Valve-in-Valve for Bioprosthetic Valve Failure Technique and Outcomes

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial Interest /arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship	Company
Grant/ Research Support:	
Consulting Fees/Honoraria:	**Edwards Lifesciences (consultant & proctor)**
Major Stock Shareholder/Equity Interest:	
Royalty Income:	
Ownership/Founder:	
Salary:	
Intellectual Property Rights:	
Other Financial Benefit:	

- Approximately 200,000 surgical aortic valve replacements are performed annually.
- Over the last 10 years, the majority of surgically implanted aortic valves have been bioprosthetic.
- With a life expectancy of 10-20 years, and implantation in younger patients, there will be a significant increase in the number of patients requiring redo surgery for failed bioprostheses.

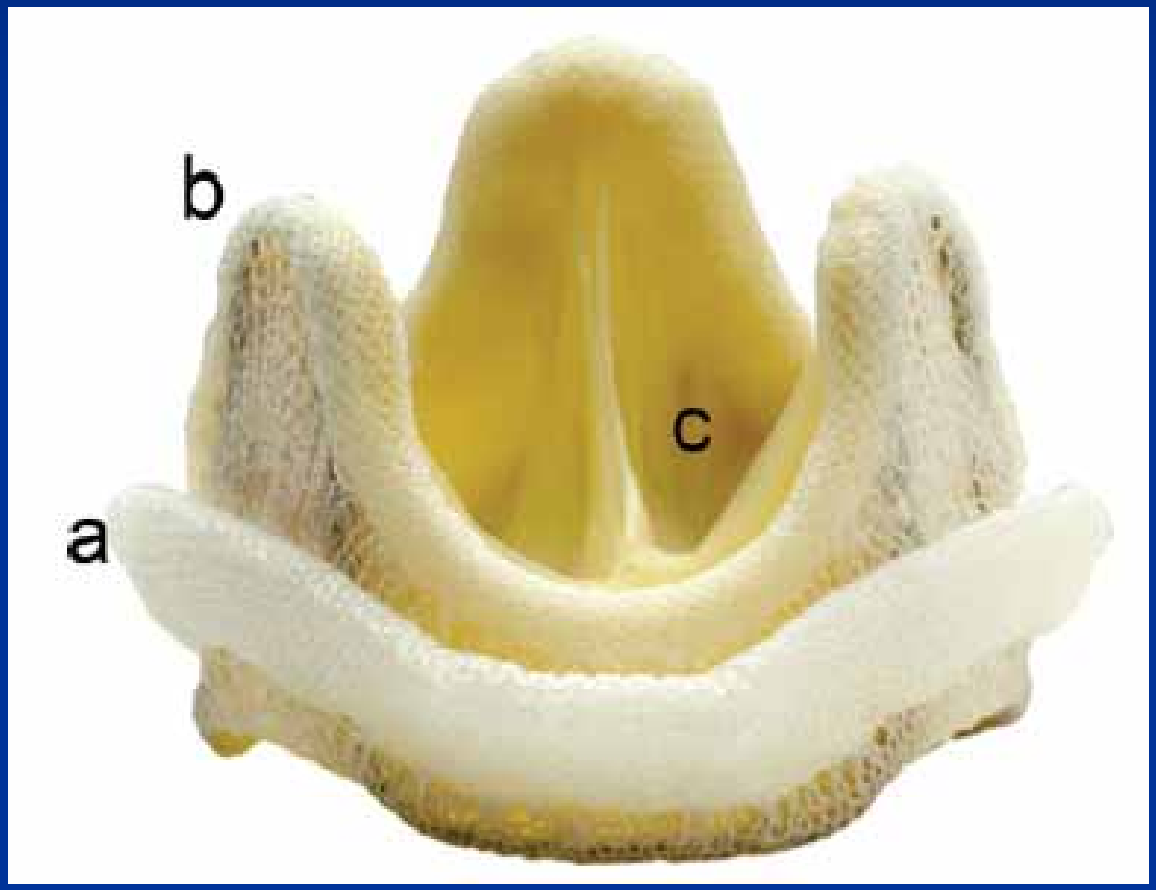
Brown JM et al; The Journal of Thoracic and Cardiovascular Surger; V.137; No.1; 1/09; p82

- Reoperation (redo) is the standard of care for failed bioprosthetic valves.
- Operative mortality for an elective redo aortic valve surgery ranges from 2% to 7%; however, it can increase to 30% in high-risk or frail patients
- TAVI provides a minimally invasive alternative to conventional redo surgery.

Piazza et al.; JACC: CARDIOVASCULAR INTERVENTIONS, VoL. 4, NO. 7, 2011

TECHNIQUES

Anatomy of (Stented) Bioprosthetic Valve



A – Sewing ring

B – Frame / Stent Post

C - Leaflets

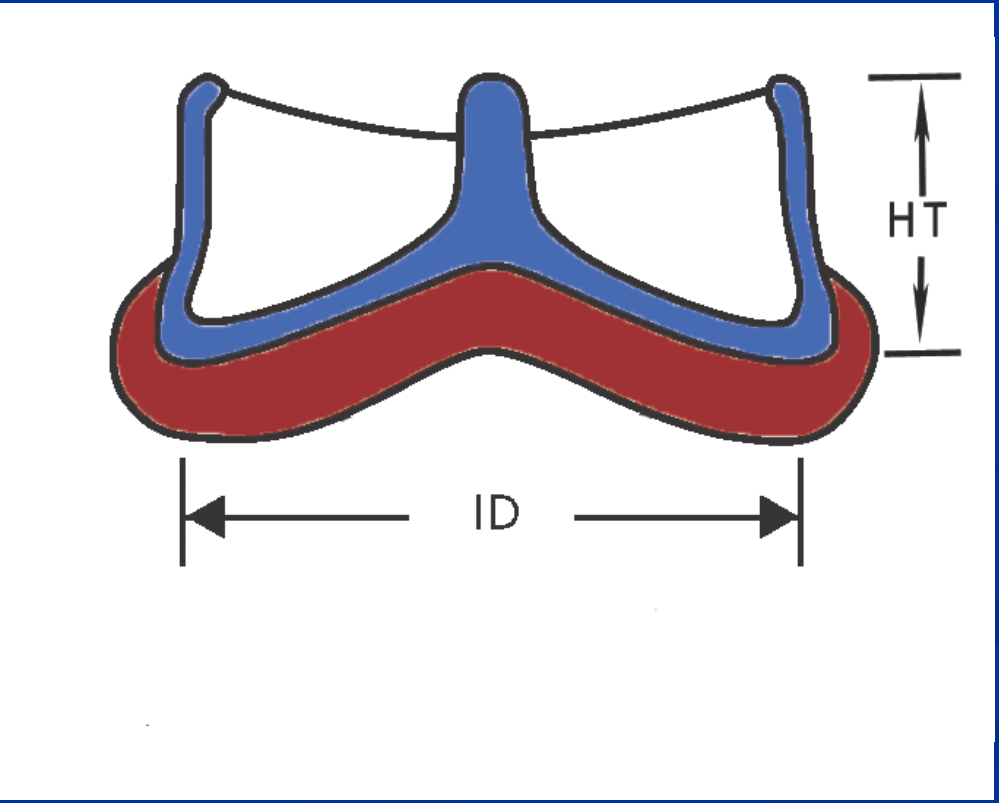
Important Technical Steps

- Choose correct size
- Position transcatheter valve in correct position

Choosing Correct Size

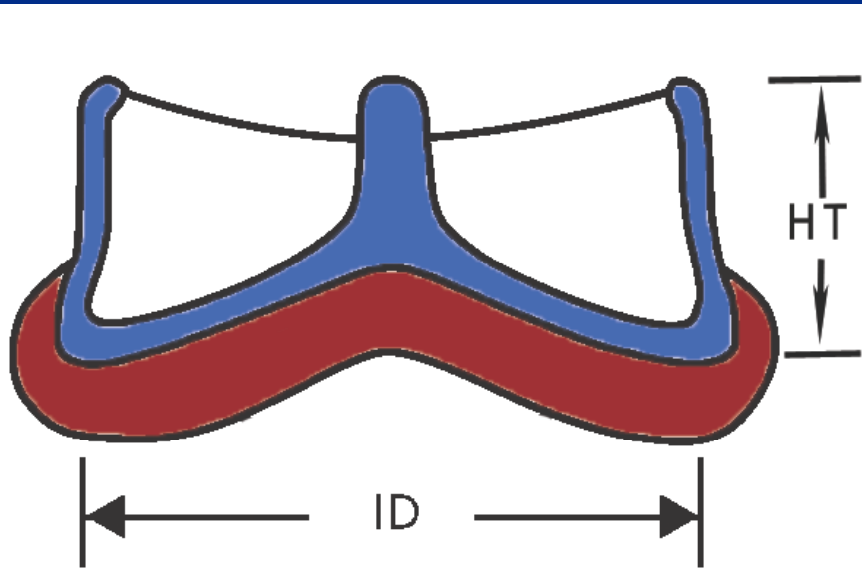
Need to know true internal diameter of valve

- To choose the right size of TAVI device
- To avoid PP mismatch and valve dysfunction



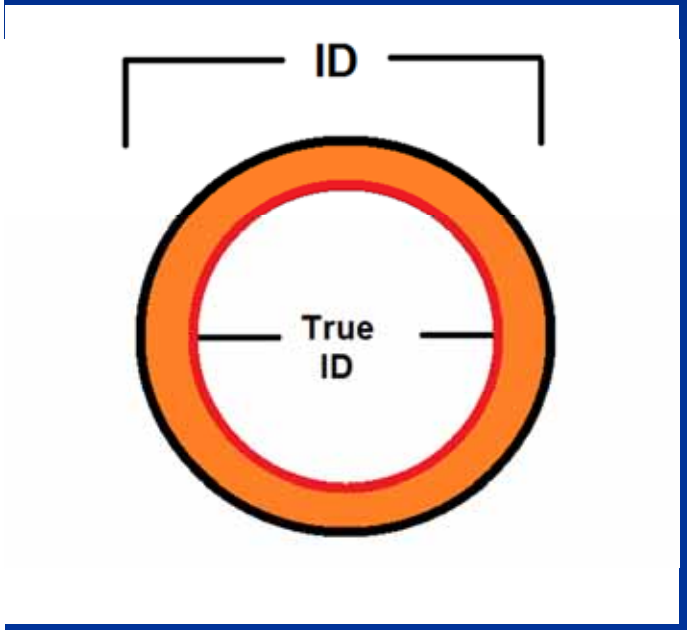
ID Charts

Size	Type	Stent Internal Diameter (mm)	Profile Height (mm)
19	Perimount	18	14
	Perimount Magna Ease	18	13
	Mitroflow	15.4	11.0
	Mosaic	17.5	13.5
21	Perimount	20	15
	Perimount Magna Ease	20	14
	Mitroflow	17.3	13.0
	Mosaic	18.5	15
23	Perimount	22	16
	Perimount Magna Ease	22	15
	Mitroflow	19.0	14.0
	Mosaic	20.5	16
25	Perimount	24	17
	Perimount Magna Ease	24	16.0
	Mitroflow	21.0	15.0
	Mosaic	22.5	17.5



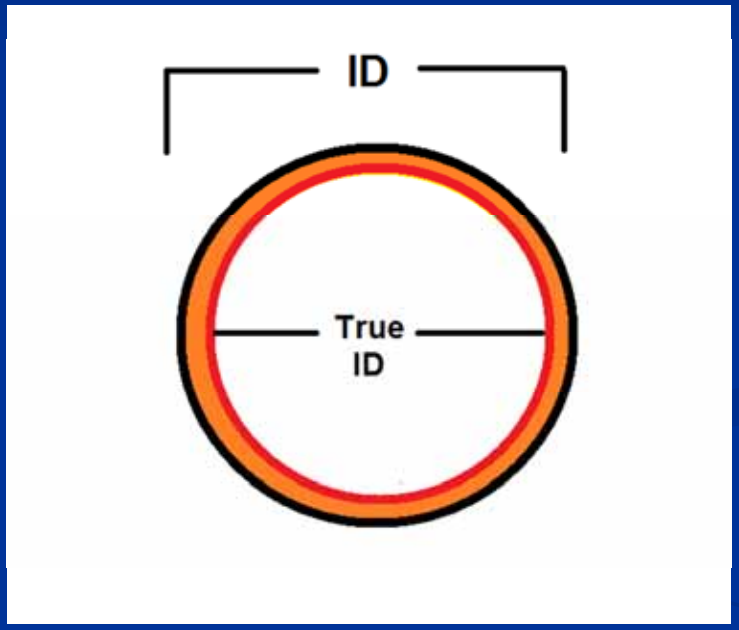
True ID ?

Effect of leaflet mounting – reduction in ID



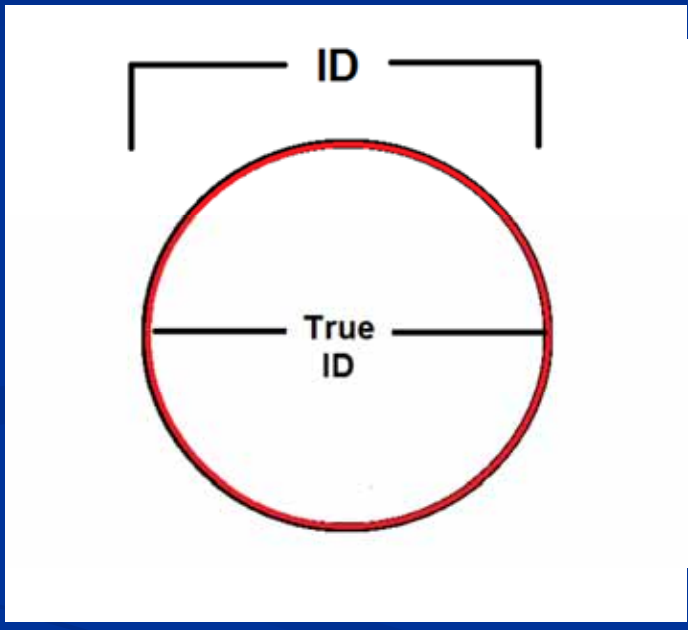
Porcine Valves

CE Porcine std, CE Porcin SAV,Hancock 2, Mosaic, Intact, Biocor/Epic, Biocor/Epic Supra,



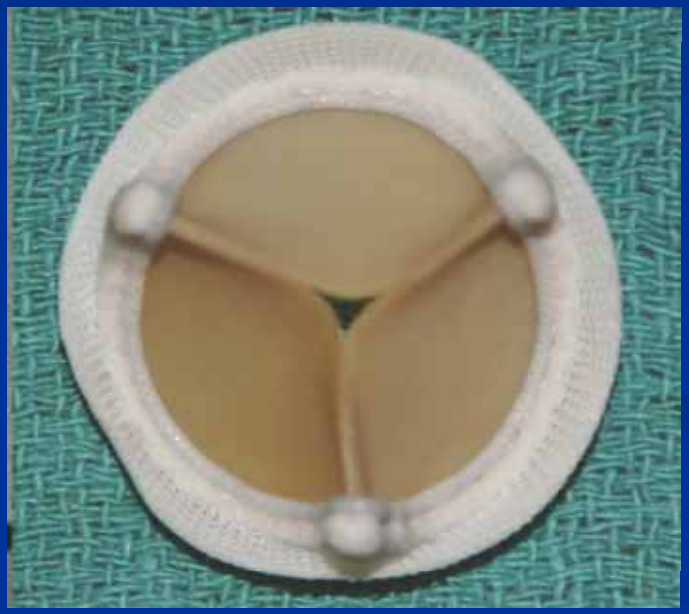
Thin Pericardial Leaflets insideThe stent

