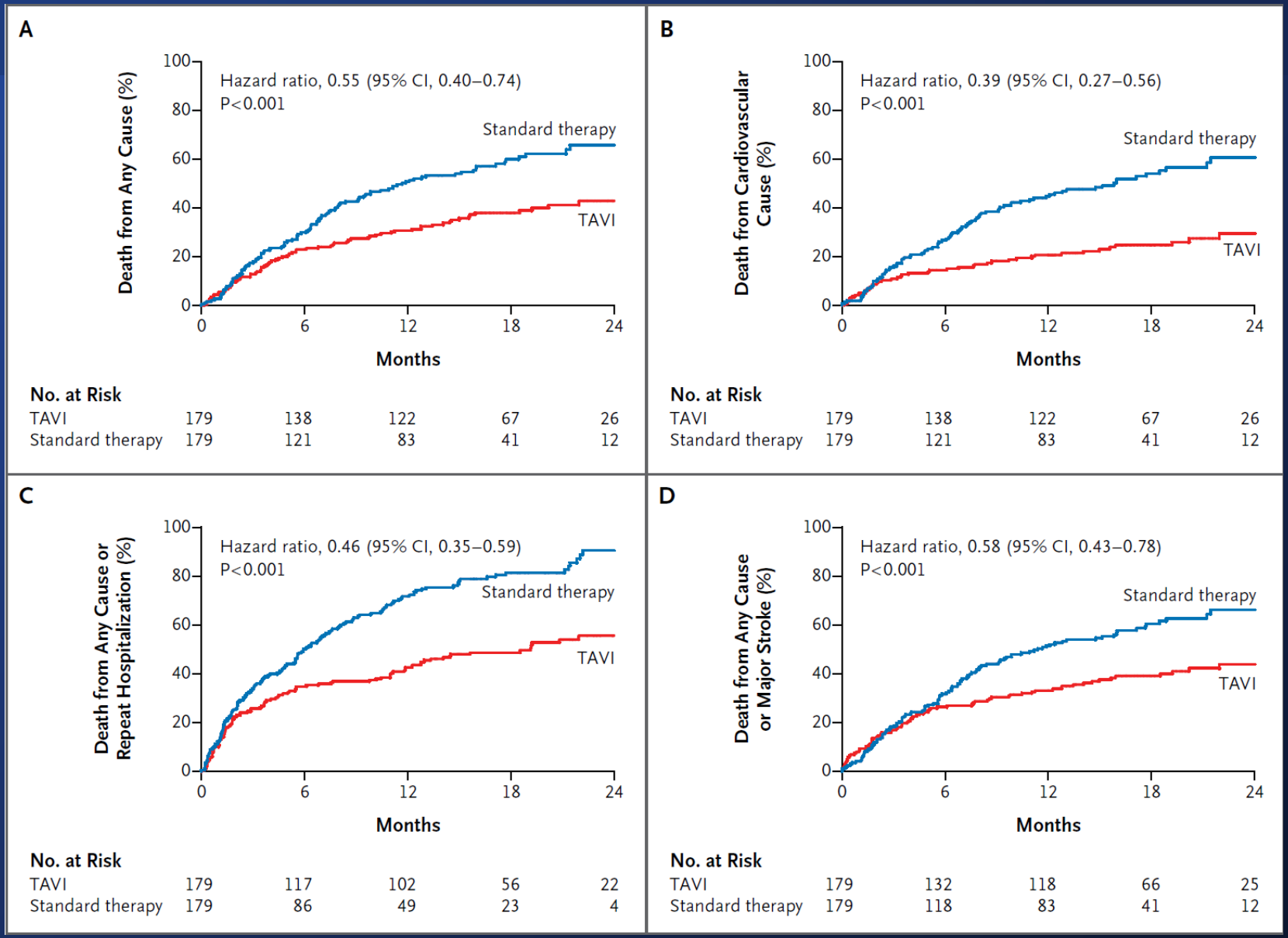

Leon MB et al. N Engl J Med. 2010;363:1597-607

High-Risk PARTNER cohort A: Result

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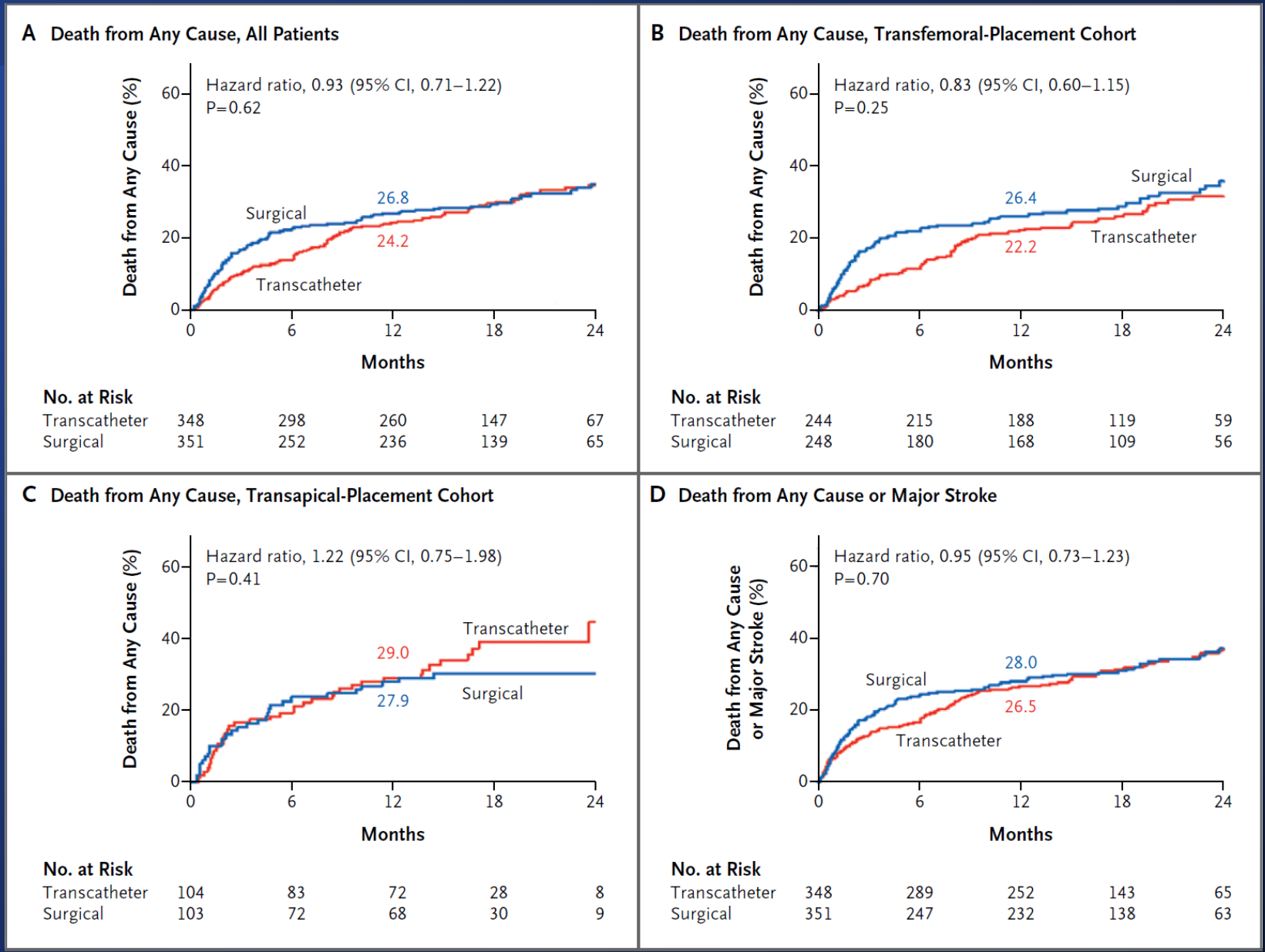
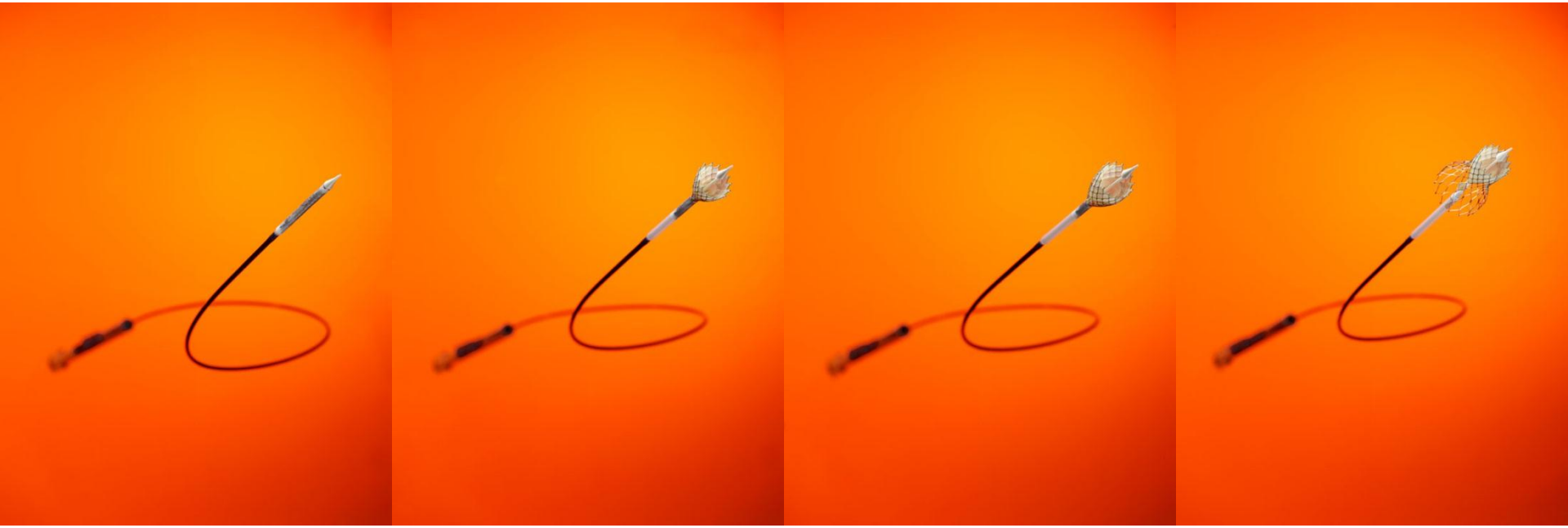


Smith CR et al. N Engl J Med. 2011;364:2187-98

The CoreValve System



Delivery Catheter Evolution

2004 2005 2006

Photograph provided by Piazza, Serruys, and DeJaegere

CoreValve Bioprosthesis

Outflow Portion

1. Sits in ascending aorta
2. Orientation

Constrained Portion

(with leaflets)

1. Supra-annular leaflet function
2. Designed to avoid coronaries

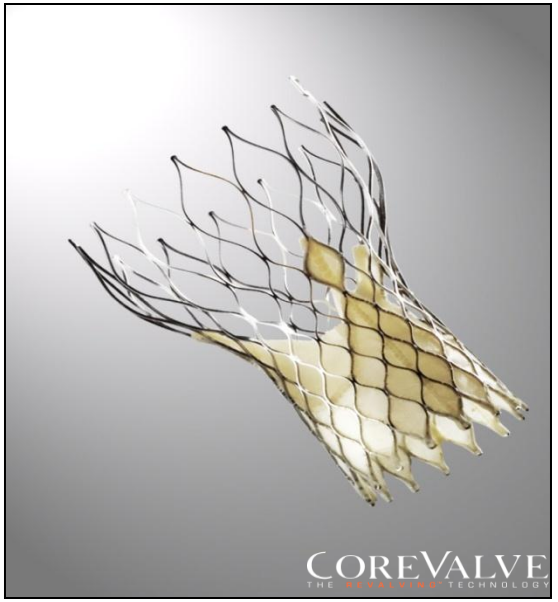
Inflow Portion

(with skirt)

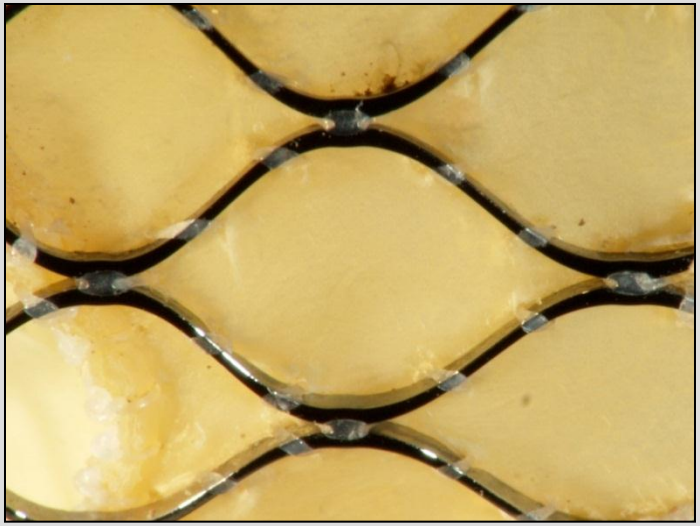
1. Intra-annular anchoring
2. Mitigates paravalvular aortic regurgitation

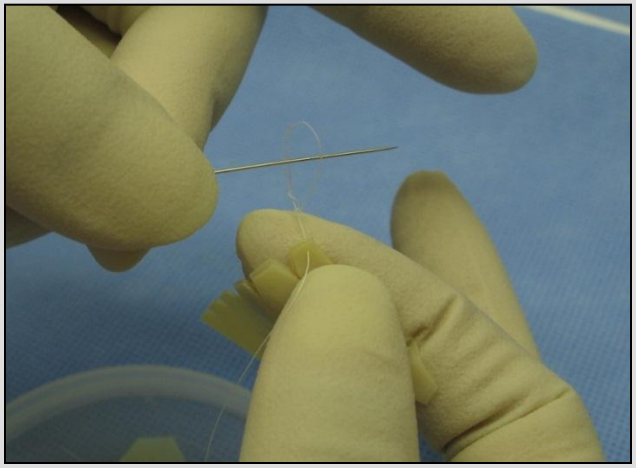
CoreValve Bioprosthesis

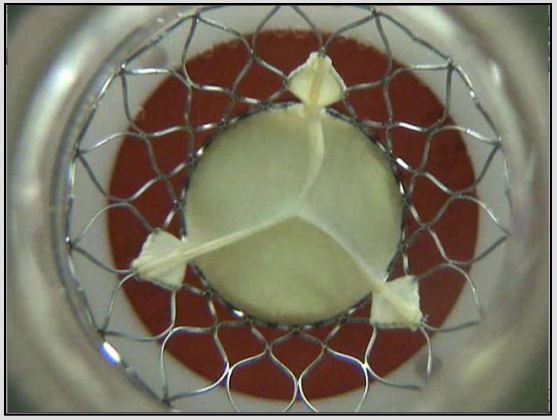
- Single layer porcine pericardium
  - Tissue valve sutured to frame
  - Tri-leaflet configuration
- Skirt
  - Primary function is sealing
- Scalloped for flow dynamics
- Supra-annular leaflet function
- Leaflet function unaffected by annulus shape or dimensions
- Ten-year bench testing (FDA)



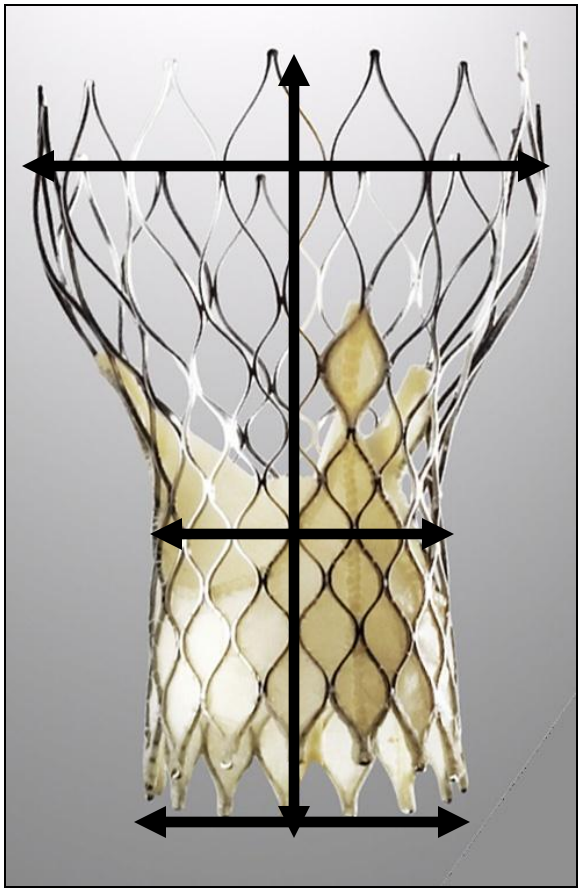
CoreValve Construction: expensive
manual, not automatic







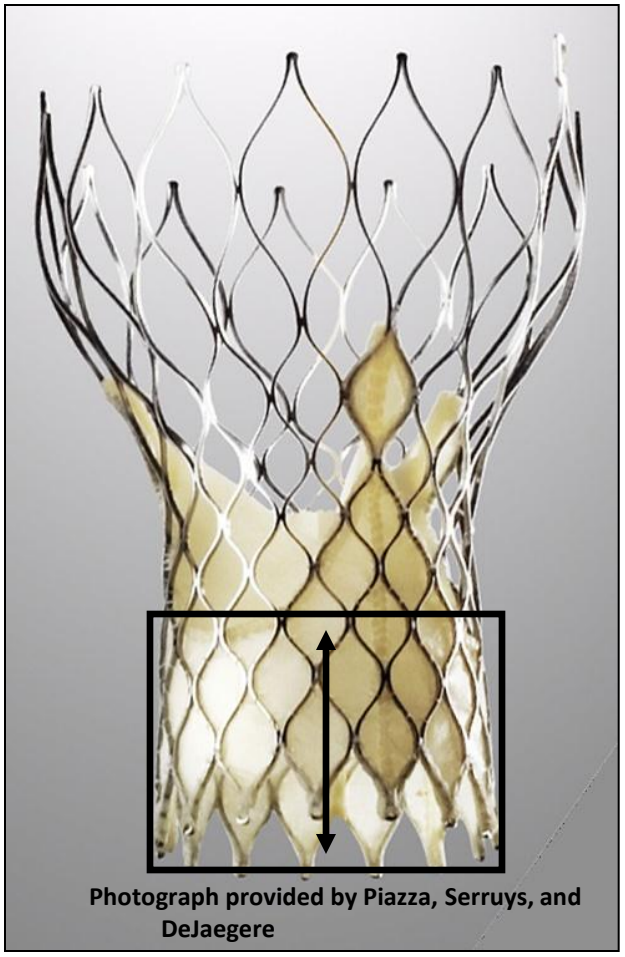
CoreValve Bioprosthesis: Two Sizes



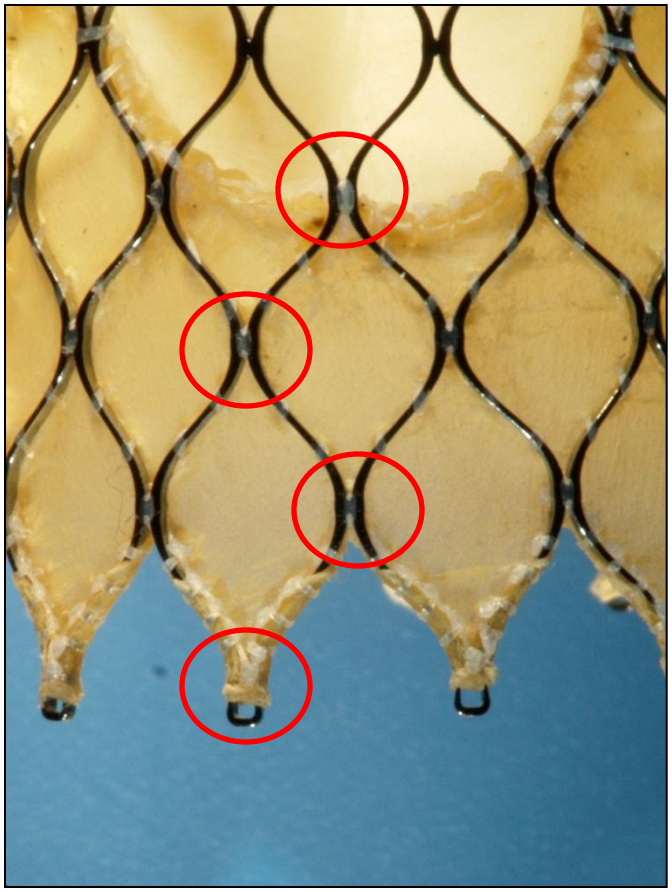
Photograph provided by Piazza, Serruys, and DeJaegere

	"Small"	"Large"
Height	55 mm	53 mm
Outflow	40 mm	43 mm
Constrained	22 mm	24 mm
Inflow	26 mm	29 mm
Accomodates Annulus of:	20 mm to 23 mm	23 mm to 27 mm