Perimount, Perimount 2700, Magna/Magna ease



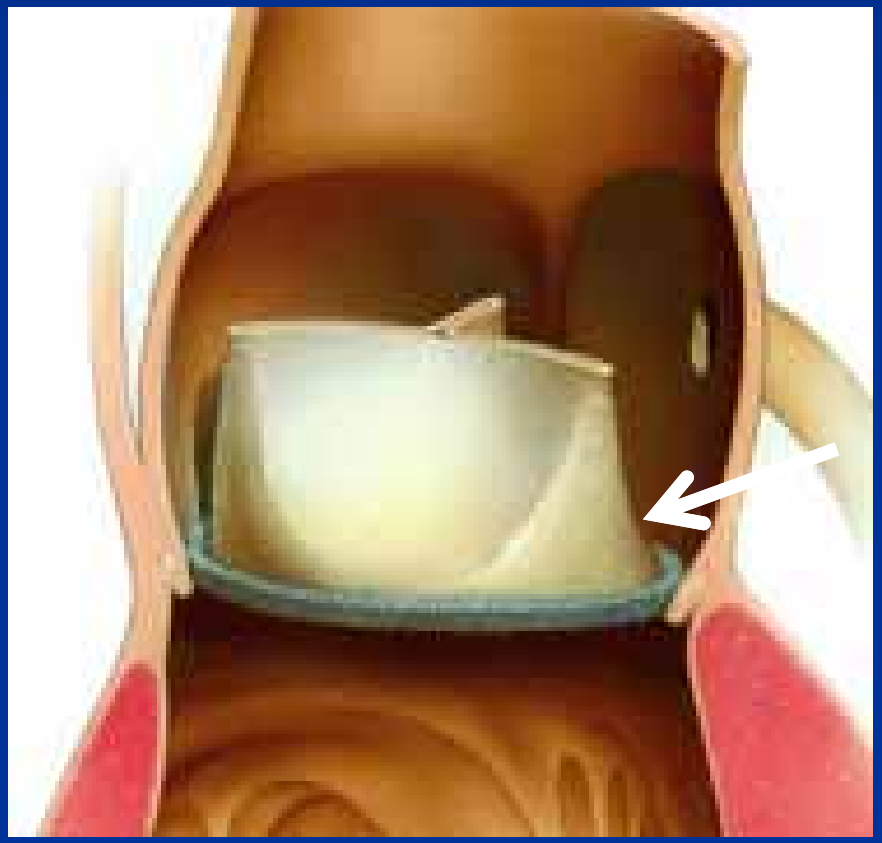
Leaflets outside The stent

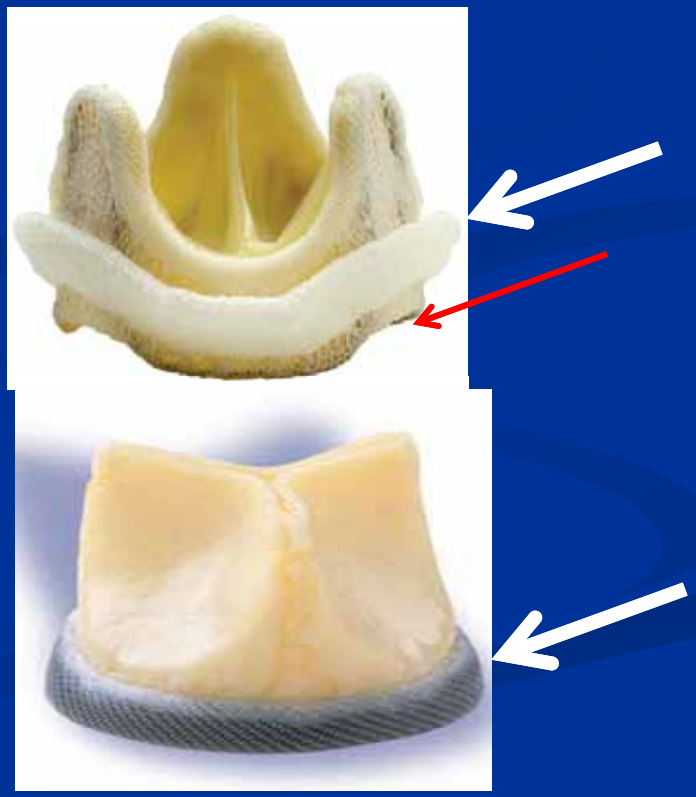
Mitroflow, Soprano, Trefecta

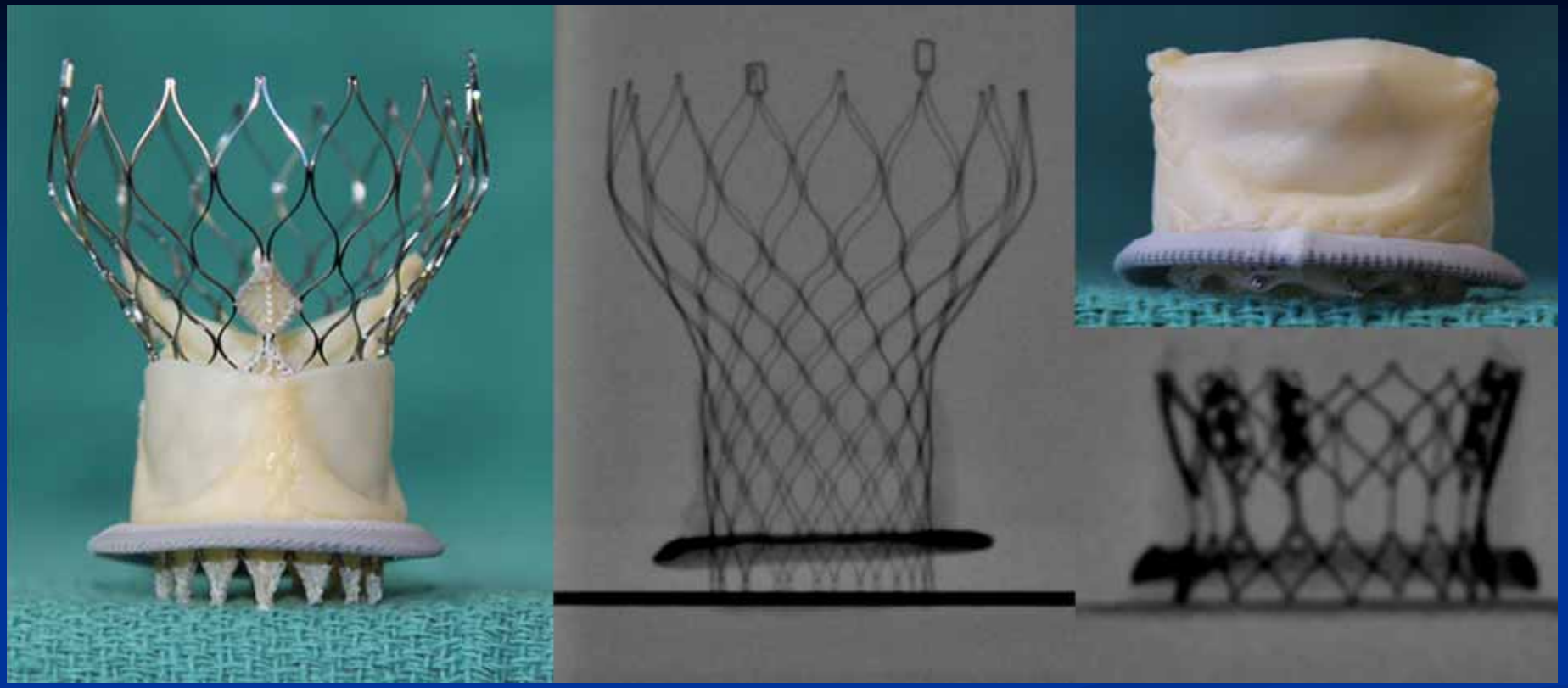




Correct Placement
Sewing Ring provides the Anchor

- Narrowest diameter is at the level of sewing ring







CoreValve

SAPIEN

Typically positioned ~6mm below sewing ring

Typically positioned ~4mm below sewing ring; Ensure not too low to leave uncovered leaflets

Radio-opaque Markers

- Sewing ring
- Frame
- None

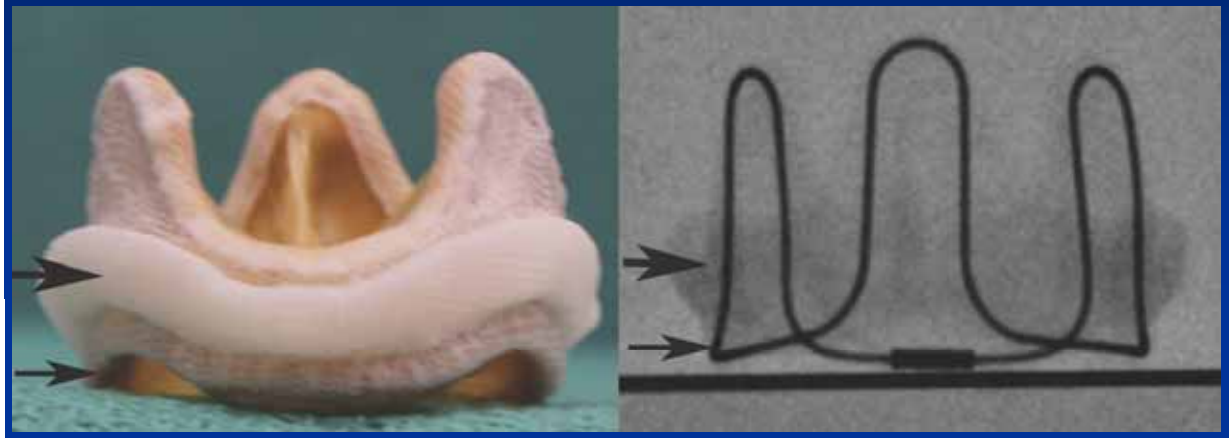
Radio-opaque Sewing Ring

Hancock II, Epic, Soprano, Mitroflow

Place CoreValve 6mm below radio-opaque sewing ring

Place SAPIEN 4mm below radio-opaque sewing ring
(due to foreshortening, may need to start ~1/3 below sewing ring

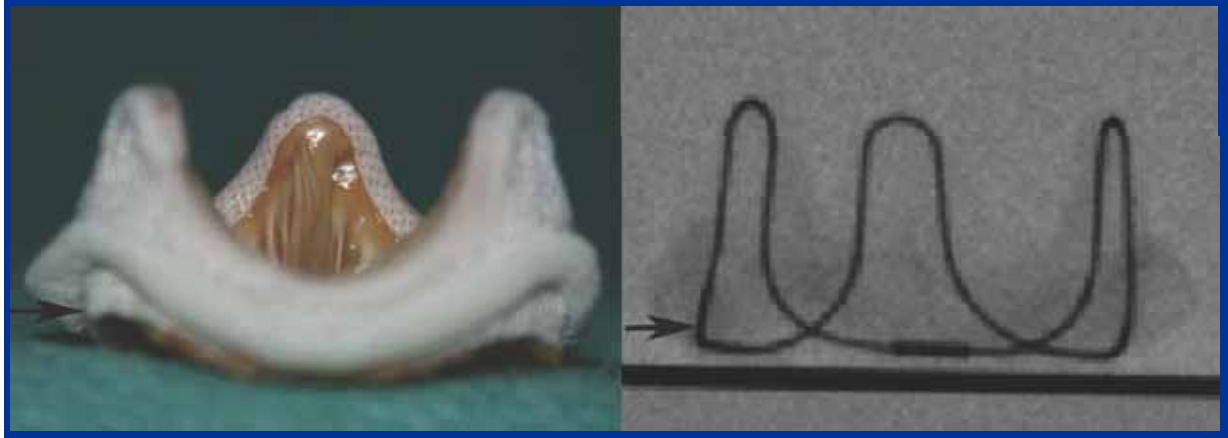
Radio-opaque Frame



Frame below sewing ring

Perimount, CE Porcine

Place transcatheter valve inflow
At same level as frame inflow



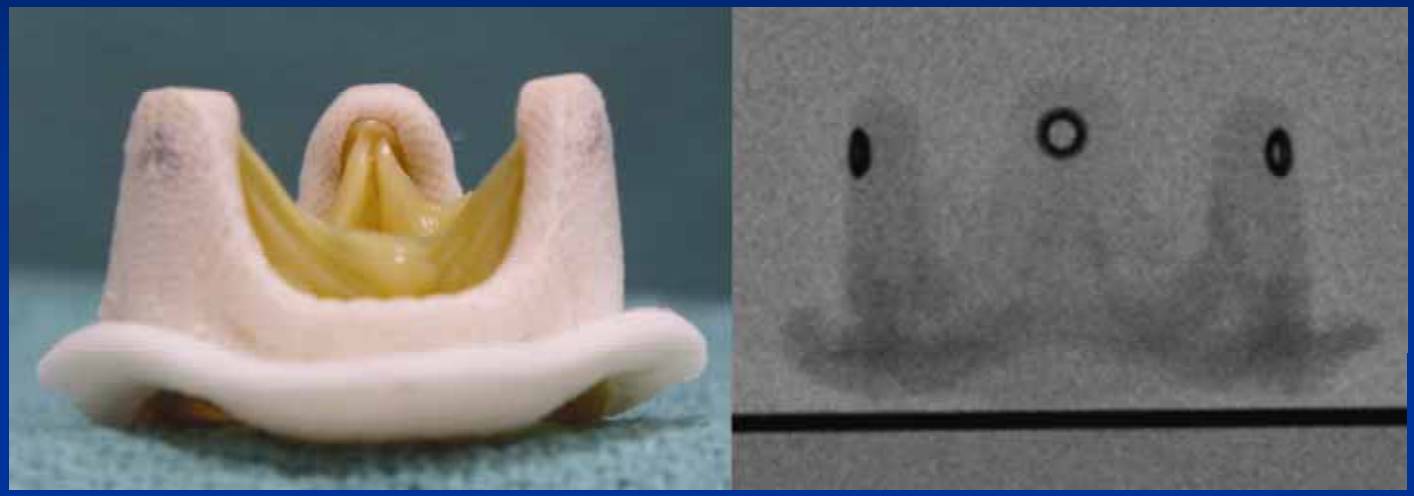
Frame same level as sewing ring

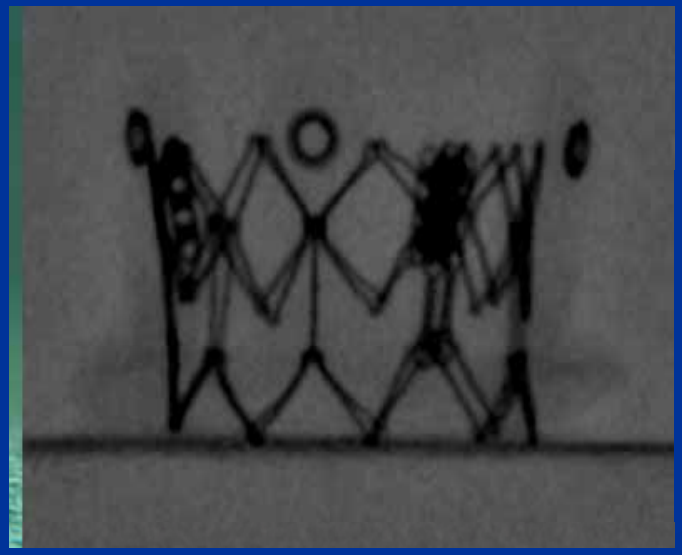
Magna, Trifecta

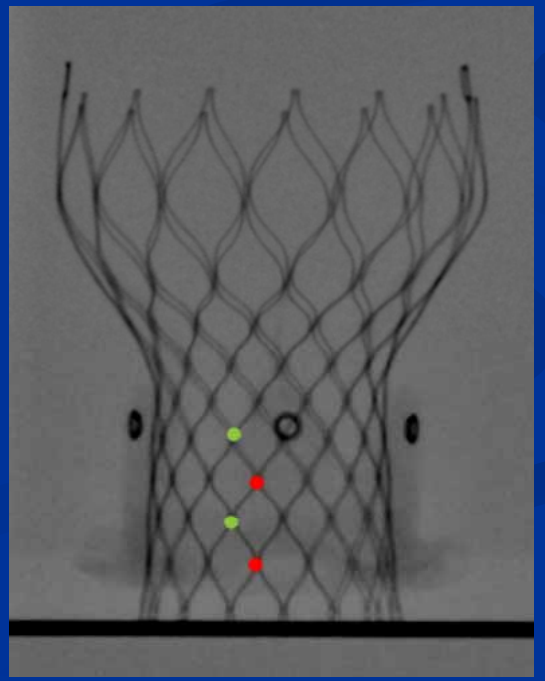
Place transcatheter valve inflow below frame inflow