CoreValve Bioprosthesis



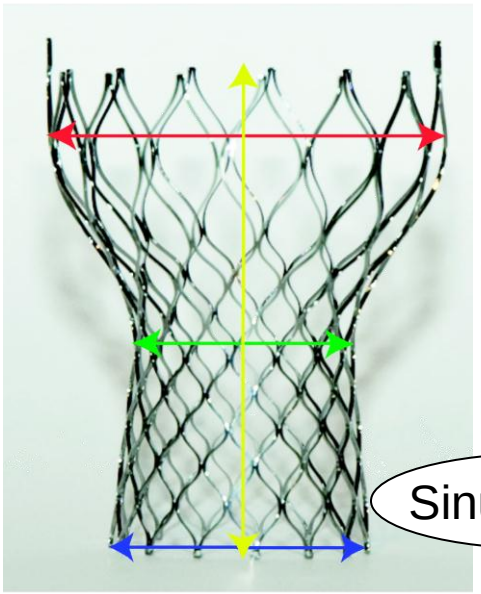
Skirt height = ~ 12 mm

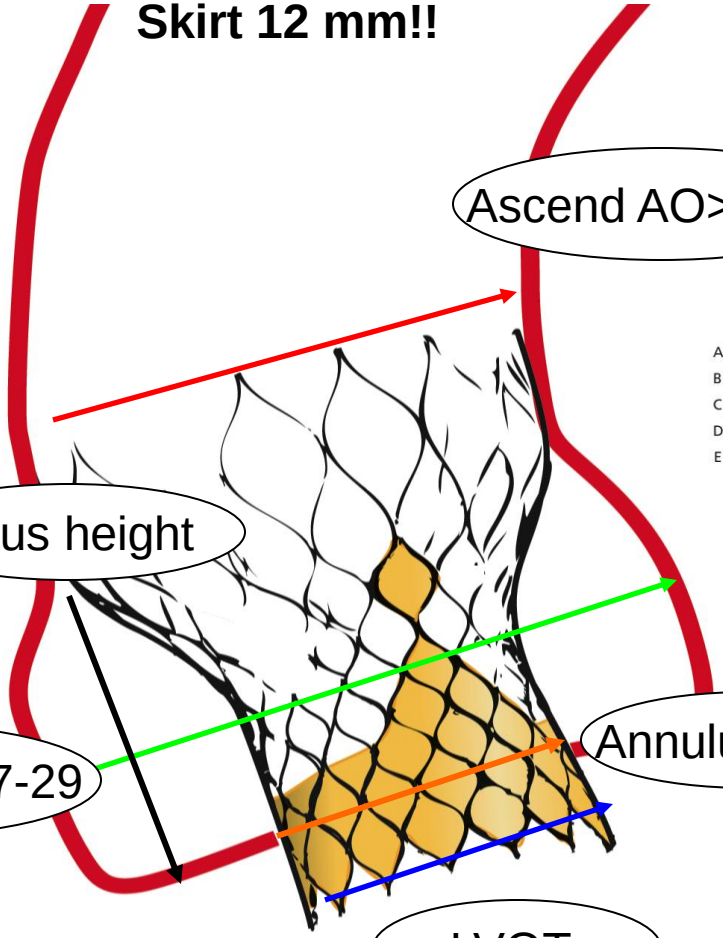


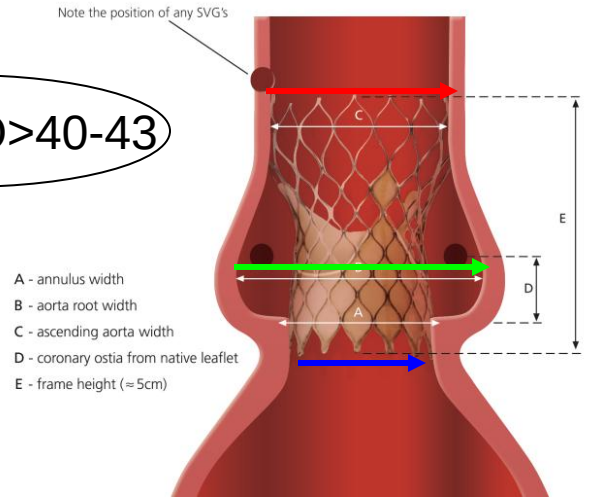
Vertical distance from joint to joint ~ 4 mm

Measurements of CORE-VALVE & Aortic Root

Sinus height > 15 mm
Skirt 12 mm!!

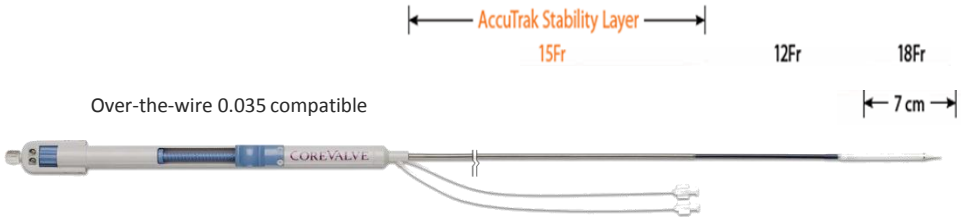


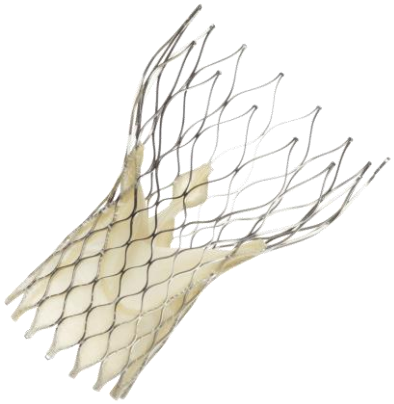


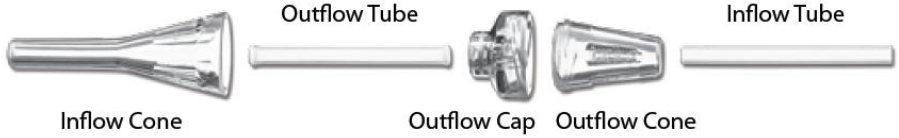


Medtronic CoreValve® System Components

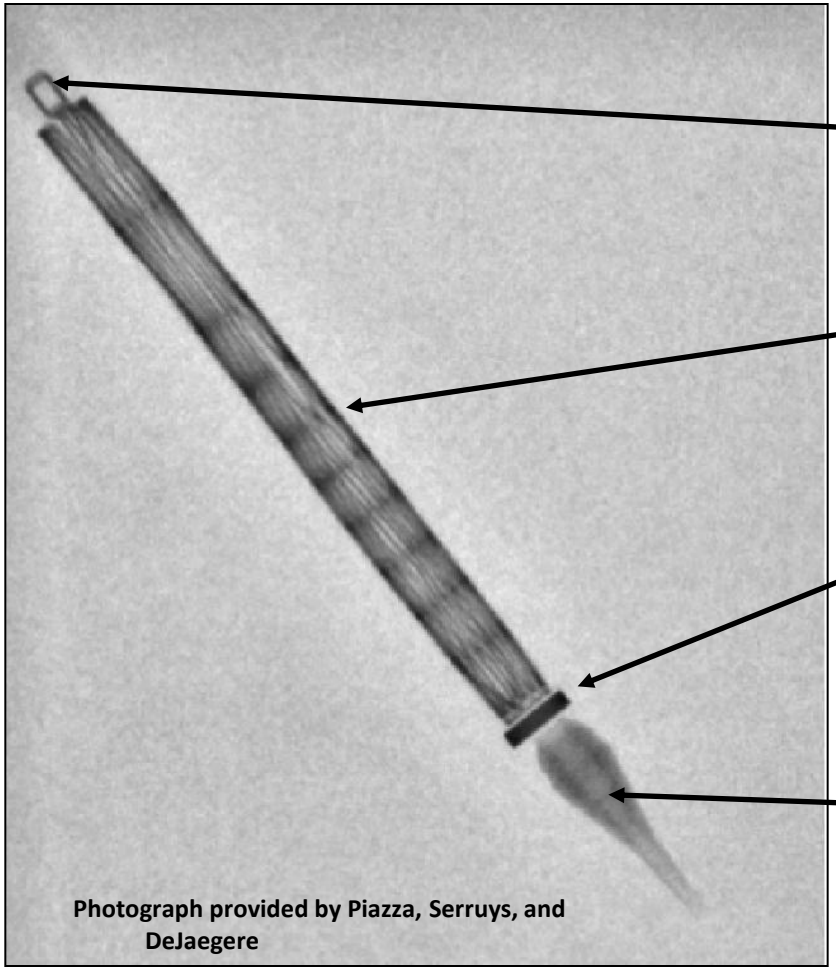
- 18F delivery system catheter
- Percutaneous Aortic Valve
  - Porcine pericardial tissue valve
  - Self-expanding multi-level Nitinol frame
- Disposable loading system







Delivery Catheter with Loaded Bioprosthesis Under Fluoroscopy



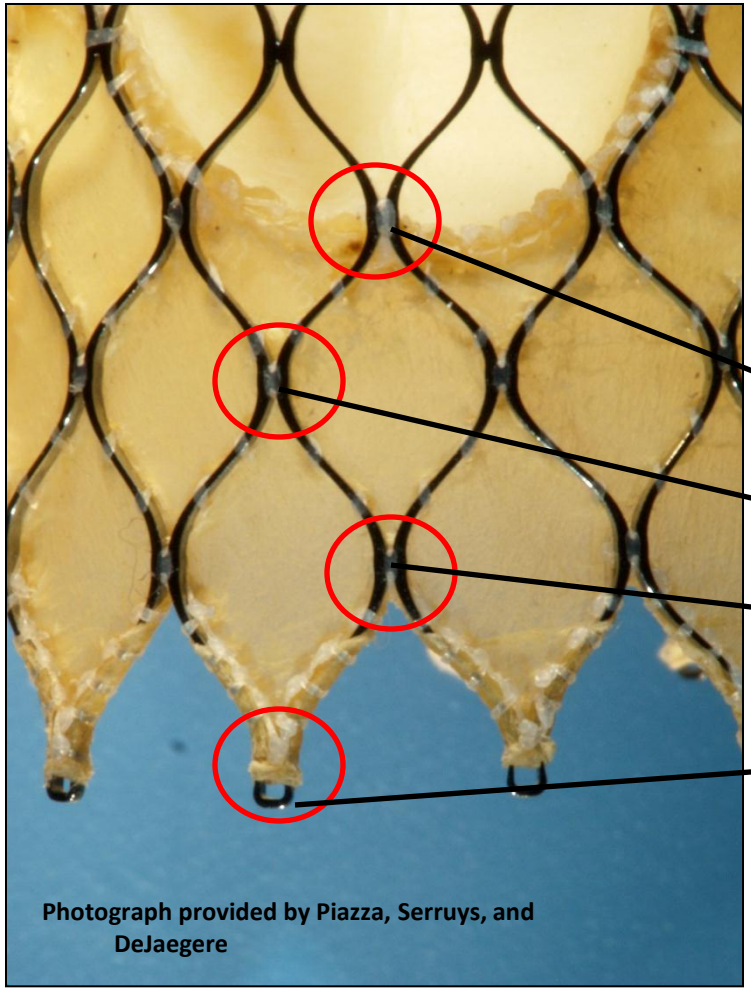
Frame loading hooks

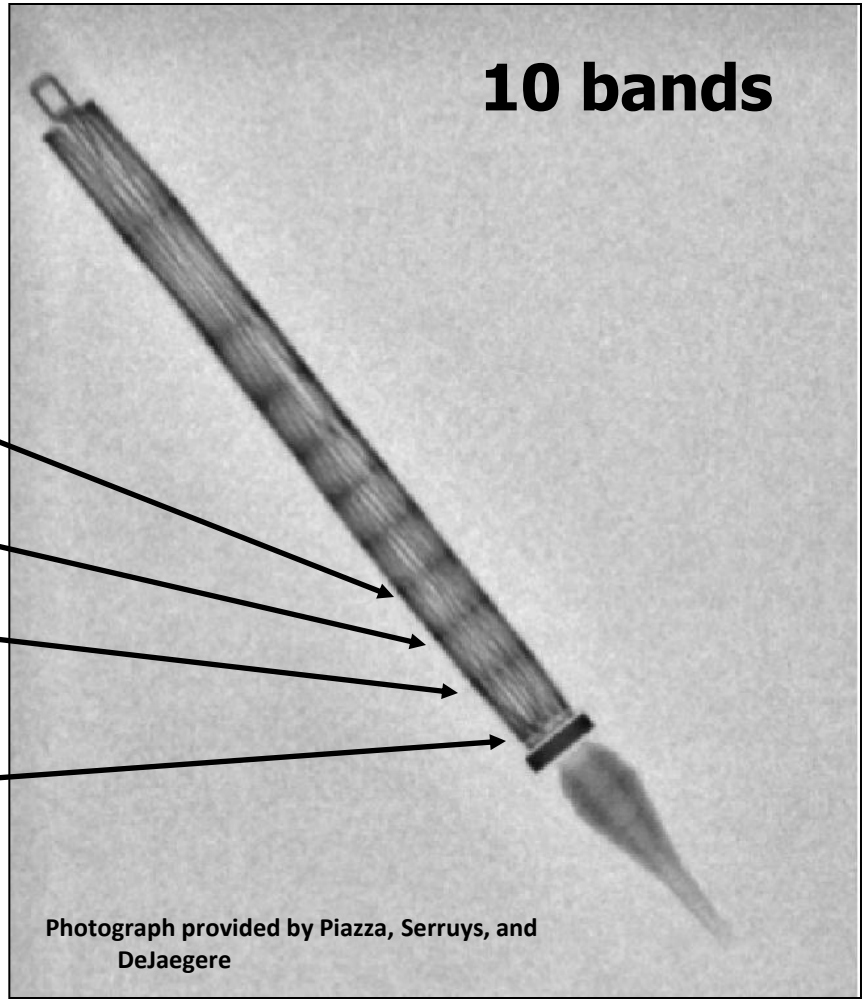
Valve bioprosthesis

Radio-opaque marker - distal end of valve capsule

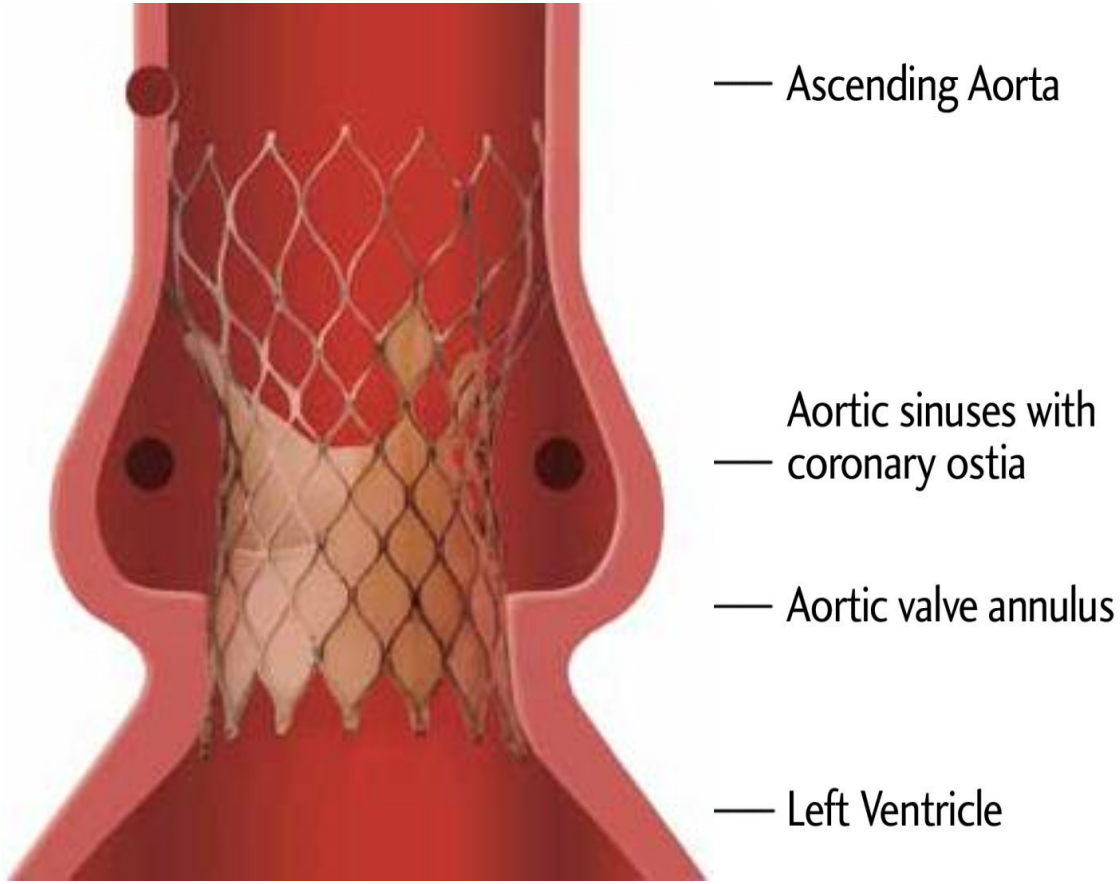
Nose cone

Bioprosthesis Under Fluoroscopy

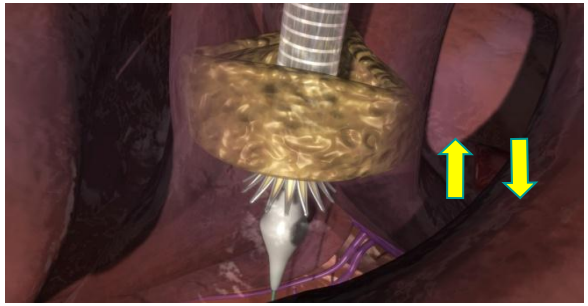


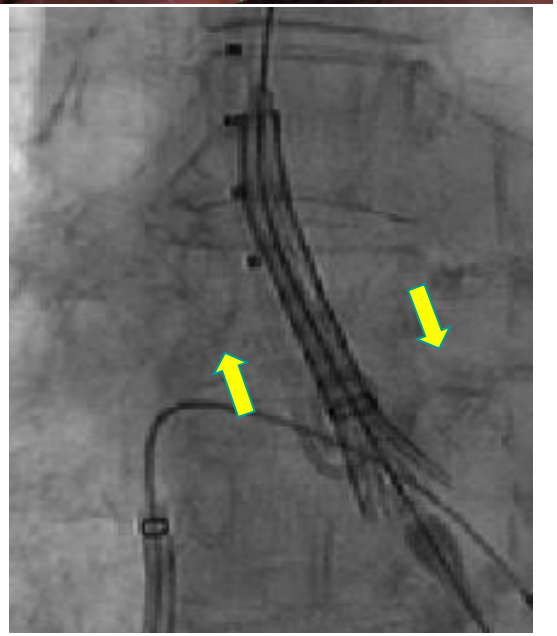


IMPLANTATION SITE



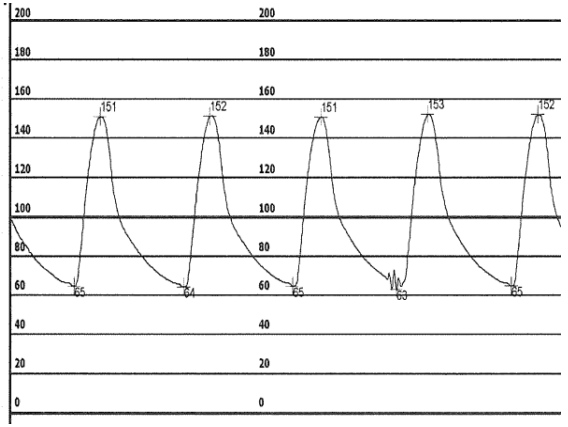
Repositionable Deployment: Before Annular Contact





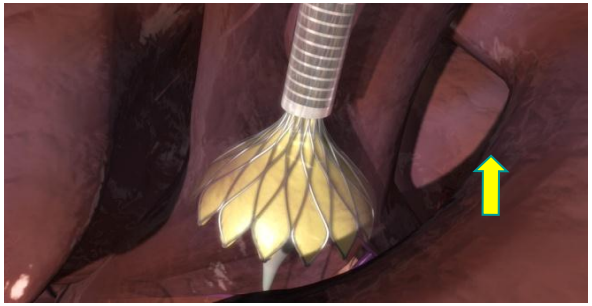
"No need to rush"

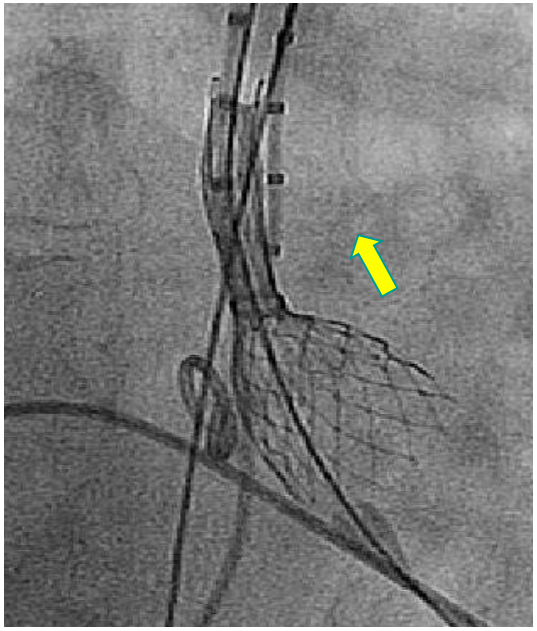
"Slow and stepwise"