- CoreValve 6mm below
- SAPIEN 4mm below

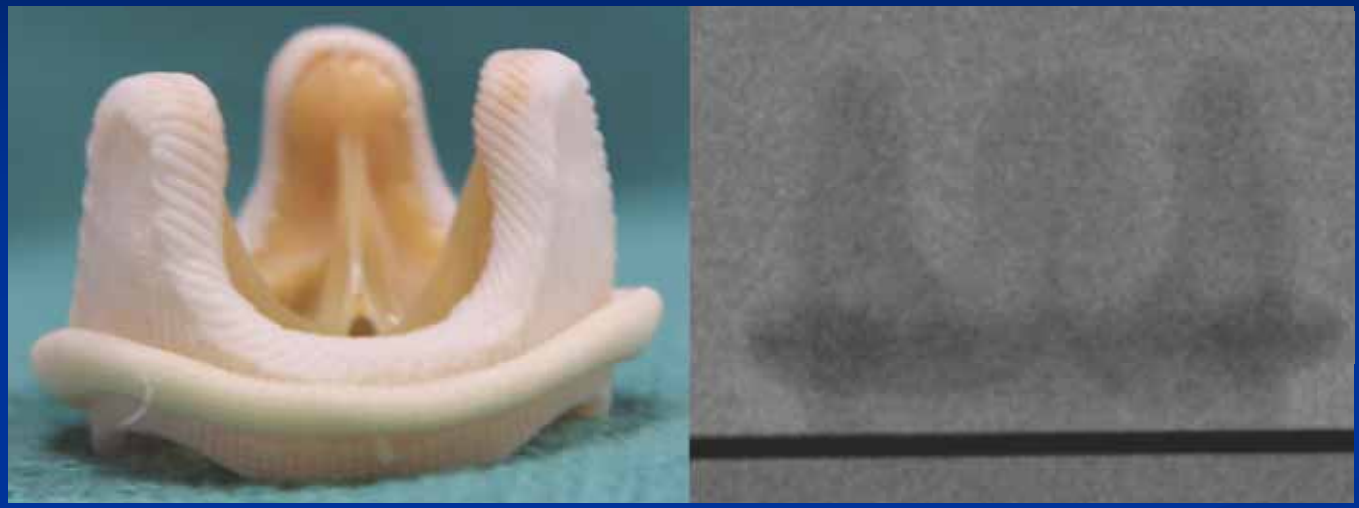
Radio-opaque stent tips
Mosaic





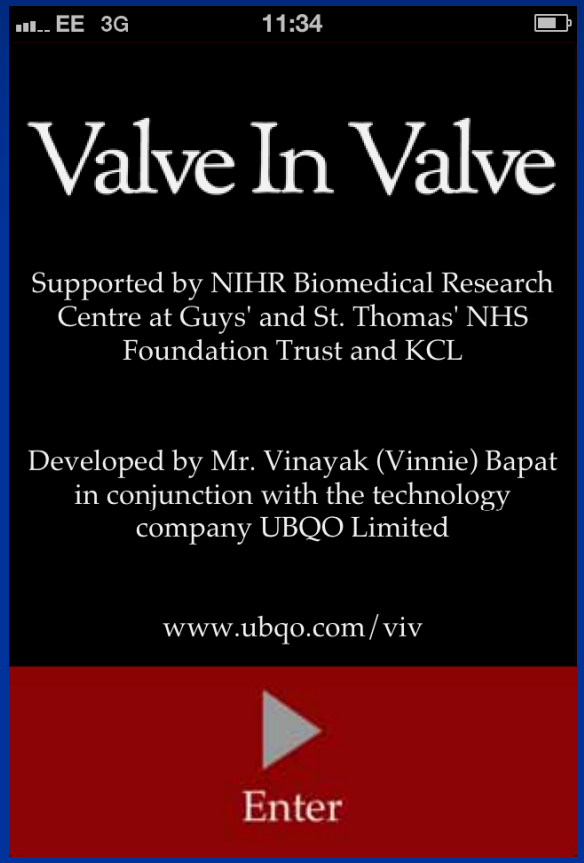


No Radio-opaque Markers

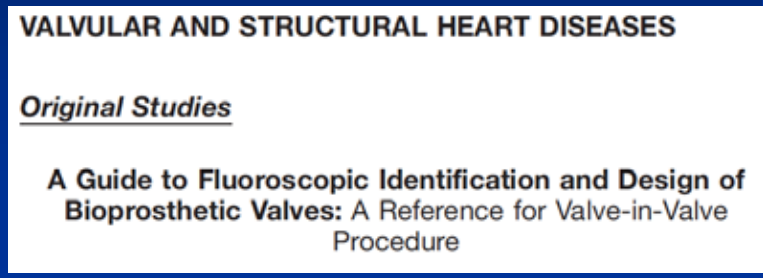


Aspire; Medtronic Intact

Use TOE and aortography



Vinnie Bapat
St Thomas' Hospital, UK



Bapat, V., et al. *Catheter Cardiovasc Interv.* 2013;81:853-61

OUTCOMES

Global valve-in-valve registry

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Transcatheter Aortic Valve Replac
Results from t

Danny Dvir, John Webb, Stephen E
Colombo, Fleur Descoutures, Christia
Napodano, Luca Testa, Thierry Lefevre,
Roy, Rui C. Teles, Amit Segev, Nicol
Tchetche, Mohamed Abdel-Wahab, Fe

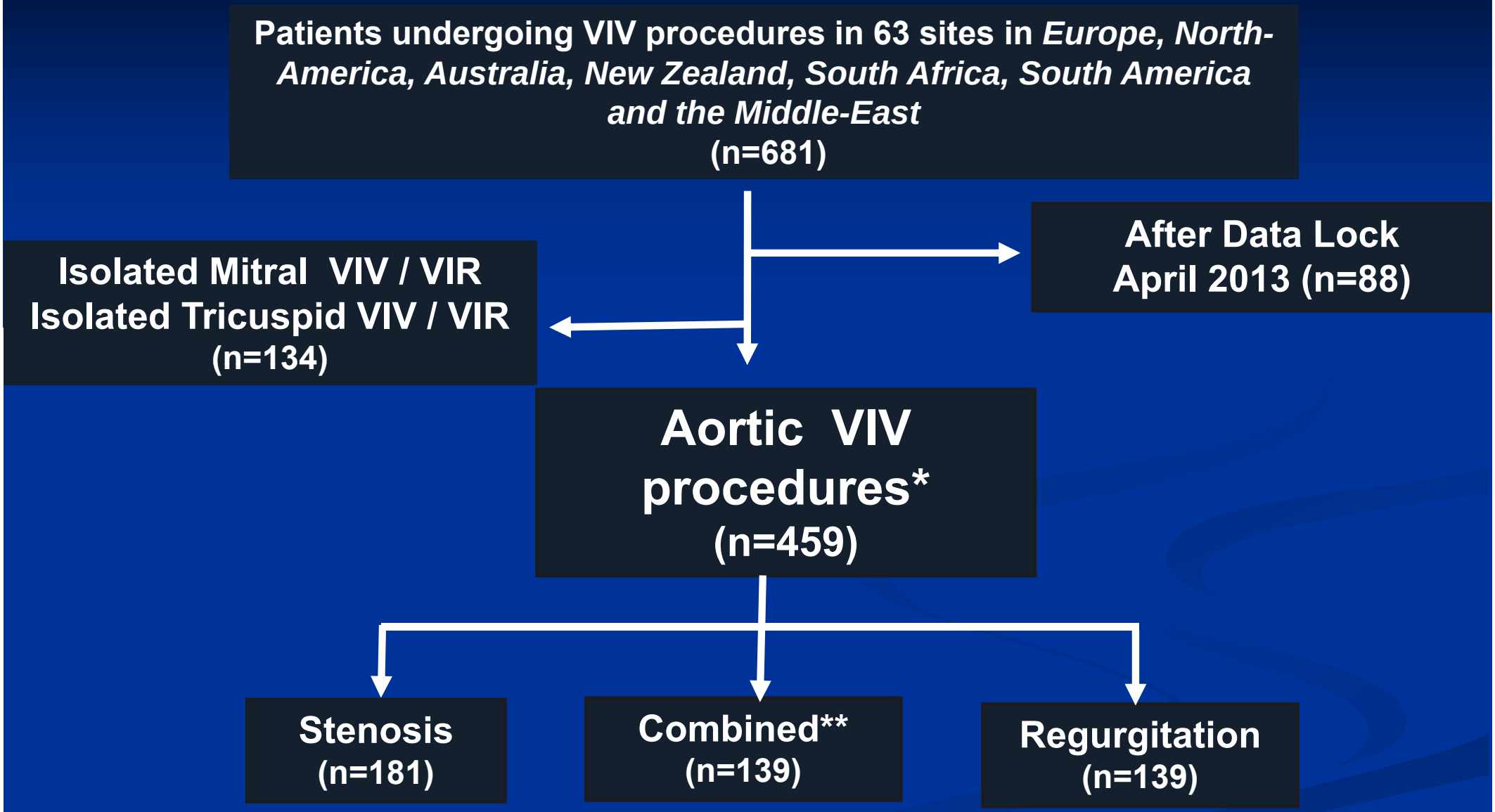
Transcatheter Valve Implantation in Failed Surgical Aortic Valves: Update from the Global Registry

Danny Dvir, MD
St Paul's Hospital, University of British Columbia
Vancouver, Canada

TVT Transcatheter Valve Therapies

NewYork-Presbyterian | Columbia University Medical Center | Cardiovascular Research Foundation

Global Valve in Valve Registry



* Including 3 cases of combined aortic VIV and mitral VIV.

** At least a moderate degree of both stenosis and regurgitation while both mechanisms are comparable in their severity.

Baseline Demographics

	Stenosis *n= 181*	*Regurgitation* *n= 139*	*Combined* *n= 139*	*P*
Age (yrs)	78.8± 7.8	77.1± 10.6	76.6± 11.1	0.10
Gender (% male)	48	66.9	55.4	0.002
LogEuroSCORE	32.3 ± 17.1	30.3 ± 18.8	34.1 ± 18.6	0.24
STS score (%)	12.3 ± 10.3	11.2 ± 8.4	13.4 ± 13.1	0.24
NYHA class IV	26.2%	36.7%	38.1%	0.001
Height (cm)	167.1 ± 9.9	168.1± 9.7	166.5 ± 9.8	0.20
Weight (kg)	77.6 ± 16.5	72 ± 13.3	70.8 ± 14.1	0.0003
BMI (kg/m2)	27.7 ± 4.8	25.4 ± 3.9	25.5 ± 4.2	<0.0001
BSA (m2)	1.89 ± 0.24	1.83 ± 0.2	1.8 ± 0.21	0.002
Stented bioprosthesis	95.6%	60.4%	78.4%	<0.0001
Label size <=21mm	37%	20.9%	26.6%	0.005

Baseline Demographics

	Edwards SAPIEN *n= 246*	*CoreValve* *n= 213*	*P*
Age (yrs)	77.6 ± 9.7	77.6 ± 10	0.95
Gender (% male)	58.5%	53.1%	0.25
LogEuroSCORE	33 ± 19.2	31.3 ± 16.8	0.31
STS score (%)	11.9 ± 10.5	12.8 ± 10.6	0.42
Chronic renal failure	57.3%	38%	<0.0001
PVD	31.3%	17.4%	<0.0001
Stented bioprosthesis	87%	71.4%	<0.0001
Label size <=21mm	26.4%	31.9%	0.19

Procedural Characteristics

	All (n=459)	CoreValve (n=213)	SAPIEN (n=246)	p Value*
Device size				<0.0001
20-mm	1 (0.2%)	-	1 (0.4%)	
23-mm	183 (39.9%)	5 (2.3%)	178 (72.4%)	
26-mm	236 (51.4%)	171 (80.3%)	65 (26.4%)	
29-mm	36 (7.8%)	34 (16%)	2 (0.8%)	
31-mm	3 (0.7%)	3 (1.4%)	-	
Access				<0.0001
Transfemoral	270 (58.8%)	197 (92.5%)	73 (29.7%)	
Transapical	171 (37.3%)	-	171 (69.5%)	
Transaxillary	13 (2.8%)	13 (6.1%)	-	
Transaortic	5 (1.1%)	3 (1.4%)	2 (0.8%)	
General anesthesia	321 (69.9%)	116 (54.5%)	205 (83.3%)	<0.0001
TEE usage	293 (63.8%)	96 (45.1%)	197 (80%)	<0.0001
Pre-implantation valvuloplasty	137 (29.8%)	41 (19.2%)	96 (39%)	<0.0001

Procedural Characteristics

	All (n=459)	CoreValve (n=213)	SAPIEN (n=246)	p Value*
Attempted device retrieval	22 (10.3%)	22 (10.3%)	NA	NA
Post-implantation valvuloplasty	48 (10.5%)	40 (18.8%)	8 (3.3%)	<0.0001
Second TAVR device implantation	26 (5.7%)	16 (7.5%)	10 (4.1%)	0.052

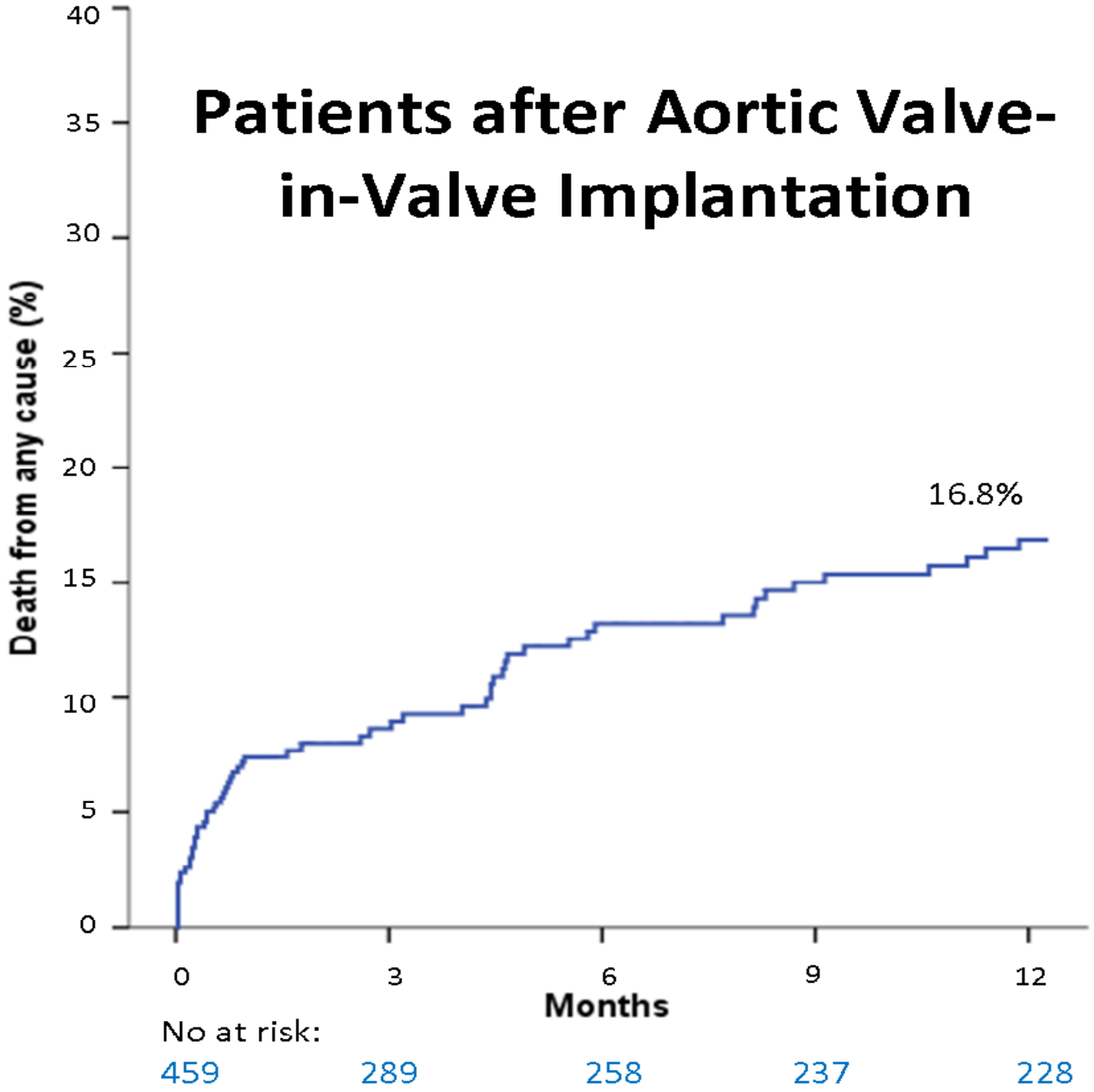
Post procedure Echocardiography

	Stenosis *n=181*	*Regurgitation* *n=139*	*Combined* *n=139*	*P*
AV area (cm^2)	1.37± 0.33	1.56± 0.49	1.56± 0.65	0.01
AV max gradients (mmHg)	32.2± 14.7	22.4± 11.6	29.1± 13.6	<0.001
AV mean gradients (mmHg)	18.4± 9.8	12.0± 6.7	16.0± 8.3	<0.001
AR (≥2)	2.8%	9.4%	5%	0.04
LVEF (%)	53.7± 9.9	49.0± 11.6	51.2± 12.9	0.002