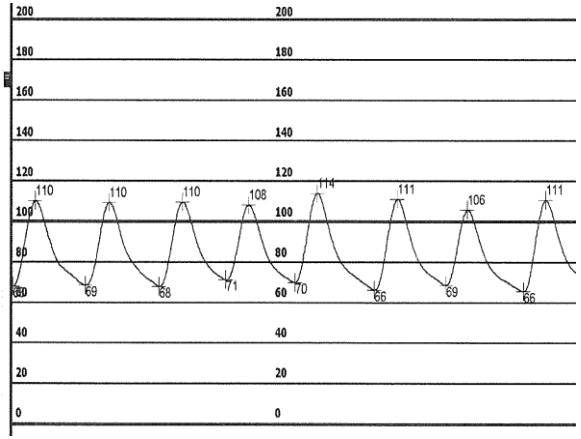
Normal blood pressure before annular contact

Repositionable Deployment: After Annular Contact



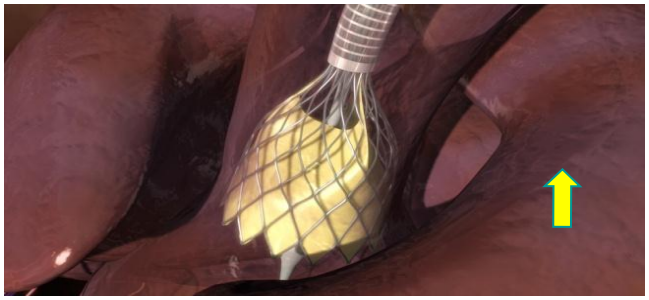


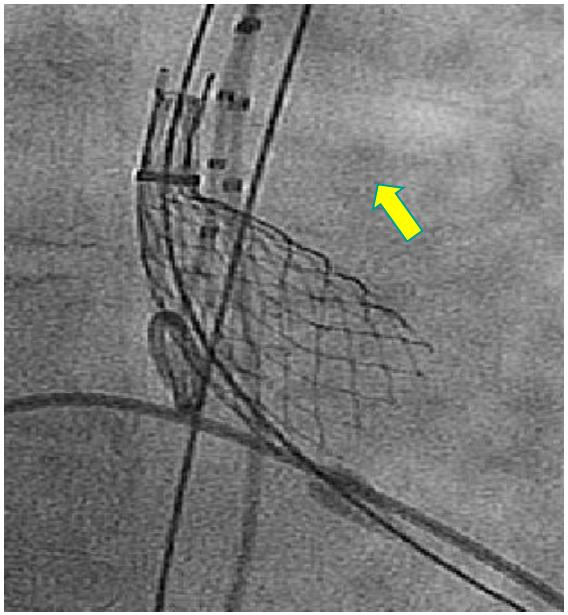
"Continue to turn"



Reduced blood pressure only between 1/3 & 2/3 of the deployment

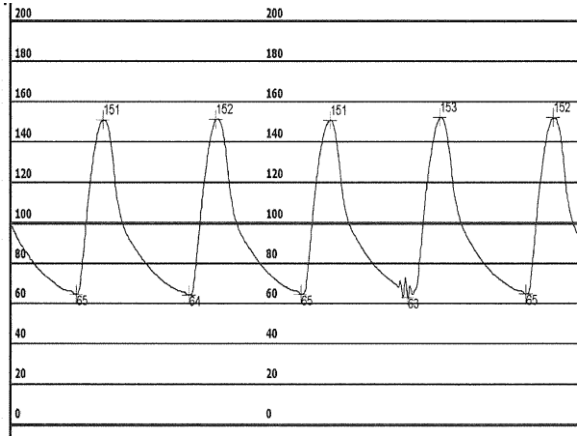
Repositionable Deployment: Before Device Release





"No need to rush"

"Slow and stepwise"



At 2/3 point, BP returns to normal and valve is still repositionable

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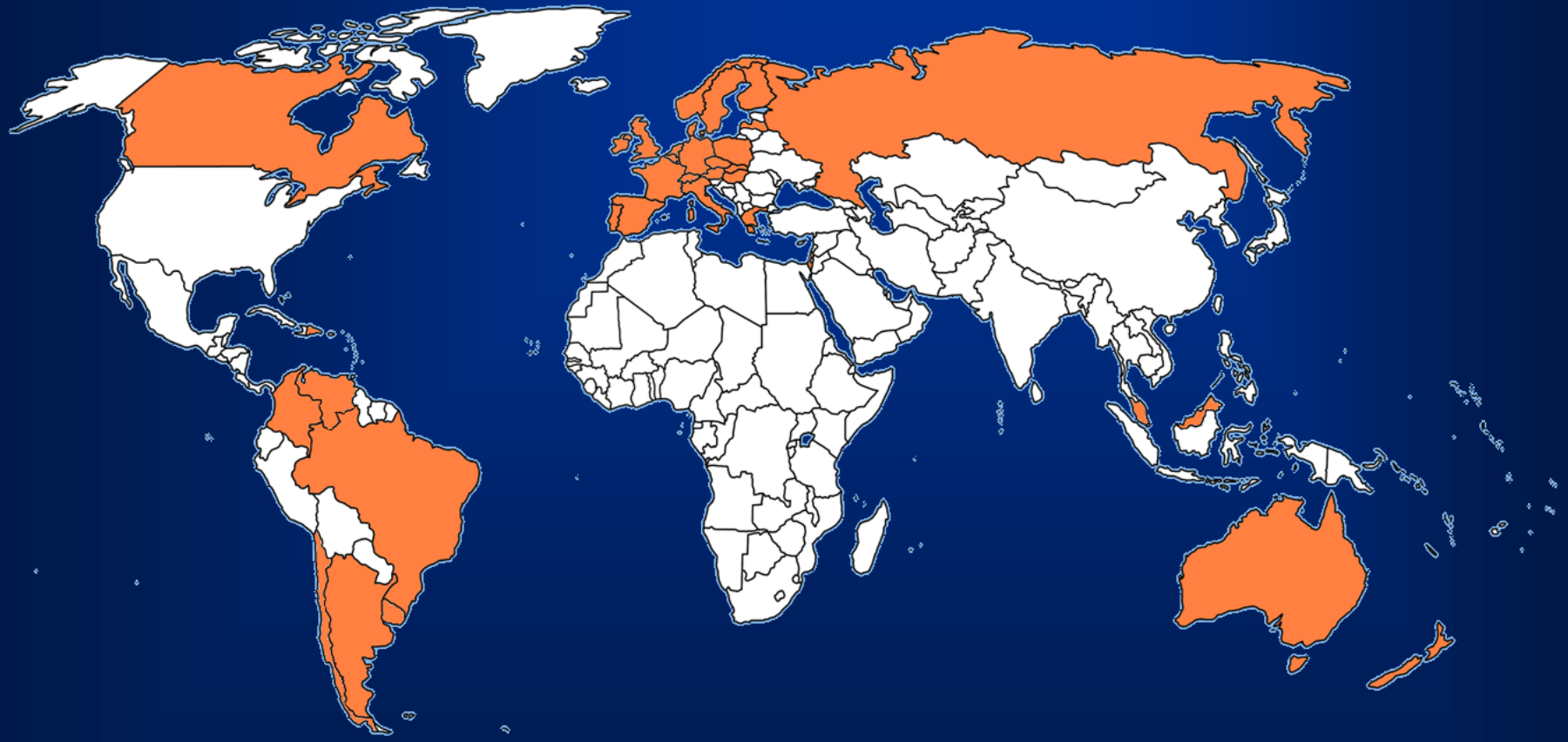
CoreValve Experience



More than 12,000 implants over 30 countries

Short-Term Clinical Outcomes

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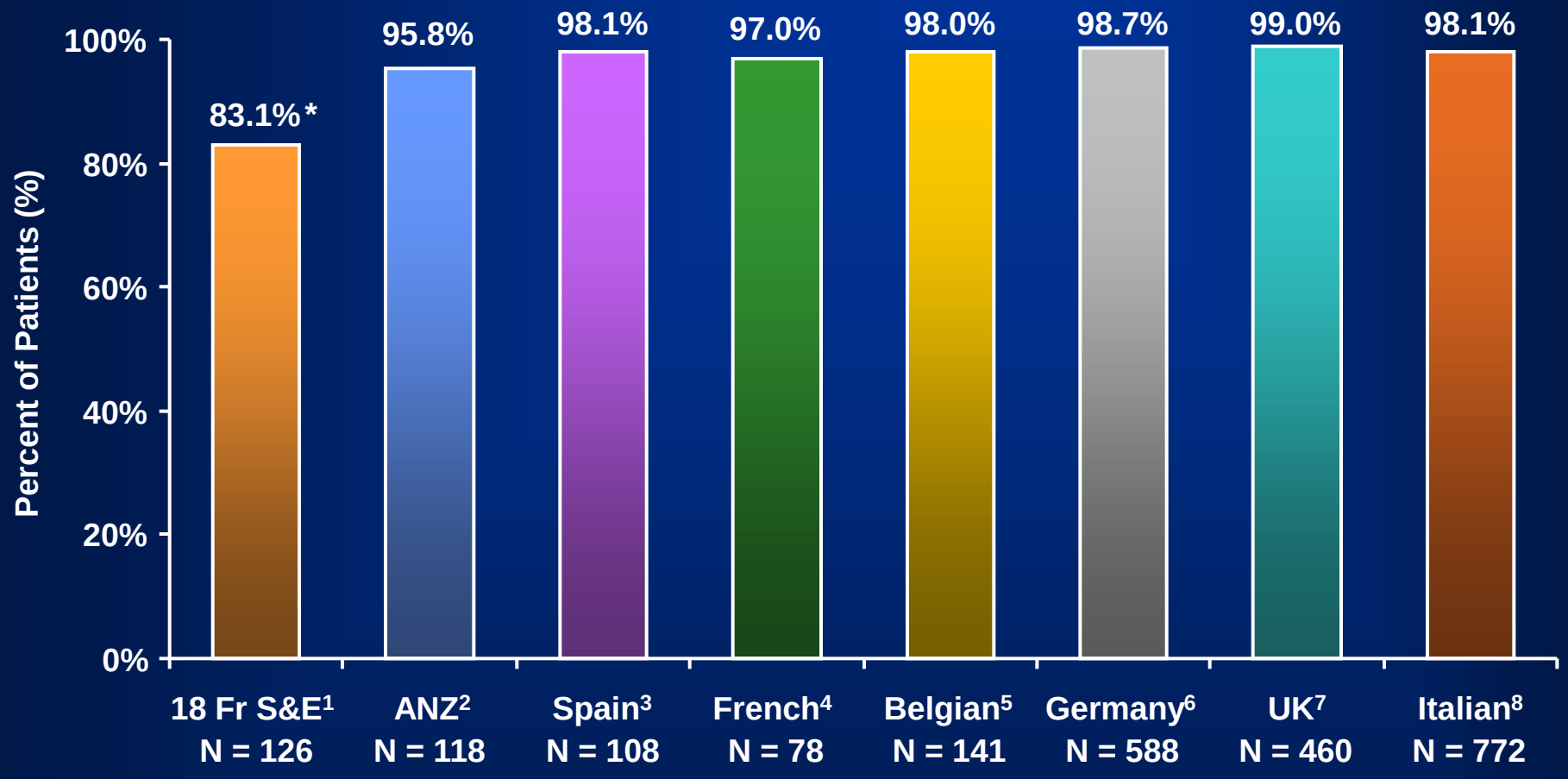
Procedural Success