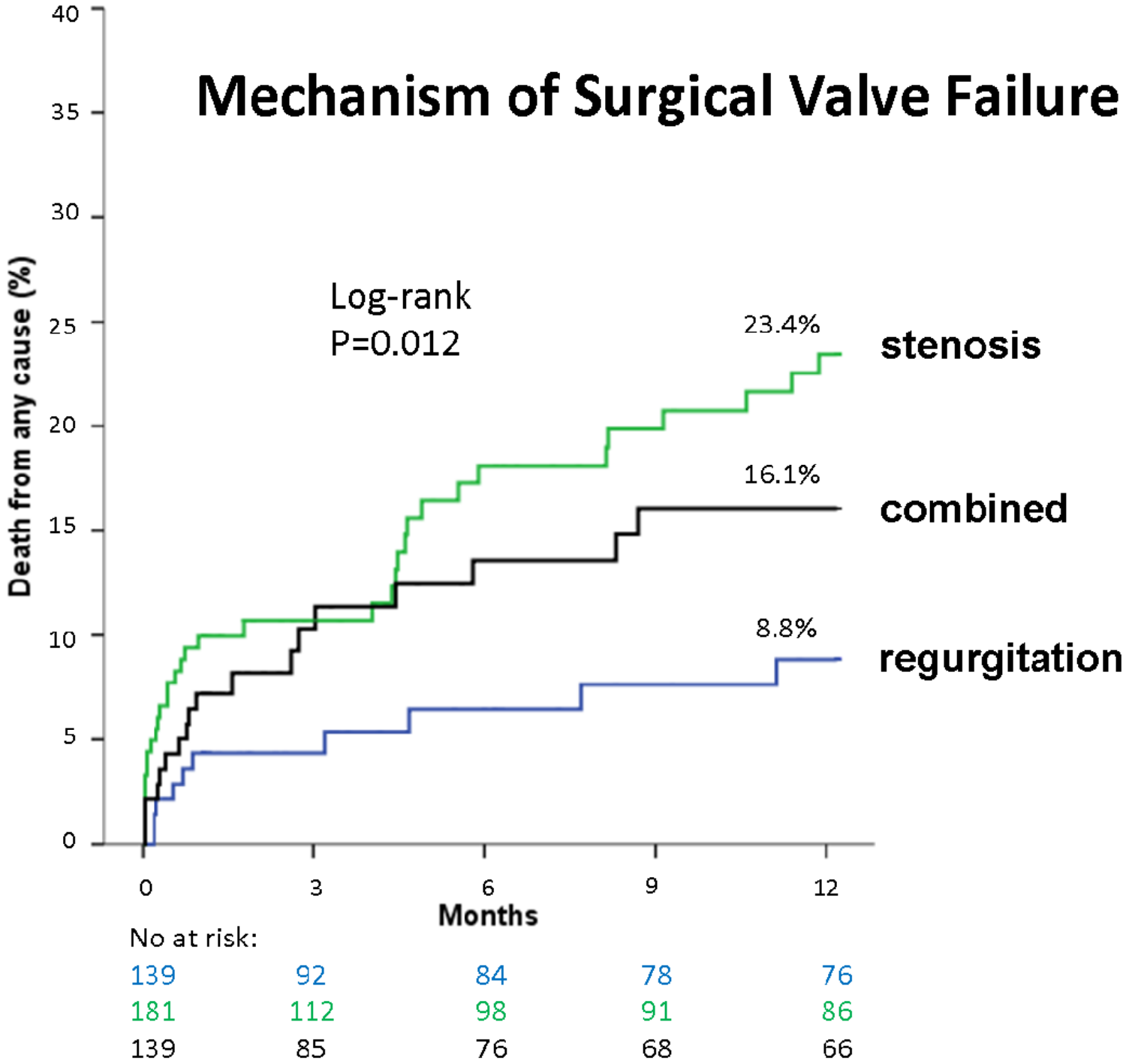
30-day Clinical Outcomes

	Stenosis *n=181*	*Regurgitation* *n=139*	*Combined* *n=139*	*P*
Death	10.5%	**4.3%**	**7.2%**	**0.04**
Cardiovascular death	8.8%	**3.6%**	**6.5%**	**0.06**
Major stroke‡	0.6%	**2.2%**	**2.9%**	**0.26**
Death or major stroke	10.5%	**6.5%**	**10.1%**	**0.42**
Major vascular complication‡	7.7%	**7.2%**	**12.9%**	**0.11**
Major/life-threatening bleeding	11%	**3.6%**	**8.6%**	**0.01**
Acute kidney injury * (VARC≥2)	8.8%	**7.2%**	**5.8%**	**0.58**

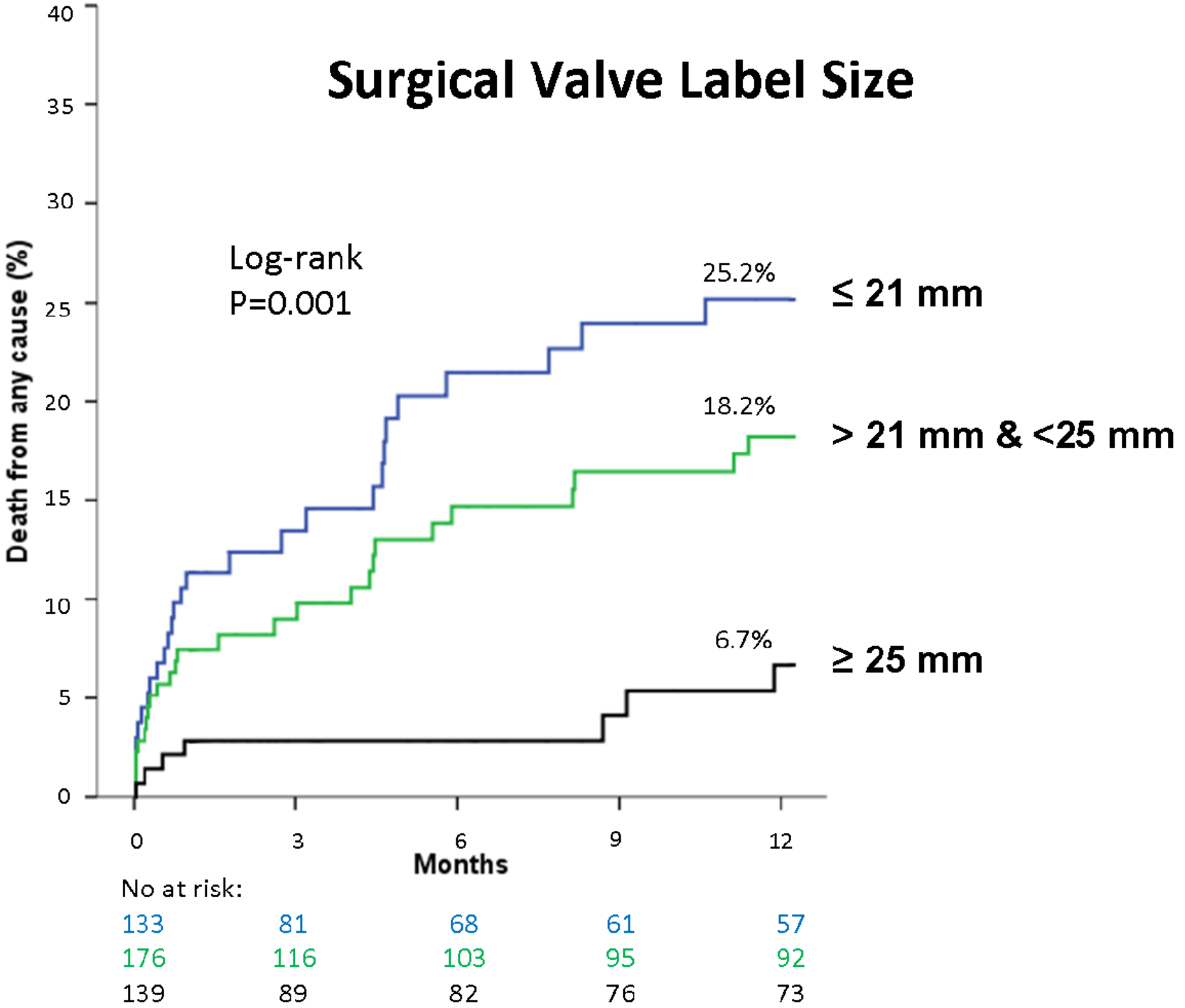
Patients after Aortic Valve-in-Valve Implantation