Procedure Success is not defined consistently across all studies.
*** Technical Success is reported here.**

1. Medtronic Data on File. COR 2006-02: 18 Fr Safety & Efficacy Study Re-Analysis, August 14, 2009.
2. Meredith I. VARC-adjudicated Outcomes in Inoperable and High Risk AS Patients. Transcatheter Cardiovascular Therapeutics 2010, Washington, DC.
3. Avanzas P, Munoz-Garcia AJ, Segura J, et al. Percutaneous implantation of the CoreValve® self-expanding aortic valve prosthesis in patients with severe aortic stenosis: early experience in Spain. *Rev Esp Cardiol*. 2010;63:141-148.
4. Eltchaninoff. French Registry, TAVI Facts, Figures and National Registries. EuroPCR 2010, Paris, France.
5. Bosmans. Belgian Registry, TAVI Facts, Figures and National Registries. EuroPCR 2010, Paris, France.
6. Zahn. German Registry, TAVI Facts, Figures and National Registries. EuroPCR 2010, Paris, France.
7. Ludman. UK Registry, TAVI Facts, Figures and National Registries. EuroPCR 2010, Paris, France.
8. Petronio. Italian Registry, TAVI Facts, Figures and National Registries. EuroPCR 2010, Paris, France.

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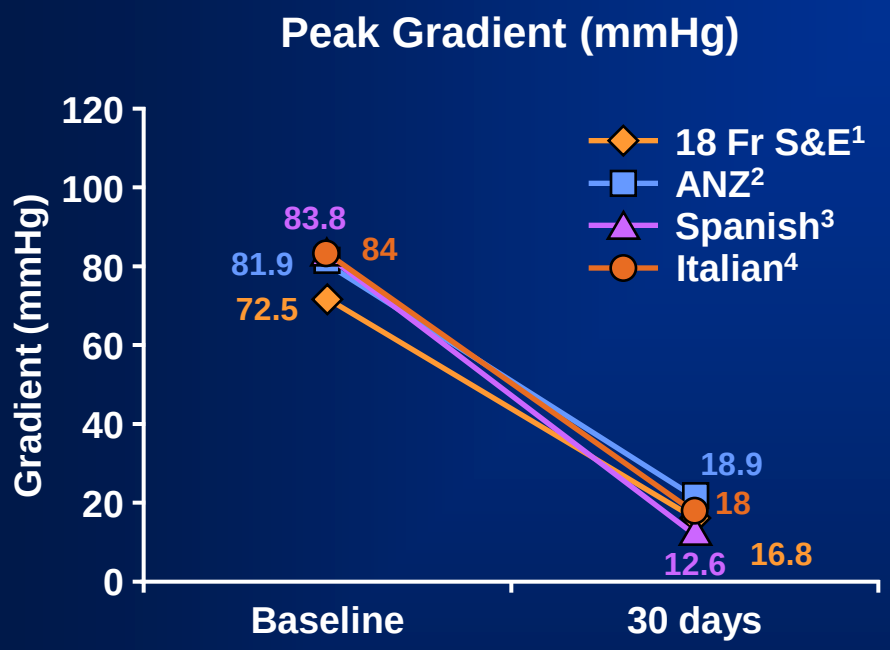
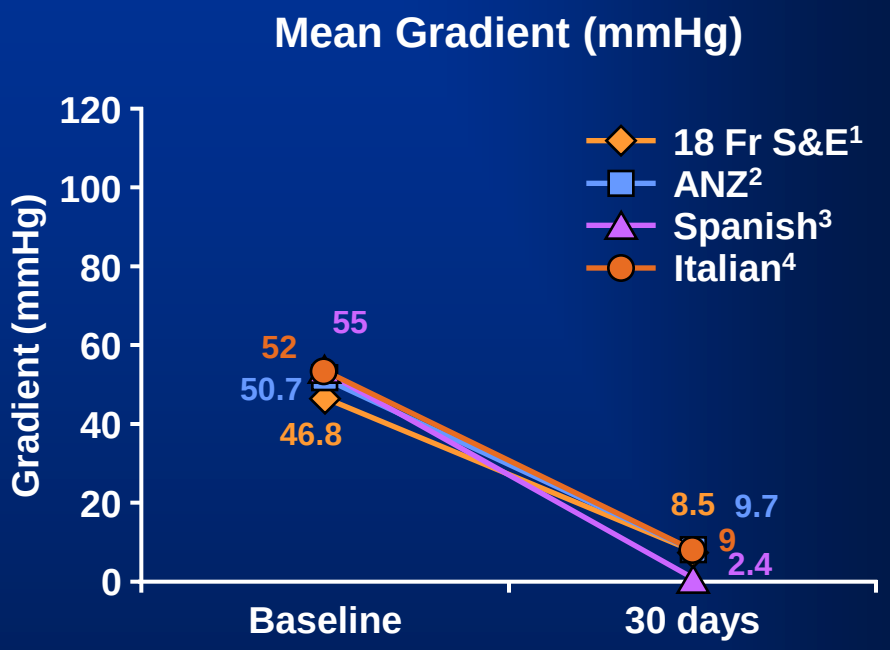
Haemodynamic Performance

Consistent Improvement Across Studies





1. Medtronic Data on File. COR 2006-02: 18 Fr Safety & Efficacy Study Re-Analysis, August 14, 2009.
2. Meredith I. VARC-adjudicated Outcomes in Inoperable and High Risk AS Patients. TCT 2010, Washington, DC.
3. Avanzas P, Munoz-Garcia AJ, Segura J, et al. Percutaneous implantation of the CoreValve® self-expanding aortic valve prosthesis in patients with severe aortic stenosis: early experience in Spain. *Rev Esp Cardiol*. 2010;63:141-148.
4. De Carlo. Serial Echocardiographic Evaluation of the CoreValve Aortic Bioprosthesis: Italian Registry EuroPCR 2010.

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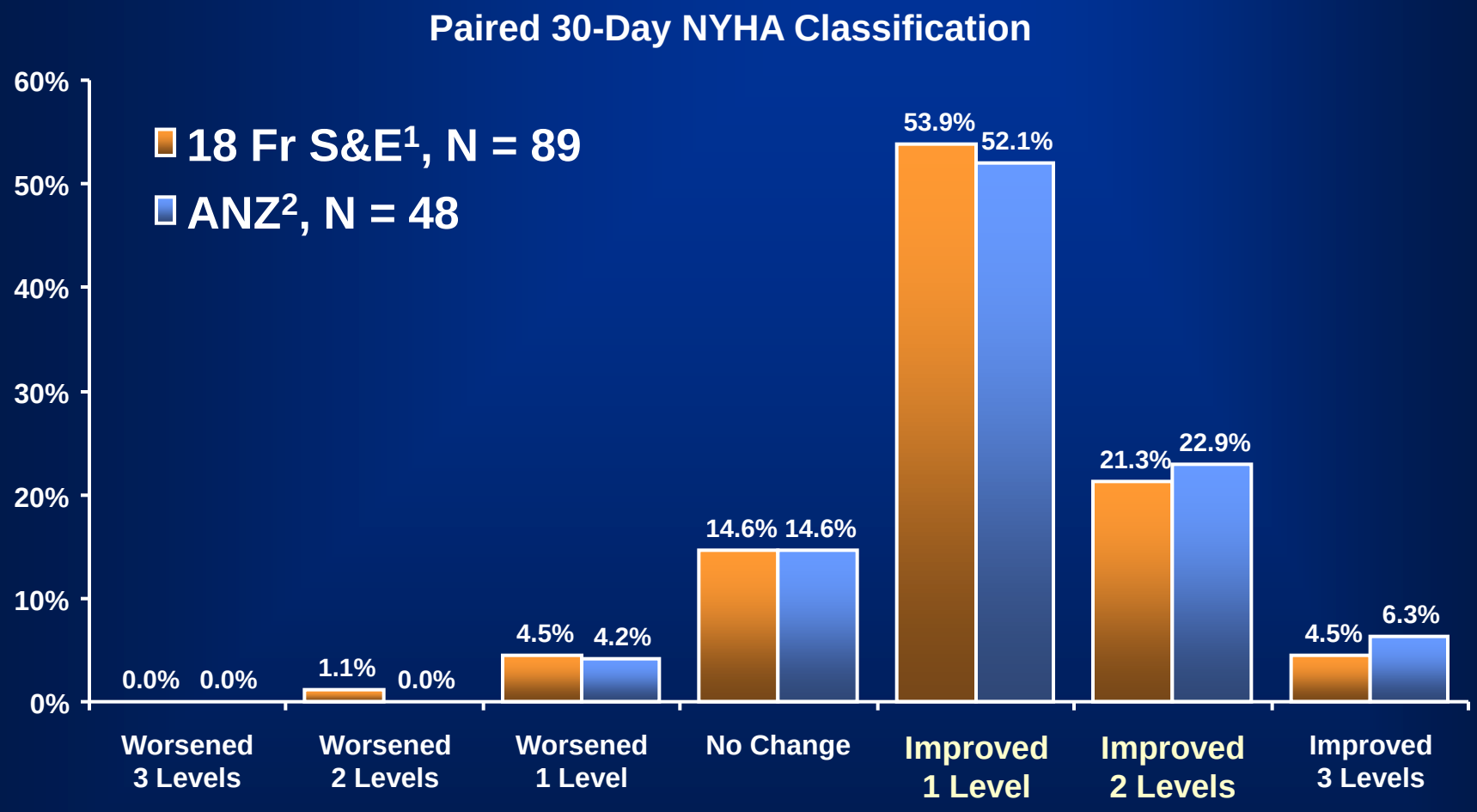
Improvement in Functional Status



Approximately 80% of patients improved at least 1 NYHA class post-implant.

1. Medtronic data on file. COR 2006-02: 18 Fr Safety & Efficacy Study Re-Analysis, August 14, 2009.
2. Meredith. A Snapshot from the Ongoing Australia-New Zealand Medtronic CoreValve® Registry. Transcatheter Cardiovascular Therapeutics 2009, September 21-25, 2009. San Francisco, CA.