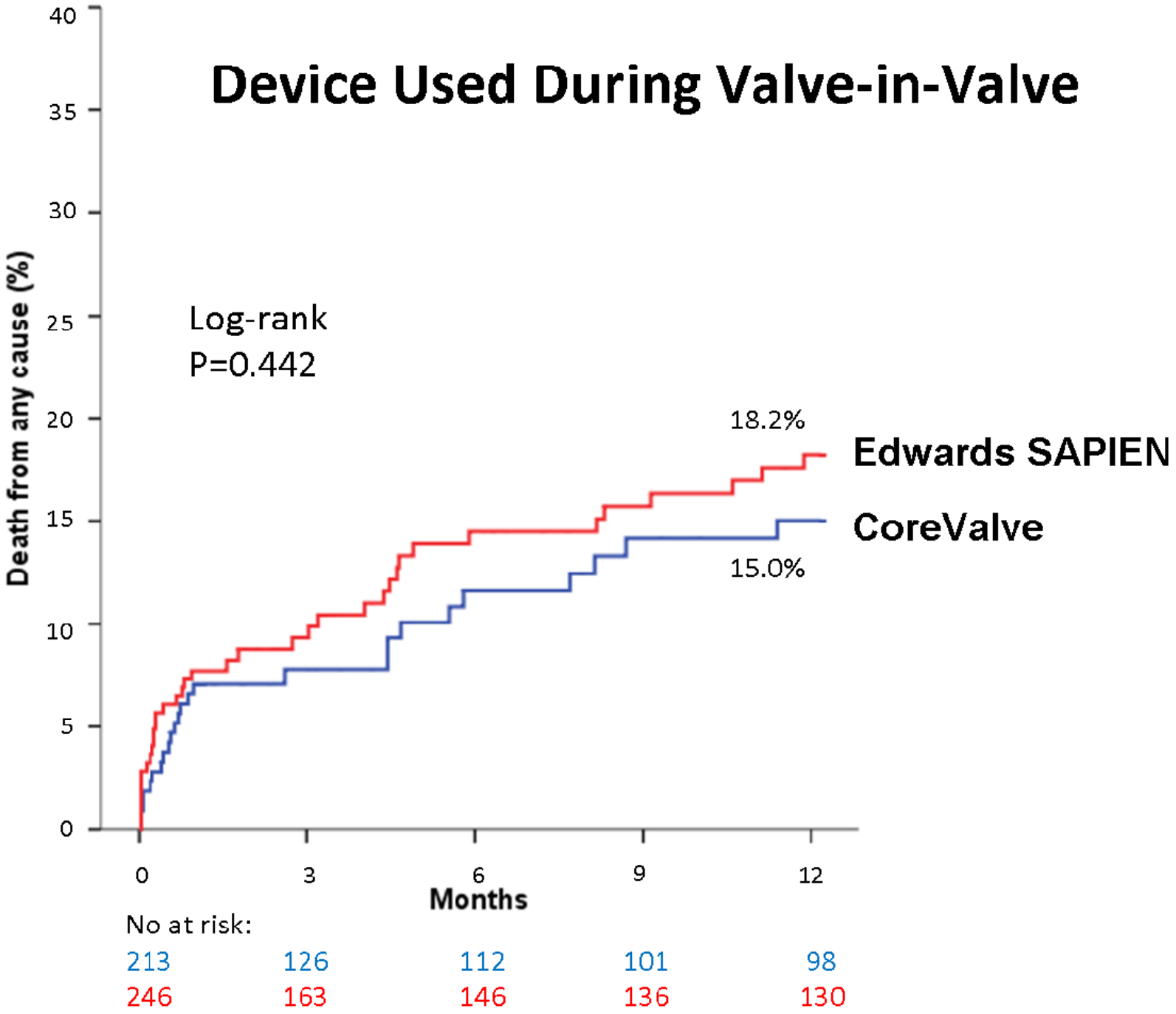
Mechanism of Surgical Valve Failure

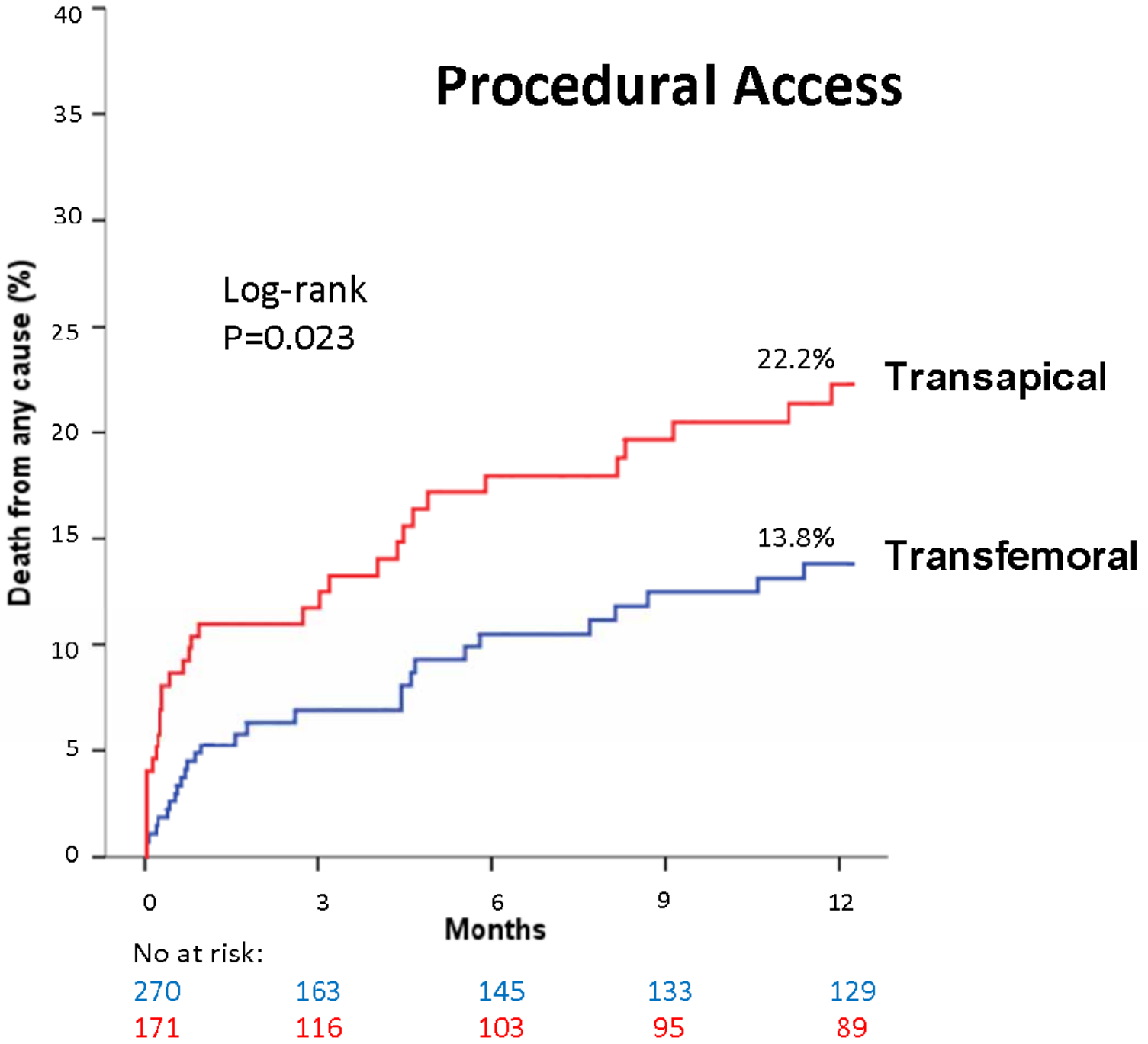


Surgical Valve Label Size

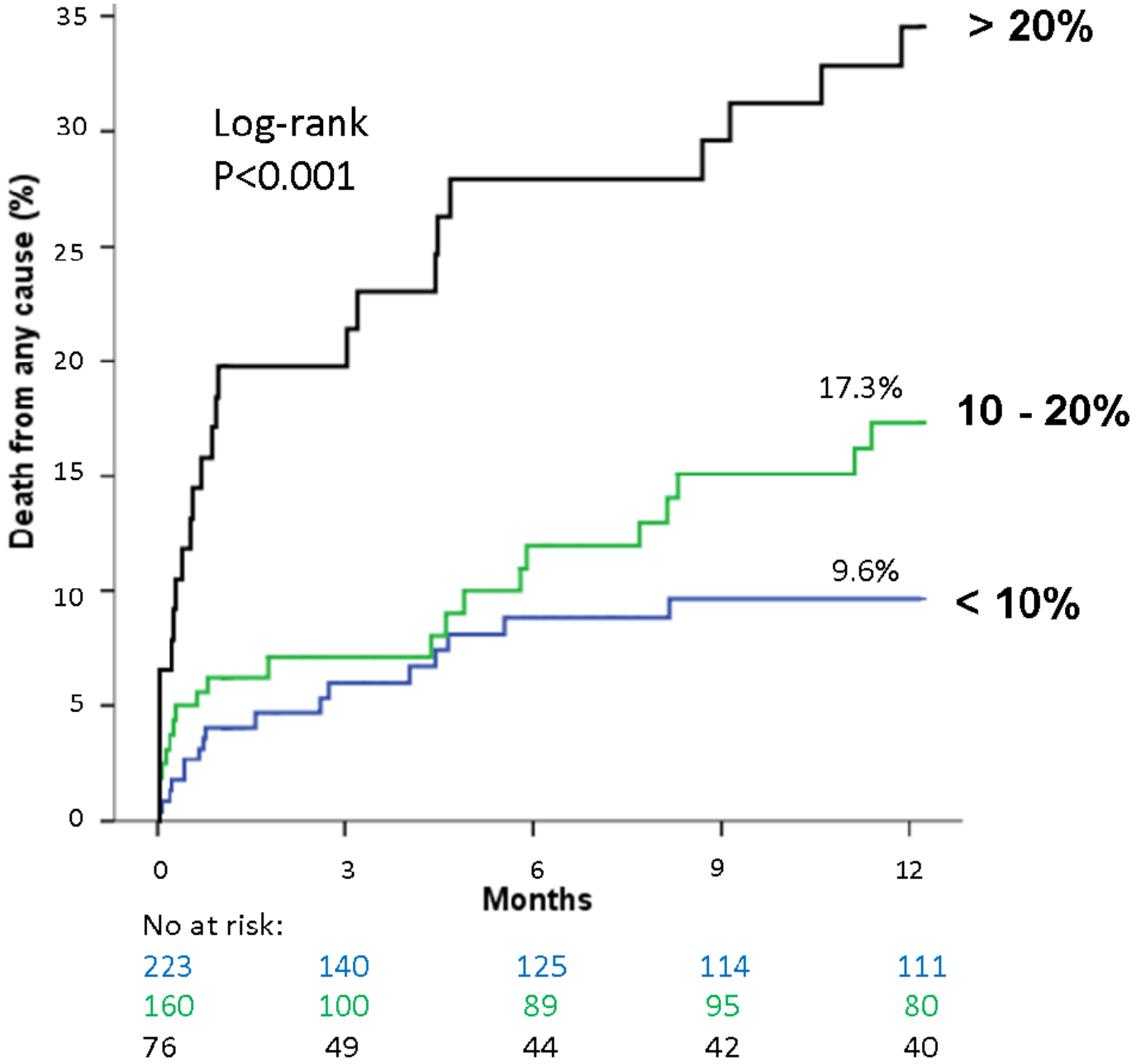


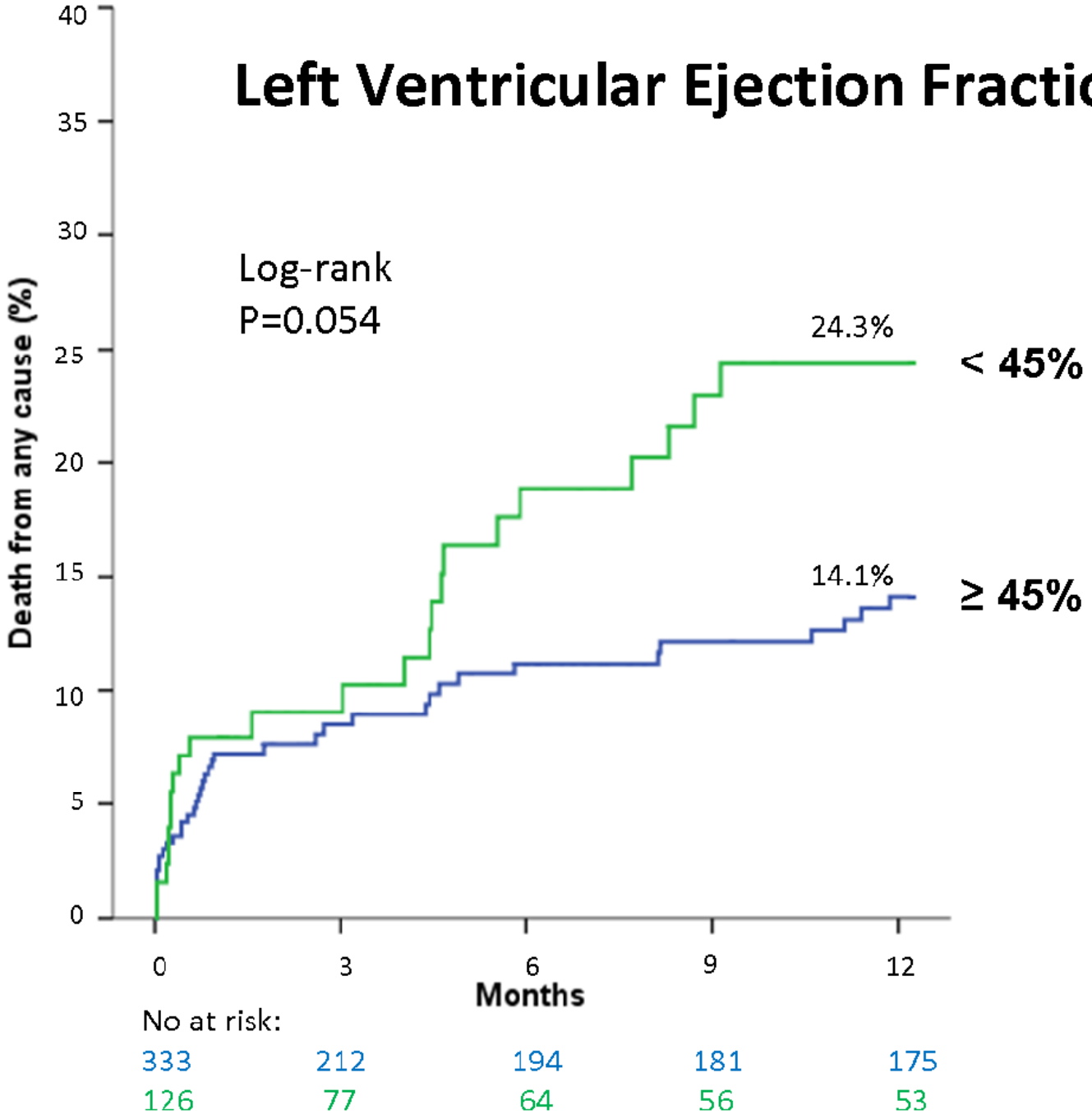
Device Used During Valve-in-Valve




Procedural Access
Death from any cause (%)
40
35
30
25
20
15
10
5
0
Log-rank
P=0.023
22.2%
Transapical
13.8%
Transfemoral
0
3
6
9
12
Months
No at risk:
270 163 145 133 129
171 116 103 95 89

STS score


Death from any cause (%)
35
30
25
20
15
10
5
0
Log-rank
P<0.001
> 20%
17.3%
10 - 20%
9.6%
< 10%
0
3
6
9
12
Months
No at risk:
223 140 125 114 111
160 100 89 95 80
76 49 44 42 40


Left Ventricular Ejection Fraction (%)
Log-rank
P=0.054
24.3%
< 45%
14.1%
≥ 45%
Death from any cause (%)
40
35
30
25
20
15
10
5
0
0
3
6
9
12
Months
No at risk:
333 212 194 181 175
126 77 64 56 53

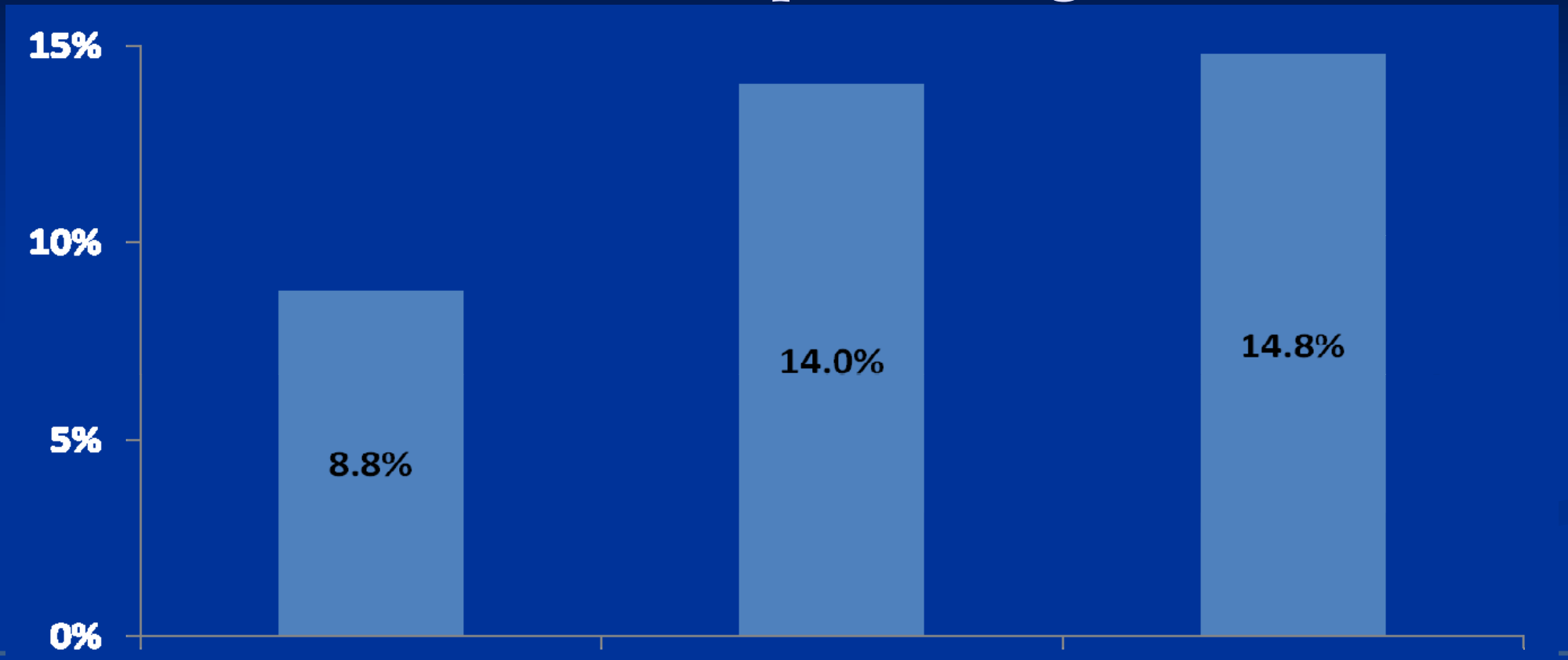
Independent Predictors for 1-Year Mortality Post Aortic VIV

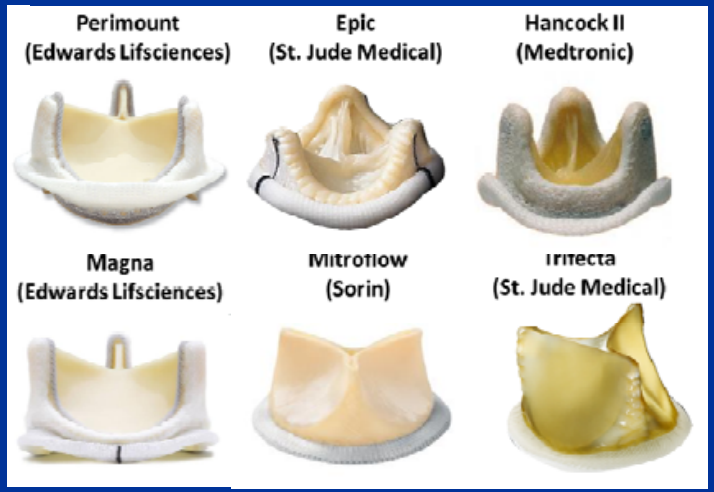
The strongest independent predictor is bioprosthesis stenosis.

	HR	95% Confidence Interval	p
Baseline stenosis vs. combined	4.8	1.8 – 12.5	0.002
Baseline stenosis vs. regurgitation	3.2	1.4 – 7.7	0.008
STS score (%)	1.03	1.01 – 1.05	0.002
Baseline left-ventricular ejection-fraction (%)	0.98	0.95 – 1.0	0.09

Included in the analysis and found non- significant:
Patient age during VIV procedure, gender, diabetes mellitus, baseline renal failure the access used and device used during VIV procedure (Edwards SAPIEN vs. CoreValve).

Safety & Efficacy Concern 1: Device Malpositioning

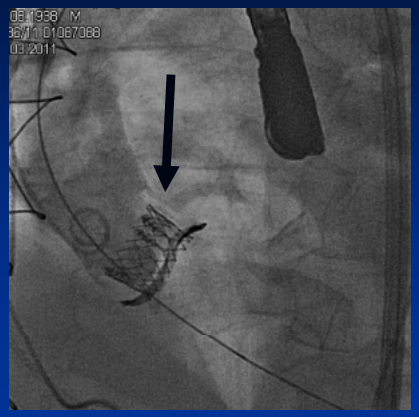




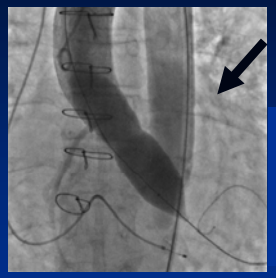
Safety & Efficacy Concern 2: Ostial Coronary Obstruction

	Stenosis	*Regurgitation*	*Combined*	*P*
Coronary Obstruction	**3.9%**	**0.7%**	**0.7%**	**0.02**

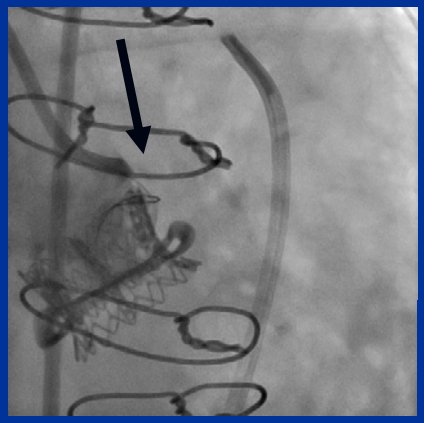
Examples of Ostial Coronary Obstruction



Center #30, case#3
Mitroflow 25mm (ID 21mm)
Tranapical Edwards-SAPIEN 23mm



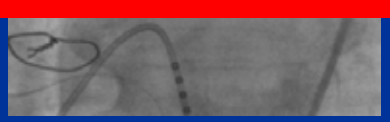
Center #29, case#7
Sorin Freedom Stentless 21mm (ID 19mm)
Balloon Valvuloplasty
before attempted CoreValve implantation



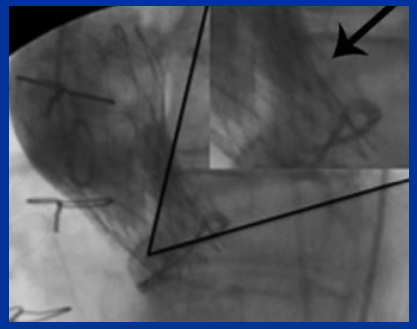
Center #37, ca
Mitroflow
Transapical

Sorin Mitroflow
Sorin Freedom Stentless
CryoLife O'Brien Stentless
Mosaic

#4
m Stentless 23mm (ID 21mm)
CoreValve 26mm



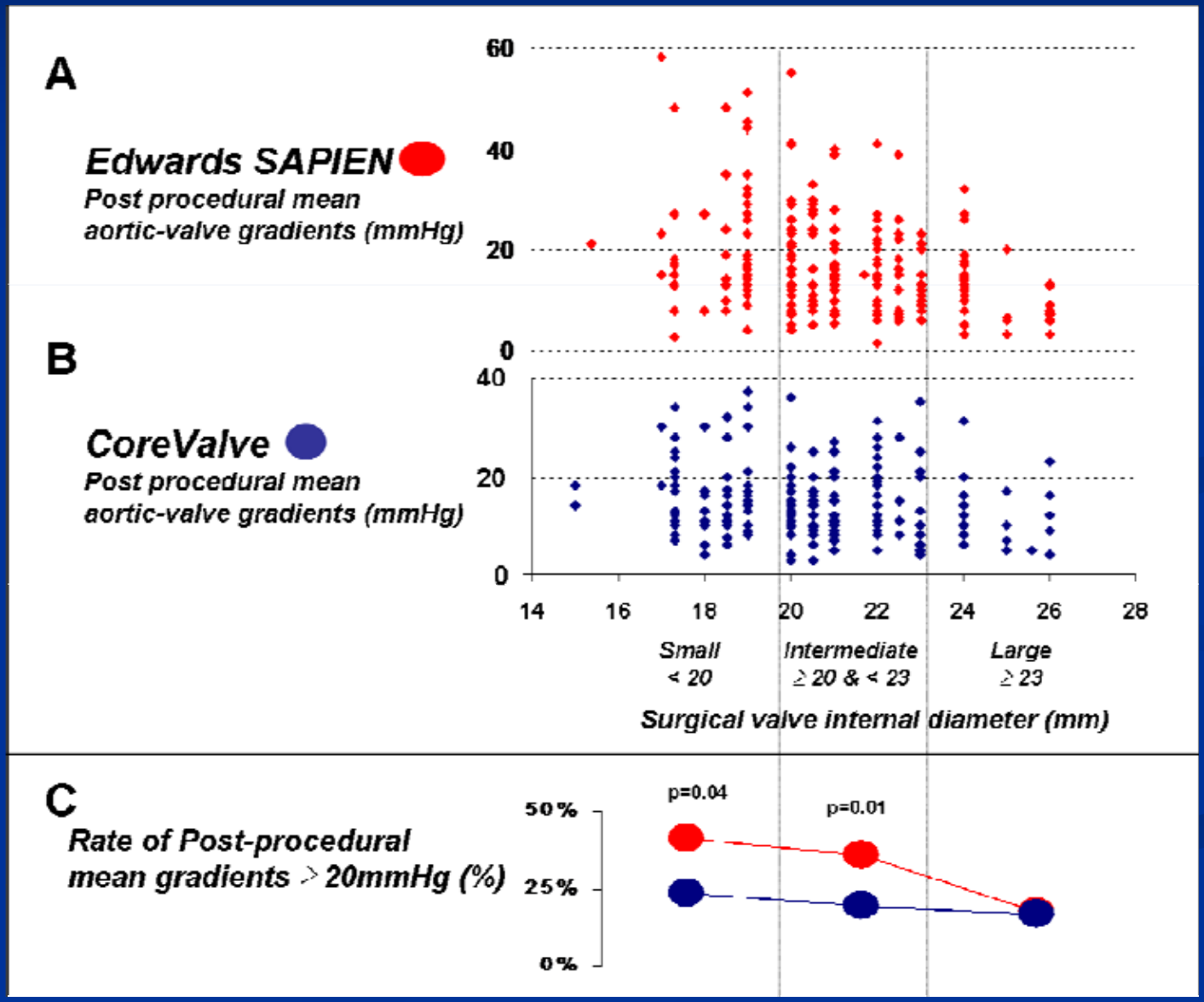
CryoLife O'Brien (stentless) 25mm (ID 23mm)
Transfemoral CoreValve 29mm