Longer-Term Clinical Outcomes

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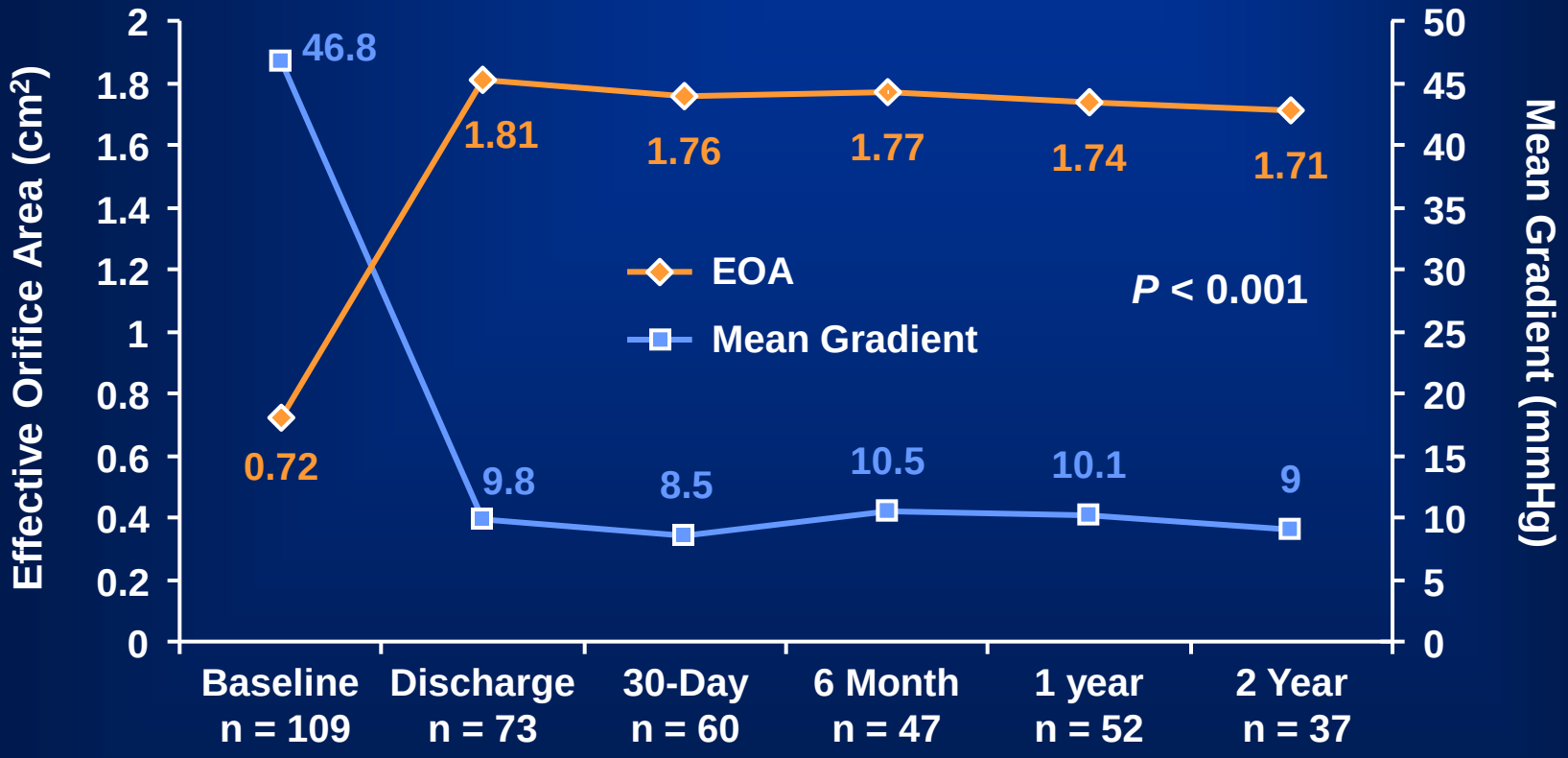
Haemodynamic Performance at 2 Years



18 Fr S&E Study[1,2]

1. Gerckens, Ulrich, MD. Safety, Durability and Effectiveness at Two Years with the 18 Fr CoreValve Transcatheter Aortic Valve. EuroPCR 2010.
2. Medtronic data on file. Addendum to COR 2006-02: 18 Fr Safety & Efficacy Study Re-Analysis, April, 2010.

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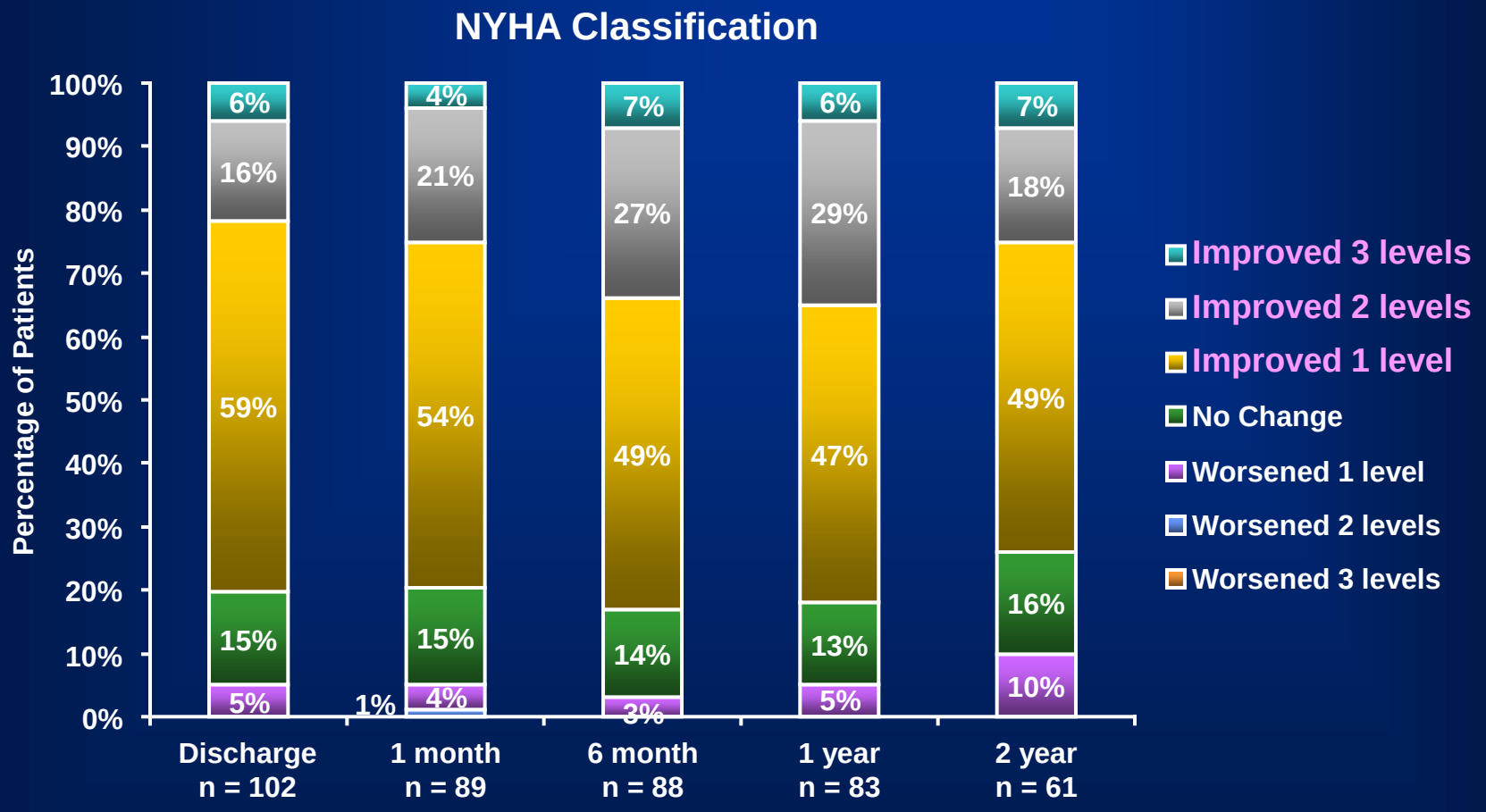
Sustained Functional Improvement at 2 Years



74% of patients sustained improvement of at least one functional class at 2 years (p<0.01).

18 Fr S&E Study

Gerckens, Ulrich, MD. Safety, Durability and Effectiveness at Two Years with the 18 Fr CoreValve Transcatheter Aortic Valve. EuroPCR 2010.

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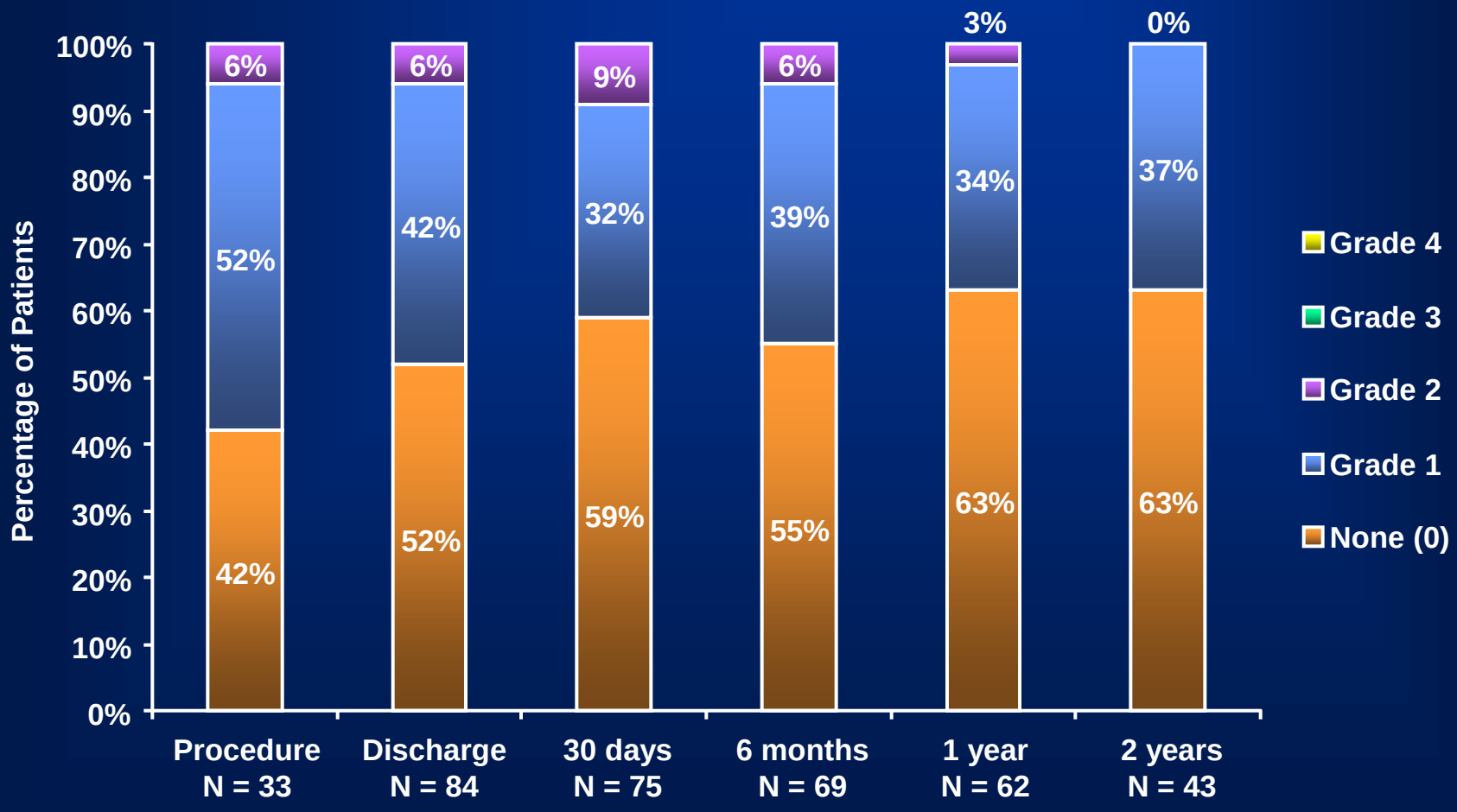
Aortic Regurgitation at 2 Years