Center #34, case#6
Mitroflow 21mm (ID 17.3mm)
Tranfemoral CoreValve 26mm

Center #11, case#11
Mosaic 21mm (ID 18.5mm)
Transapical Edwards-SAPIEN 23mm

Safety & Efficacy Concern 3: Elevated Post Procedural Gradients

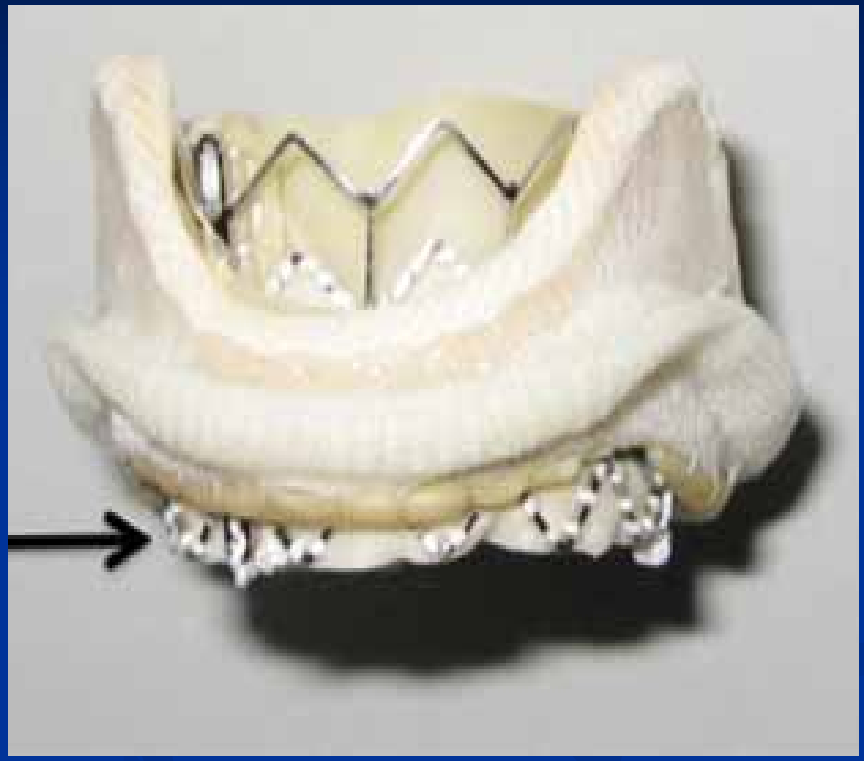


Safety & Efficacy Concern 3: Elevated Post Procedural Gradients

Independent Predictors for Elevated Gradients

	HR	95% Confidence Interval	p
Baseline stenosis vs. regurgitation	6.25	2.94 – 12.50	<0.001
Edwards SAPIEN (vs. CoreValve)	2.05	1.23 – 3.40	0.006

Included in the analysis and found non- significant:
type of bioprosthesis (stented vs. stentless), bioprosthesis internal-diameter, postimplantation valvuloplasty.



The leaflets are positioned *above* the surgically implanted valve; reducing dependence on the inner dimension of the surgical bioprosthesis.

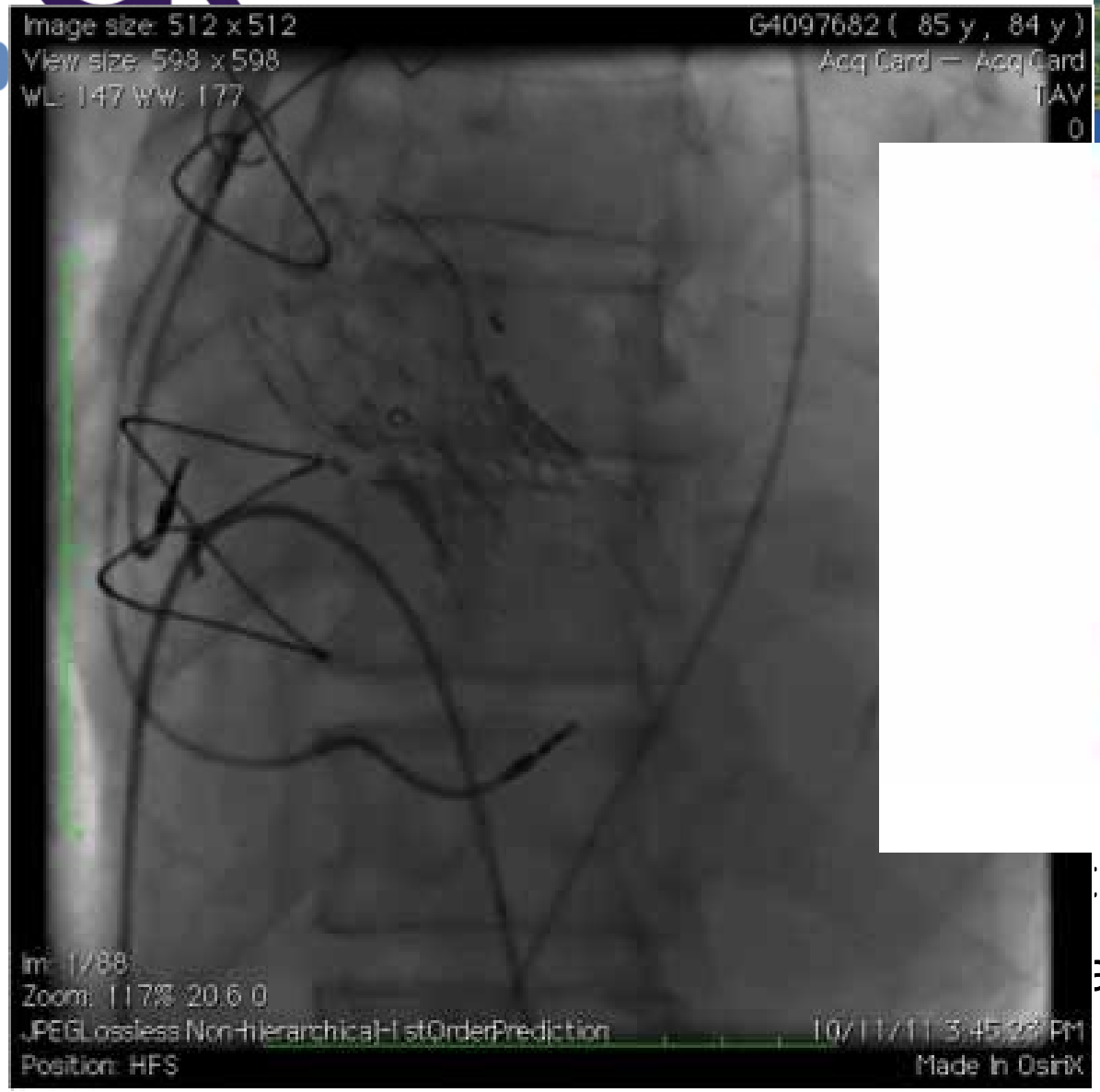
The leaflets are positioned *within* the surgically implanted valve; thus are highly dependent on the inner dimension of the surgical bioprosthesis.

Conclusion

- Valve-in-valve as a treatment for patients with a failed aortic bioprosthesis is feasible, safe and effective.
- Post-procedural gradients in Valve-in-Valve procedures are usually higher than in native aortic valve repair.
  - Especially with SAPIEN valve used in small bioprosthesis
- Malpositioning and coronary occlusion are specific concerns

Conclusion

- Pre-case planning is critical to procedural success.
- Understand
  - Correct Sizing
  - Correct positioning – and use of fluroscopic markers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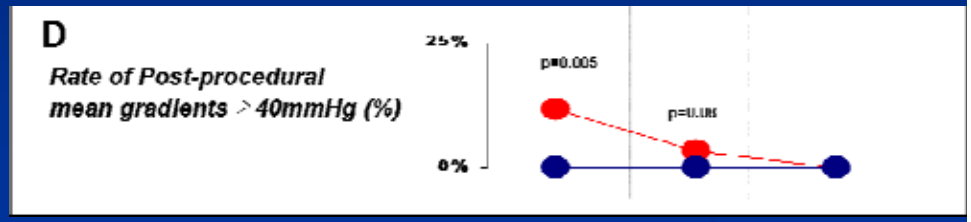
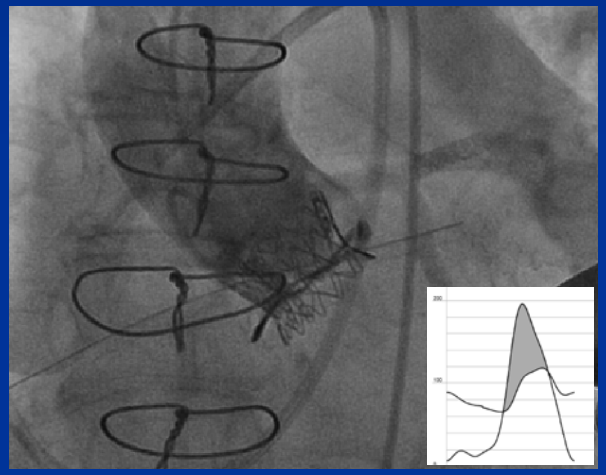
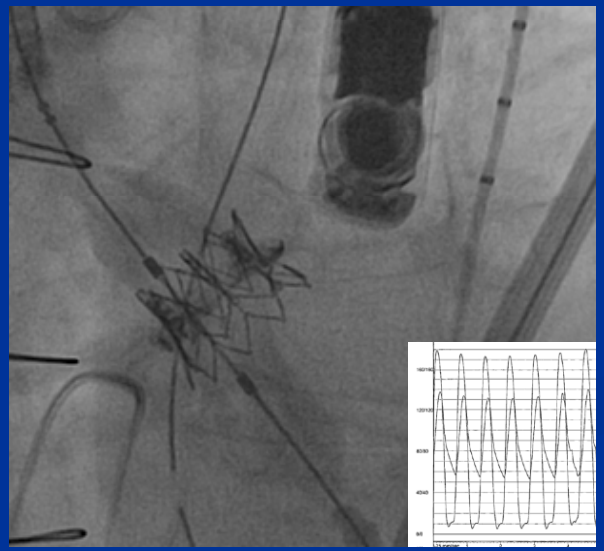
Safety & Efficacy Concern 3:
Elevated Post Procedural Gradients

Post VIV Procedure Severe Aortic-Stenosis

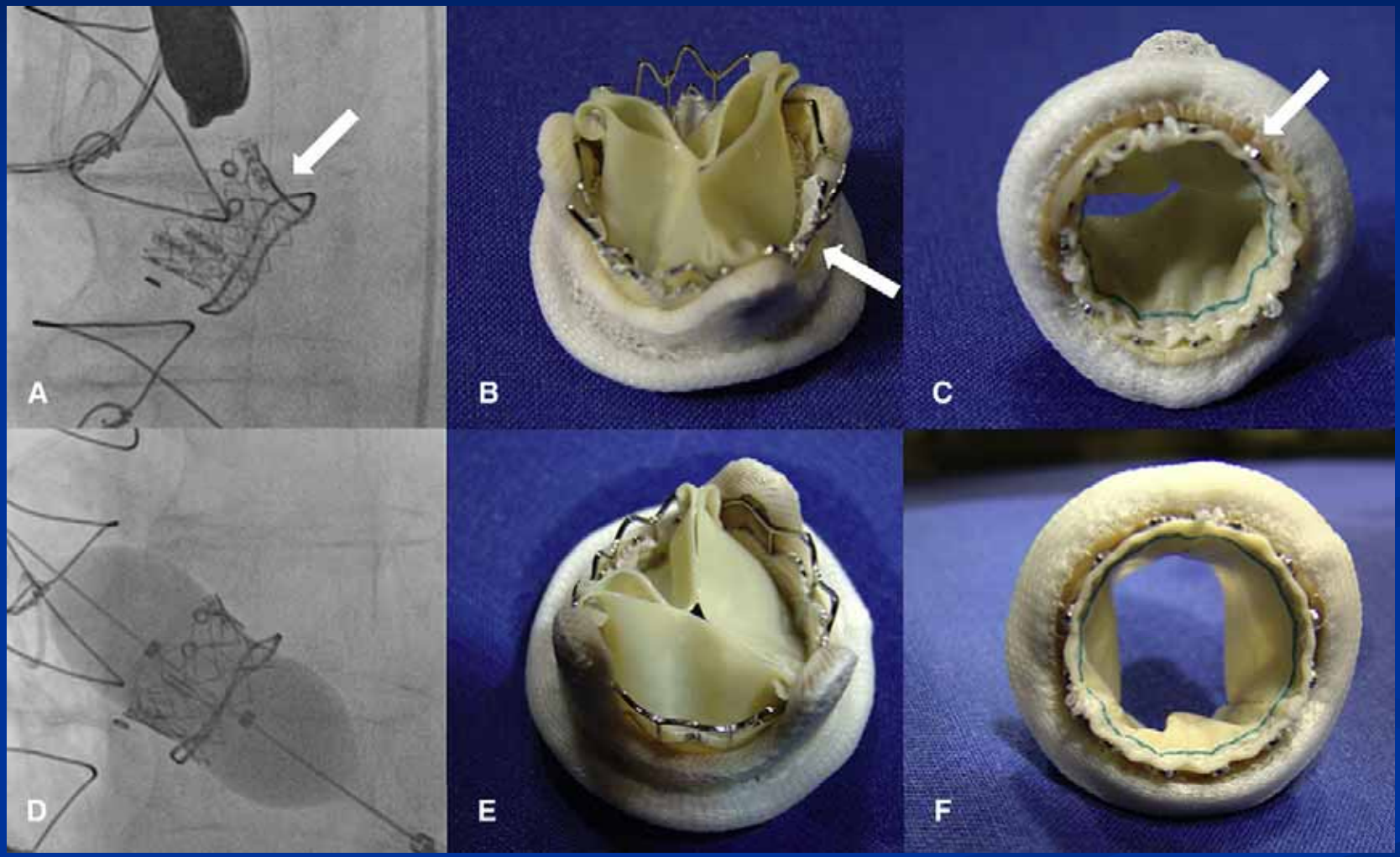




Mitroflow 21mm (ID 17.3mm)
Transapical Edwards-SAPIEN 23mm
Post TAVR mean gradients: 88/58mmHg



Mitroflow 21mm (ID 17.3mm)
Tranfemoral Edwards-SAPIEN XT 23mm
Post TAVR gradients: 93/48mmHg


A
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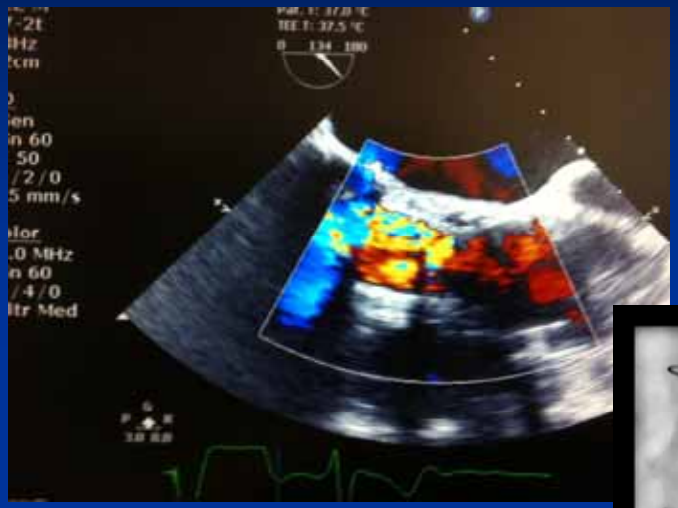
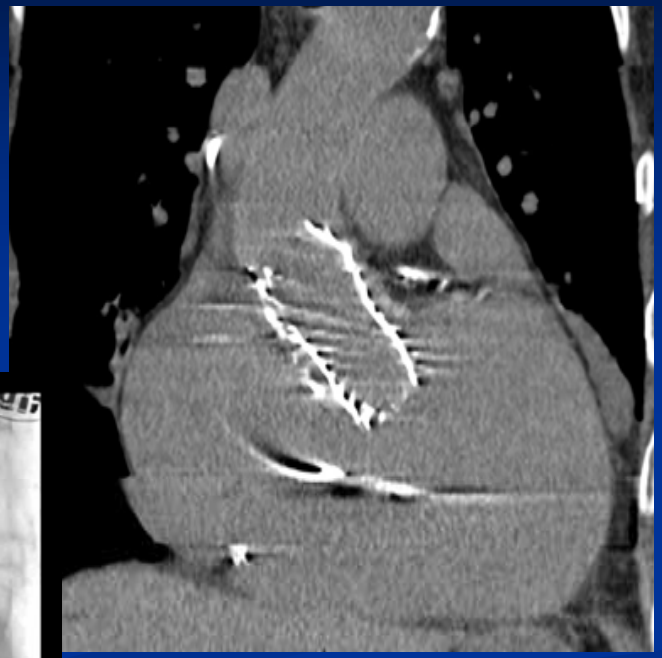
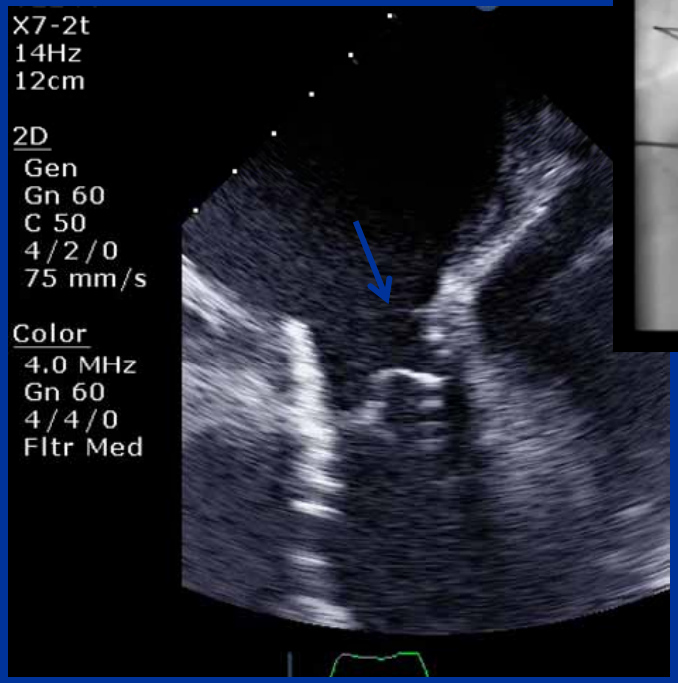
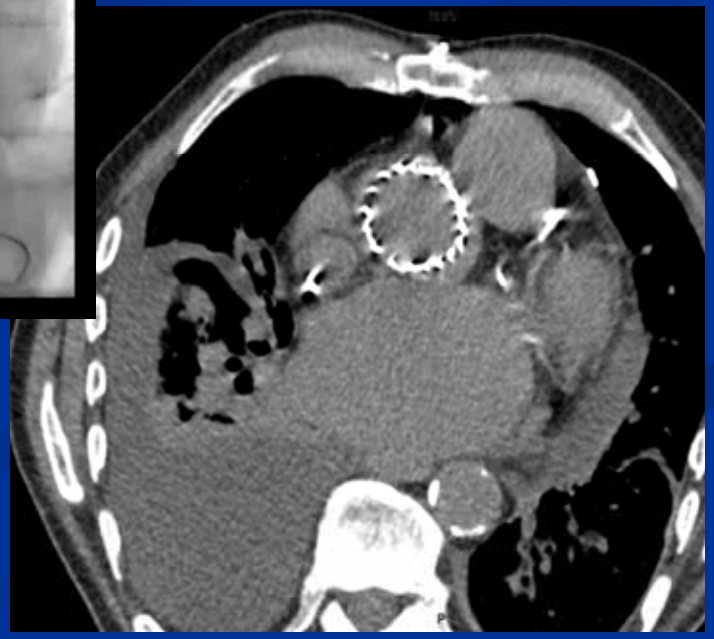
Safety & Efficacy Concern 4: Durability?