18 Fr S&E Study

Gerckens, Ulrich, MD. Safety, Durability and Effectiveness at Two Years with the 18 Fr CoreValve Transcatheter Aortic Valve. EuroPCR 2010.

Conclusions

- TAVI using the CoreValve self-expanding aortic valve provides a safe and effective alternative for patients who are at high-risk or inoperable for conventional surgical aortic valve replacement.
- Longer term follow-up studies are needed to demonstrate the continued durability of TAVR in the high-risk and inoperable patients

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Indication of COREVALVE TAVI in Clinical Trial for approval in Korea

[첫째 조건]

aortic valve area <1㎠ (<0.6㎠/㎡) , severe AS

[둘째 조건]

1. age ≥ 80세 이거나
2. or EuroSCORE ≥20% 이거나
3. or elderly > 65 yo with one or two following conditions
   - 간경변(LC child class A or B)
   - 호흡부전(pulmonary insufficiency): FEV1 < 1 liter
   - 심장수술 과거력(CABG, 판막수술)
   - 중증의 대동맥석회화 (porcelain aorta)
   - 폐고혈압(pulmonary hypertension) >60mmHg
   - 재발성 폐색전(recurrent pulmonary embolism)
   - 우심실부전(right ventricular insufficiency)
   - 개심술을 할 수 없는 흉부 후유증(thoracic burning sequelae)
   - 종격동(mediastinum) 방사선치료(radiotherapy) 이력
   - 수술이 금기증에 해당되는 중증의 결합조직(connective tissue) 질환
   - 영양결핍(cachexia)

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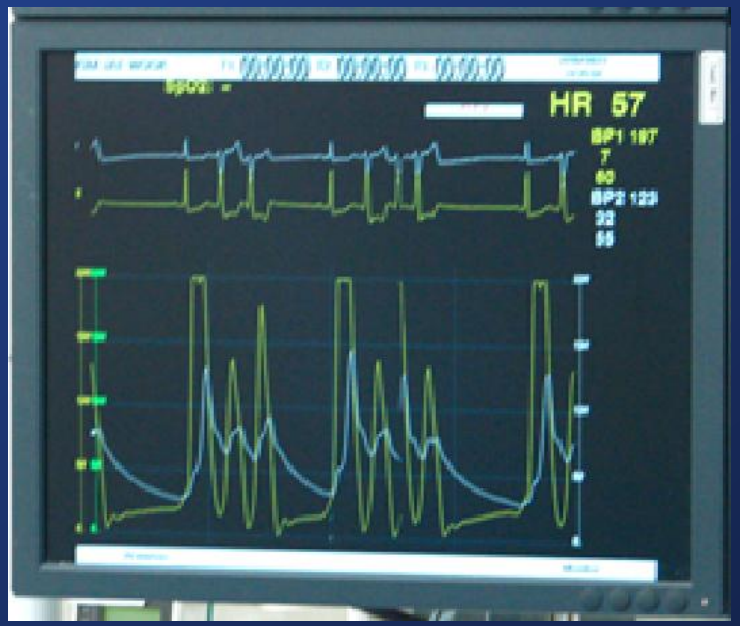
First two cases of TAVI in SNUH in 2011/7/25

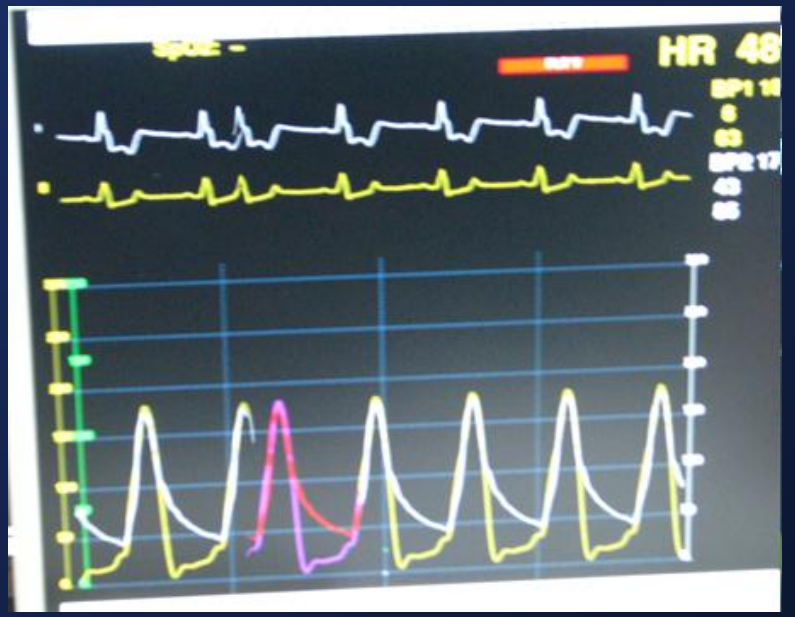
강현재

한정규

양한모

김효수

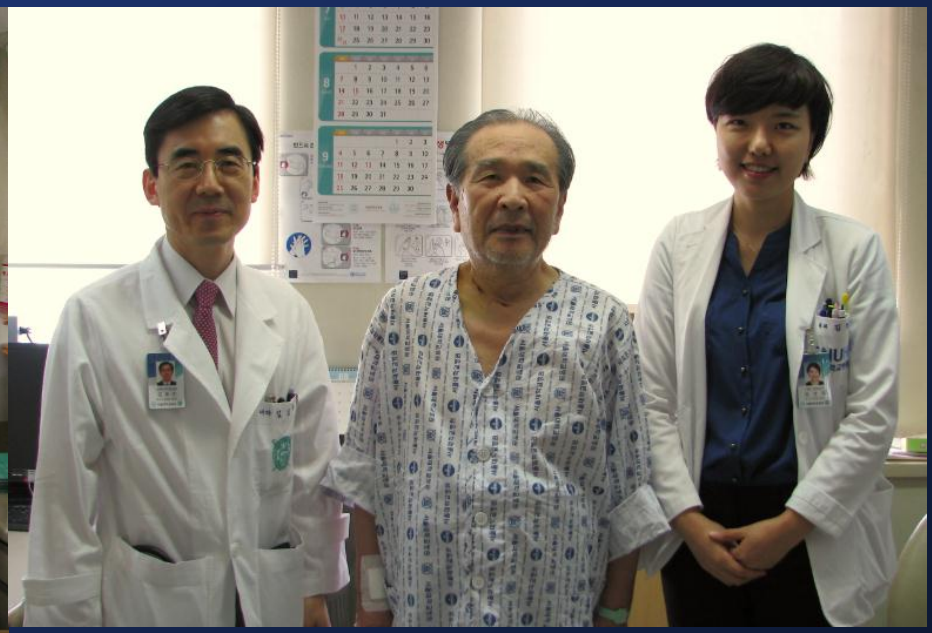




Now, six Core-valve, one Edwards valve

Improved QL immediately after TAVI

At OPD f/u two wks later



At 5th d before discharge

TAVI based on teamwork

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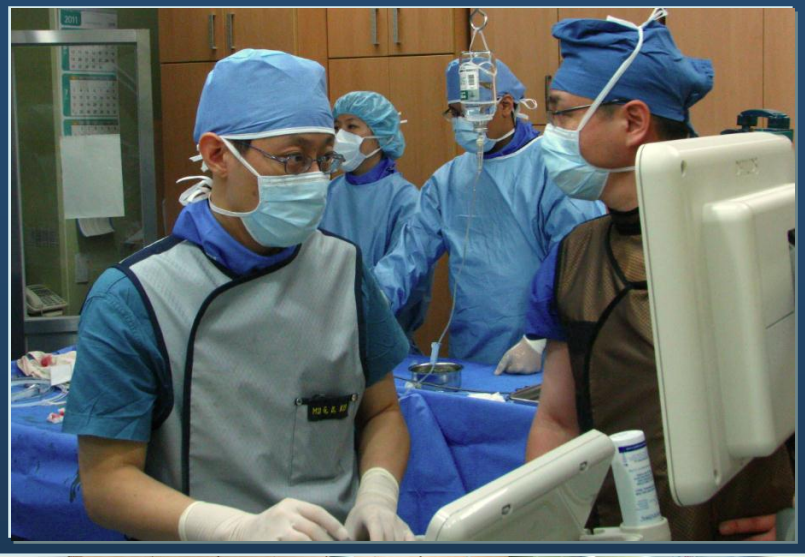

Ongoing TAVI toward broader indication

US pivotal CoreValve trial

- Extreme risk (>50% risk); single arm (n=437)
- High risk (>15% risk); 1:1 randomized trial with sAVR(n=790)

SURTAVI; CoreValve vs sAVR (n=1200, age >70)

- STS score 3-8 (Europe) (-50% of sAVR candidates)
- STS score 4-8 (US) (-25% of sAVR candidates)

PARTNER II; Sapien XT valve

- Intermediate risk (STS>3), n=1500-200, 1;1 vs sAVR
- Inoperable ; Sapien XT vs Sapien (enrolling)

TAVI

Transcatheter Aortic Valve Implantation for aortic stenosis

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