Severe AR 3 yrs following TAVI within failed stentless valve and one year after suspected endocarditis









Future Directions / Unanswered Questions

- Treatment of “operable” high-risk patients with failed bioprosthetic valves.
- Durability of VIV-procedure devices.
- Treatment of failed small surgical valves.
- Sizing during VIV procedures.
- Appropriate changes in surgical valve replacement practice.

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Bioprosthetic Market Background

- Approximately 200,000 surgical aortic valve replacements are performed annually[1].
- Over the last 10 years, the majority of surgically implanted aortic valves have been bioprosthetic.
- With a life expectancy of 10-20 years, and implantation of bioprosthetic valves in younger patients, it is expected that there will be a significant increase in the number of patients requiring redo surgery for failed bioprostheses.

Role of TAVI

- Reoperation (redo) is the standard of care for failed bioprosthetic valves.
- However, for patients who are elderly and have associated comorbidities, redo surgery may not be a viable option.
  - Operative mortality for an elective redo aortic valve surgery ranges from 2% to 7%; however, it can increase to 30% in high-risk and non-elective patients[1]
  - Risk is especially high for patients who have undergone a previous sternotomy and are typically frail.
- TAVI provides a minimally invasive alternative to conventional redo surgery.
- Results up to 1 year show positive outcomes for the use of TAVI in failed surgical bioprostheses[2].

Type of Bioprosthetic Valve Failure

Indicator	Mild	Moderate	Severe
Aortic Stenosis (AS)			
Jet Velocity (m/second)	Less than 3.0	3.0-4.0	> 4.0
Mean gradient (mm Hg)*	Less than 25	25-40	> 4.0
Valve area (cm^2)	Greater than 1.5	1.0-1.5	< 1.0
Valve area index (cm^2 per m^2)			< 0.6
Aortic Regurgitation (AR)			
Angiographic Grade	1+	2+	3-4+
Color Doppler jet width	Central jet, width less <25% of LVOT	>Mild but no signs of severe AR	Central jet, width > 65% LVOT
Doppler vena contracta width (cm)	Less than 0.3	0.3-0.6	> 0.6
Regurgitant volume (ml/beat)	Less than 30	30-59	≥ 60
Regurgitant fraction (%)	Less than 30	30-49	≥ 50
Regurtitant orifice area (cm^2)	Less than 0.10	0.10-0.29	≥ 30
Left ventricular size	--	--	Increased

Causes of Valve Failure

Type	Cause
Calcification	Residual glutaraldehyde-derived polymers may serve as potential binding sites by: 1. Residual glutaraldehyde substraction; 2. Phospholipid extraction; and/or 3. Residual glutaraldehyde substraction;
Pannus	Host tissue response and develops at the host-prosthesis interface. Early pannus is composed of myofibroblasts, fibroblasts, and capillary endothelial cells. Overtime pannus may calcify. Some pannus formation over the suture is normally expected and functions to form a nonthrombogenic surface.
Wear & Tear	Calcific deposits have a propensity to develop in areas where leaflet flexion and stress are greatest; that is, at the basal and commissural attachment points. Approximately three-fourths of patients with leaflet calcification and tears suffer from aortic regurgitation.
Thrombosis / Endocarditis	Thrombosis and endocarditis occur less frequently than the a forementioned modes of bioprosthetic failure, occurring at a rate of 0.2% per year and 1.2% per year, respectively. Patients presenting with active endocarditis are contraindicated for implantation of a CoreValve bioprosthesis.

VIV Procedure: Pre-case Planning

Careful pre-case planning is essential to Valve-in-Valve procedural success

Patient Selection

Avoid patients presenting with a degenerative surgical valve that:

- Has significant concomitant PVL
- Is not securely fixed in the native annulus
- Is not structurally intact
- Has a partially detached leaflet (could potentially obstruct coronary ostium)

Valve Identification

Verify model of failed valve through fluoroscopic imaging

- CT is highly recommended to validate ID of failed bioprosthesis
- Determine valve height

Valve Sizing

Utilize CoreValve size chart to determine appropriate size CoreValve to implant

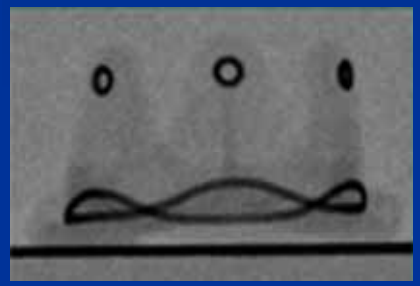
ronic CoreValve System Procedural Practices for Stented UC201304471 nd for Stentless UC201304805 EE

VIV Procedure: Procedural Tips

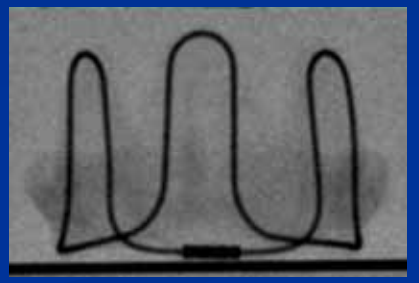
- Balloon predilatation of a stenotic surgical aortic bioprosthesis has not been evaluated. In cases where there is severe stenosis, predilatation of the surgical aortic bioprosthesis may be performed, and the steps used are identical to the native valve predilatation
- Determine valve positioning relative to the ring
  - In stentless – use anatomic or reference markers and/or root injections
- Avoid too low/ too high implantation*
- The need for rapid pacing is the same as in a native procedure
- Assess the risk of coronary occlusion by the surgical valve leaflet

Sample Surgical Valves

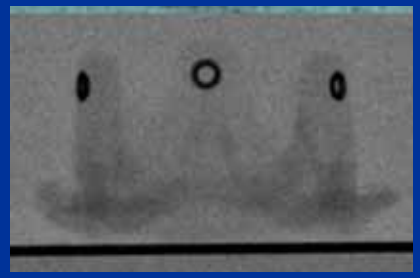
Medtronic Hancock II



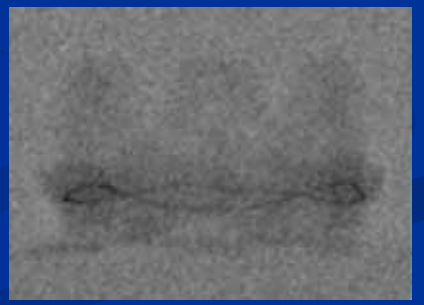
CE Porcine



Medtronic Mosaic

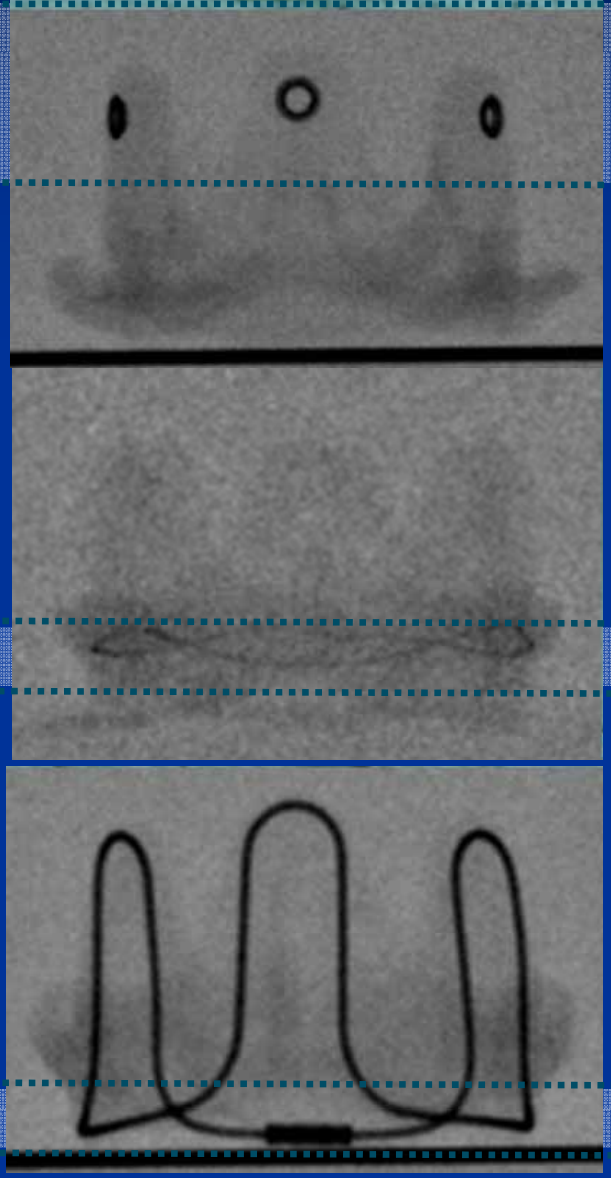


St. Jude Biocor Supra



Valve Positioning

Location of Angiographic Markers in Surgical Valves Varies



Markers located in crown

Markers located in sewing ring

Markers located below sewing ring

VIV Procedure: Hemodynamics

- Gradients measured following VIV procedures are typically higher than gradients observed in native annulus procedures. Higher post-procedural gradients can be attributed to two factors:
  - Patient-prosthesis mismatch
    - VIV procedures will not resolve gradients caused by mismatch of the originally implanted surgical valve; however, it will reduce gradients resulting from subsequent failure of that valve.
  - Decreased orifice area
    - VIV procedures inherently decrease the aortic valve area (AVA) within the annulus
    - Intra-annular designs further decreasing the aortic valve area.
    - CoreValve maximizes AVA with its supra-annular design; therefore, only the Nitinol frame and skirt rest within the failed surgical valve.

Valve-in-Valve Studies

- Multiple studies have produced results showing Valve-in-Valve implantation to be a viable treatment option for extreme and high risk patients.
- The Global Valve-in-Valve Registry has reported on Valve-in-Valve procedures in more than 460 patients using both the CoreValve bioprosthesis and SAPIEN device in a variety of different degenerative bioprosthetic valves.
- Two additional studies conducted by Bedogni et al., and Linke et al., evaluated CoreValve in Valve-in-Valve procedures with 25 and 27 patients respectively.

Global Valve-in-Valve Registry

Overview: Retrospective collection of data; 38 centers from Europe, North America, Australia, New Zealand and the Middle East.

- The CoreValve 26mm & 29mm and Sapien 23mm & 26mm devices were used in this study.

Purpose: To evaluate the efficacy and safety of ViV procedures

Objectives:

-
-
-
-
-


Circulation

American Heart Association.

Transcatheter Aortic Valve Replacement for Degenerative Bioprosthetic Surgical Valves: Results from the Global Valve-in-Valve Registry

Danny Dvir, John Webb, Stephen Brecker, Sabaue Bleiziffer, David Hildick-Smith, Antonio Colombo, Hein Descoutures, Christian Hengstenberg, Neil E. Moat, Ralli Bekeredjian, Massimo Napodano, Luca Testa, Thierry Lefèvre, Victor Guetta, Henrik Nissen, José-María Hernández, David Roy, Rui C. Teles, Amit Segev, Nicolas Dumonteil, Claudia Fiorina, Michael Gotzmann, Didier Tchetche, Mohamed Abdel Wahab, Federico De Marco, Andreas Baumbach, Jean Claude Laborde and Ran Kornowski

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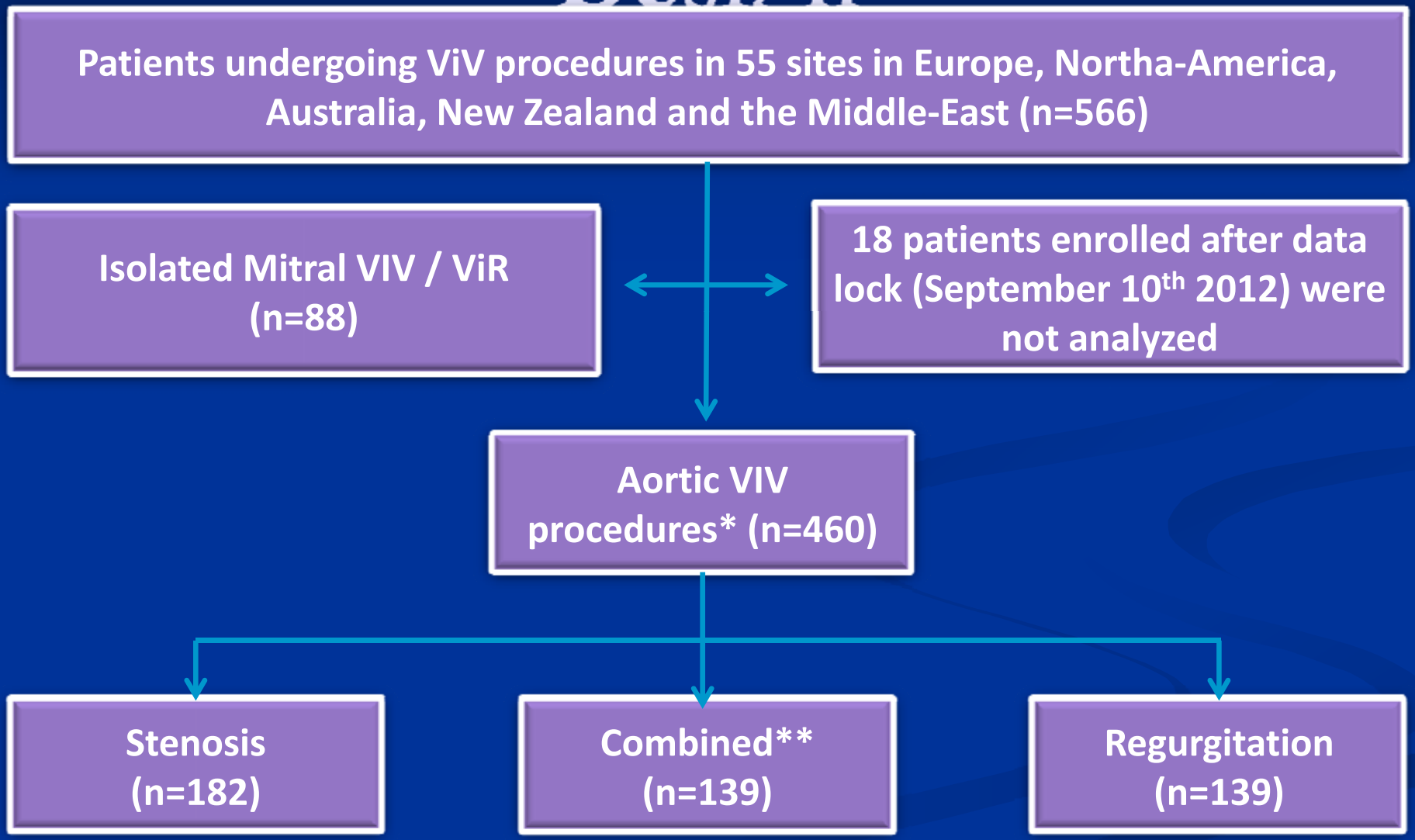
Global Valve in Valve Registry Design



Baseline Demographics

	Stenosis n= 182	Regurgitation n= 139	Combined n= 139	p Value
Age (yrs)	78.8± 7.8	77.1± 10.6	76.6± 11.1	0.10
Gender (% male)	47.5	66.9	55.4	0.002
LogEuroSCORE	32.3 ± 17.1	30.3 ± 18.8	34.1 ± 18.6	0.24
STS score (%)	12.3 ± 10.3	11.2 ± 8.4	13.4 ± 13.1	0.24
Diabetes Mellitus (%)	40.1	21.2	21.4	<0.001
Peripheral Vascular Disease (%)	30.6	23.5	22.9	0.22
Chronic Renal Failure (%)	44.5	50.8	51.9	0.37
Previous stroke (%)	13.3	12.8	9.2	0.52

Procedural Outcomes

High Procedural Success

Procedural Results	Total (n=202)	CoreValve (n=124)	SAPIEN (n=78)	p Value
Procedural Success	188 (93.1%)	120 (96.8%)	68 (87.2%)	0.009
2nd TAVR Valve	17 (8.4%)	10 (8.1%)	7 (9%)	0.82
Coronary obstruction	7 (3.5%)	4 (3.2%)	3 (3.8%)	1.0
Emergent surgery	4 (2%)	1 (0.8%)	3 (3.8%)	0.3
Post-implantation BAV	25 (12.4%)	21 (16.9%)	4 (5.1%)	0.01

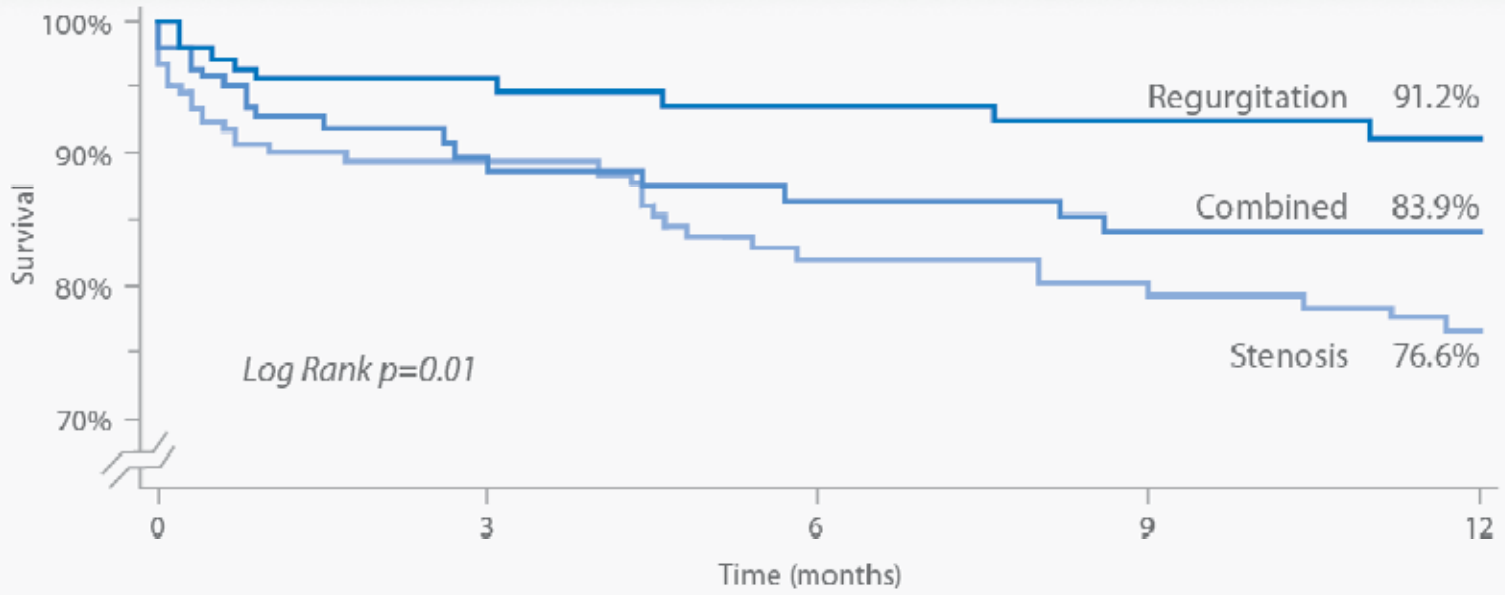
Procedural Outcomes

30-Day Outcomes	Total (n=202)	CoreValve (n=124)	SAPIEN (n=78)	p Value
Death	17 (8.4%)	9 (7.3%)	8 (10.3%)	0.45
Major Stroke	4 (2%)	2 (1.6%)	2 (2.6%)	0.64
Death or Major Stroke	20 (10.4%)	11 (8.9%)	9 (11.5%)	0.48
Major Vascular Complication	7 (3.5%)	2 (1.6%)	5 (6.4%)	0.11
Permanent pacemaker	15 (7.4%)	11 (8.9%)	9 (11.5%)	0.48
Mean gradients (mmHg)	15.9 ± 8.6	13.9 ± 7.5	19.2 ± 9.2	<0.0001

Global Valve-in-Valve Registry Survival

Survival According to Bioprosthesis Mechanism of Failure

Patients whose surgical valve failed from stenosis were at a significantly higher risk of 1 year mortality.

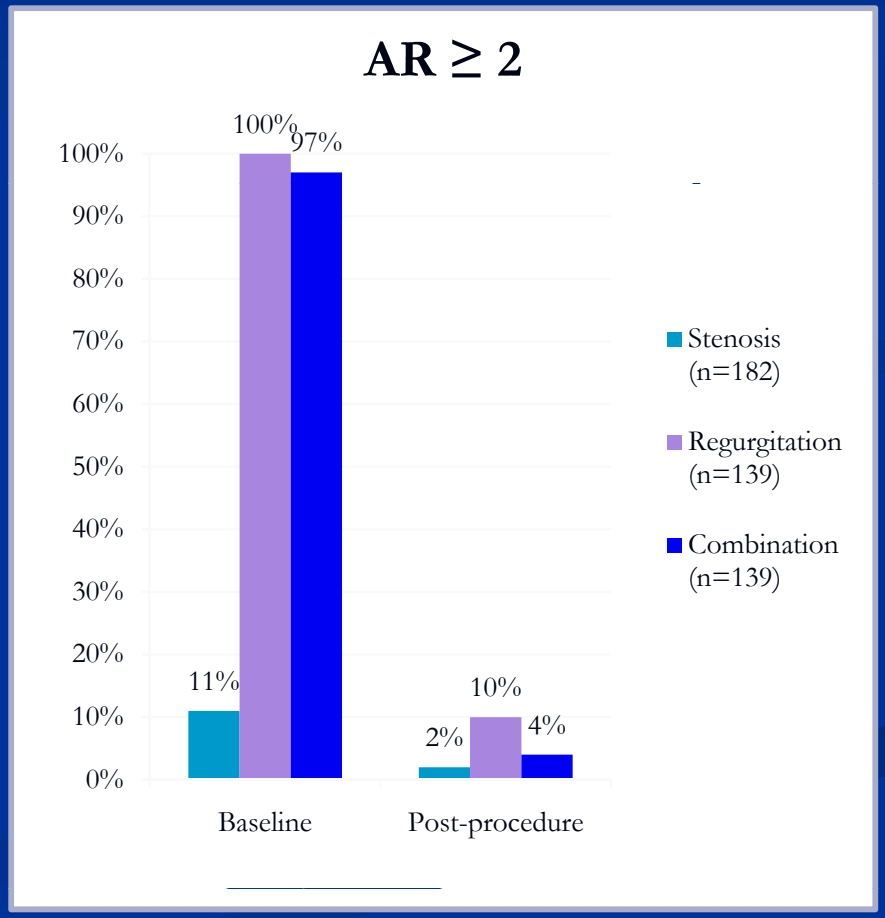


# Patients at Risk					
Regurgitation	139	92	84	78	75
Combined	139	85	76	68	66
Stenosis	182	112	98	91	86

Global Valve-in-Valve Registry Results

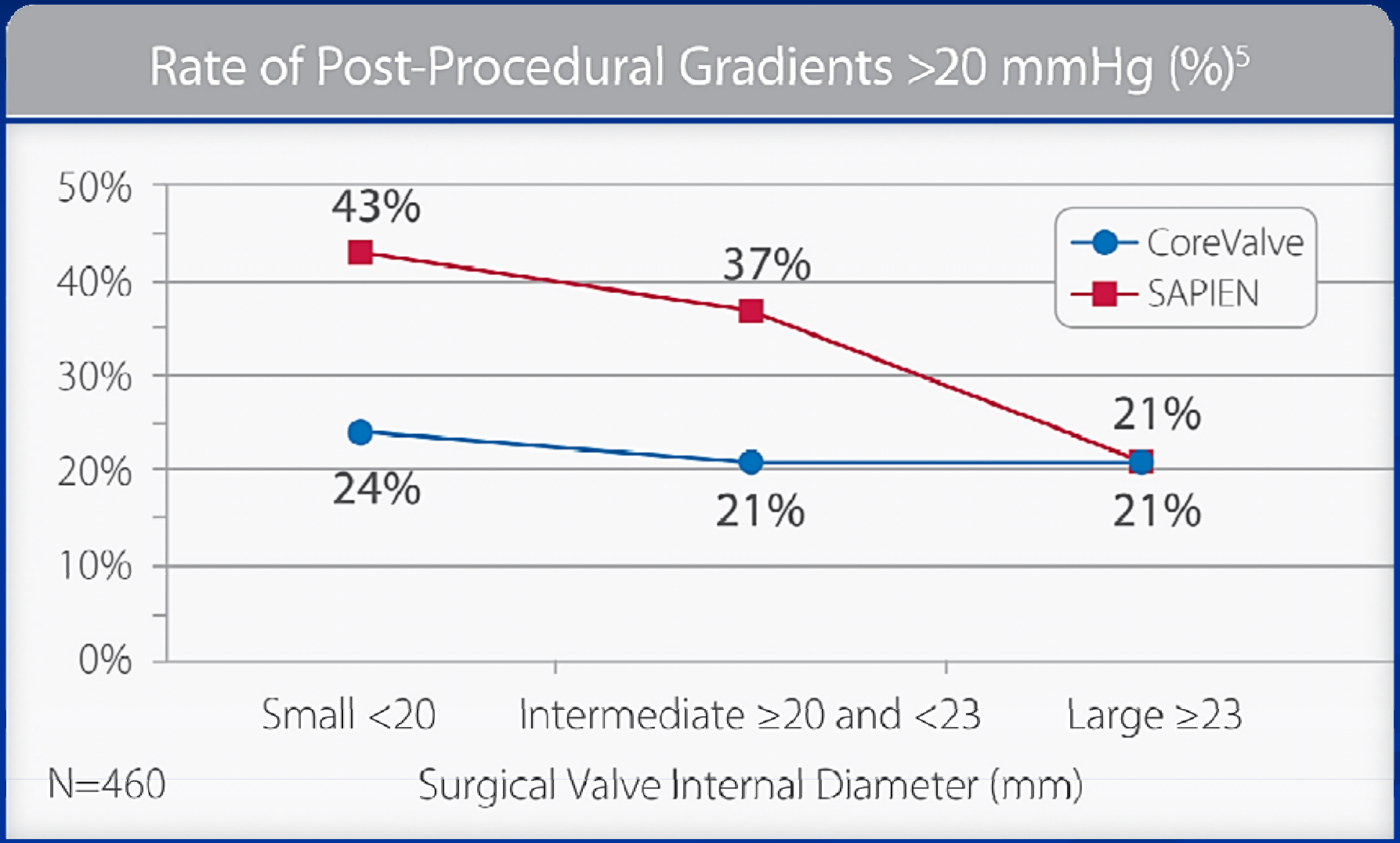
Improvements in AV area, mean gradients, and regurgitation in Valve in Valve procedures

	AV Area (cm^2)		AV Mean Gradients (mmHg)	
	Baseline	Post-Procedure	Baseline	Post-Procedure
Stenosis (n=182)	0.70 ± 0.20	1.37 ± 0.33	46.4 ± 16.1	18.4 ± 9.8
Regurgitation (n=139)	1.48 ± 0.60	1.56 ± 0.49	18.0 ± 10.1	12.0 ± 6.7
Combination (n=139)	0.91± 0.30	1.56 ± 0.65	37.6 ± 14.9	16.0 ± 8.3
p value	<0.001	0.01	<0.001	<0.001

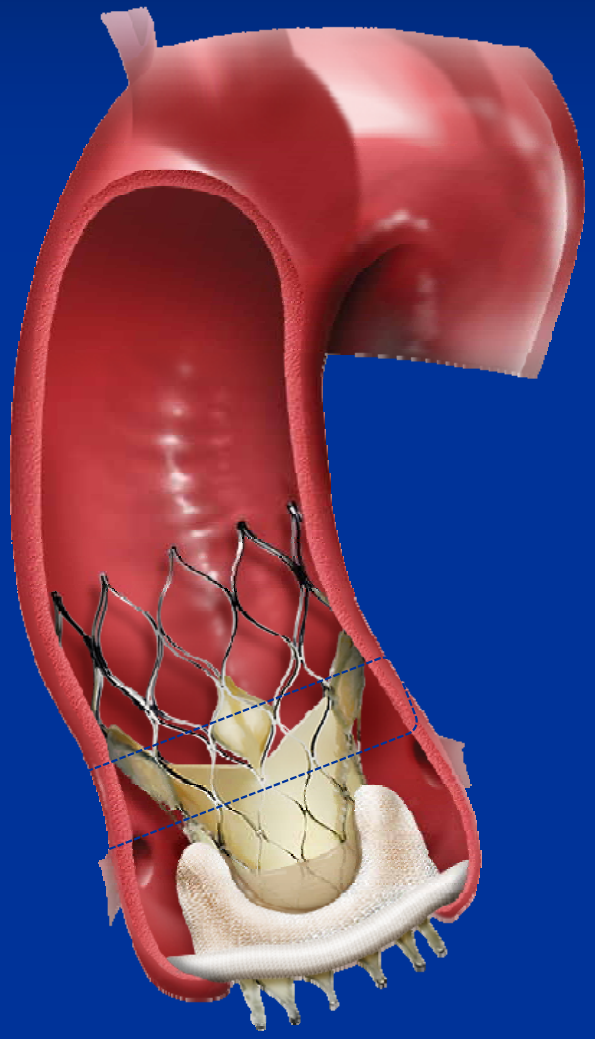


Global Valve-in-Valve Registry

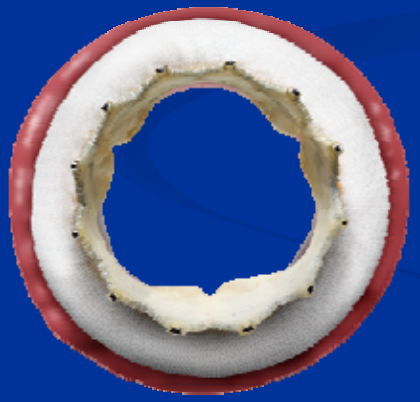
Hemodynamic Results



Hemodynamics in Valve-in-Valve Implantation



Large potential orifice area



25% larger Potential Orifice Area than SAPIEN XT

Global Valve-in-Valve Registry

Predictors of High Post-Procedural Gradient

	Multivariate Analysis		
	Odds Ratio	95% Confidence Interval	p value
Baseline Aortic-Valve Area*	0.87	0.79 - 0.94	0.001
Edwards SAPIEN	2.28	1.17 - 4.43	0.02
NYHA Functional Class IV	1.00	0.97 - 1.02	0.83
LVEF (%)	1.02	0.97 - 1.06	0.13
Baseline Aortic Regurgitation ≥ ± 2	1.04	0.49 - 2.17	0.93
Stented bioprosthesis	1.42	0.61 - 3.31	0.42
Small Bioprosthesis (ID <20mm)	1.40	0.63 - 3.10	0.35
Pre-Implantation Valvuloplasty	1.67	0.93 - 2.91	0.08
Using Small TAVR Device†	2.85	0.41 - 17.32	0.84
Post-Implantation Valvuloplasty	1.57	0.62 - 3.81	0.38

*Per 0.1cm2 increment
†CoreValve 26-mm (vs. 29-mm) and Edwards SAPIEN 23-mm (vs. 26-mm)
NYHA, New-York Heart Association; ID, internal-diameter; TAVR, transcatheter aortic-valve replacement

Additional Valve-in-Valve Studies

Low gradient, high procedural success and high survival rates were also observed in two additional studies analyzing CoreValve in valve-in-valve procedures.

	Linke et al (n=27)	Bedogni et al (n=25)
Procedural Success	100%	100%
Mean Gradient at 30 Days	13 ± 9	13.8 ± 8.5
Survival at 30 Days	92.6%	88%
Survival at 1 Year	88%	N/A*
New Pacemaker Implantation	3.7%	12%

Supra-Annular Valve Function in VIV

Medtronic Hancock II	Medtronic Mosaic