Durability of Balloon-Expandable Heart Valves

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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
► Consulting Fees/Honoraria	► Edwards Lifesciences

Durability of bioprosthesis

- Transcather valves durability is one of the major remaining issues in the context of extension of TAVI to younger patients.

- It is well known that surgical bioprosthesis have a limited durability

- Bioprosthetic durability can be altered by structural valve deterioration (SVD) but also by thrombosis and endocarditis

- When deterioration is severe, it can lead to hemodynamic and clinical deterioration and require re-intervention (common surgical definition of SVD)

- Data on durability of transcatheter valves are still scarce

Durability of TAVI vs SAVR at 5 years
From the randomized PARTNER 1 Trial
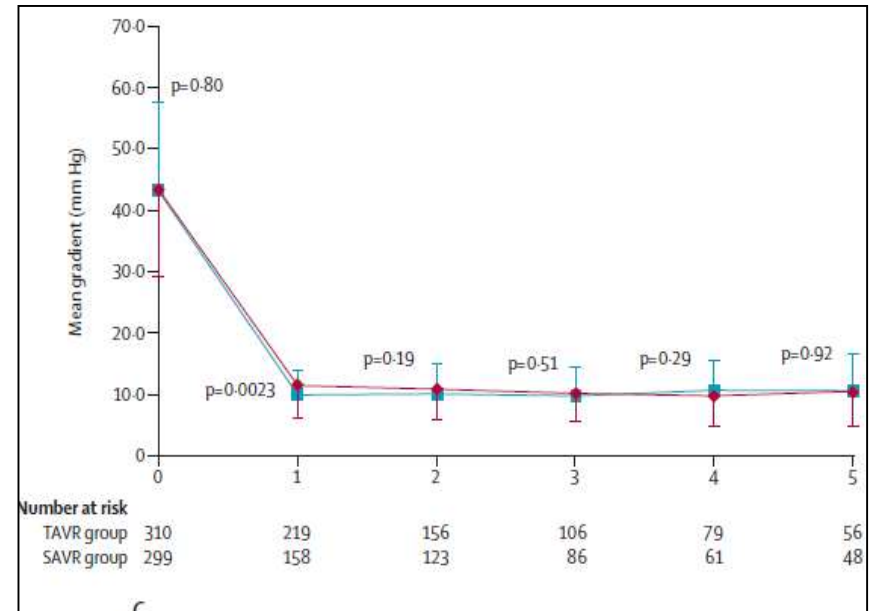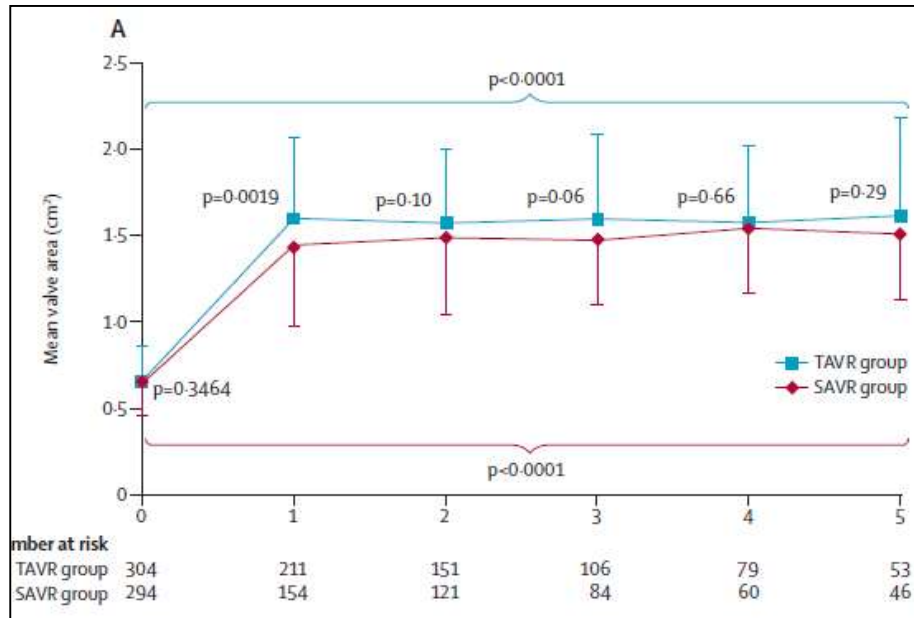
- **Unchanged AVA & gradient comparable to SAVR**
- **No valve deterioration**

M Mack et al. PARTNER 1
Lancet 2015:385(9986):2477-84

A clash of thunder at EuroPCR 2016

PUBLIC RELEASE: 17-MAY-2016

EuroPCR 2016: Half of transcatheter heart valves show degeneration within 10 years of TAVI

First study of long-term durability shows high rates of valve degeneration

Danny DVIR

2017 : 1st Consensus on Bioprosthetic Valve Deterioration

Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Davide Capodanno[1,*,†], Anna S. Petronio[2,†], Bernard Prendergast[3], Helene Eltchaninoff[4], Alec Vahanian[5], Thomas Modine[6], Patrizio Lancellotti[7], Lars Sondergaard[8], Peter F. Ludman[9], Corrado Tamburino[1], Nicolò Piazza[10], Jane Hancock[3], Julinda Mehilli[11], Robert A. Byrne[12], Andreas Baumbach[13], Arie Pieter Kappetein[14], Stephan Windecker[15], Jeroen Bax[16], and Michael Haude[17]

Standardized Definition of Structural Valve Degeneration for Surgical and Transcatheter Bioprosthetic Aortic Valves

Danny Dvir, Thierry Bourguignon et al

Durability of bioprosthetic valves
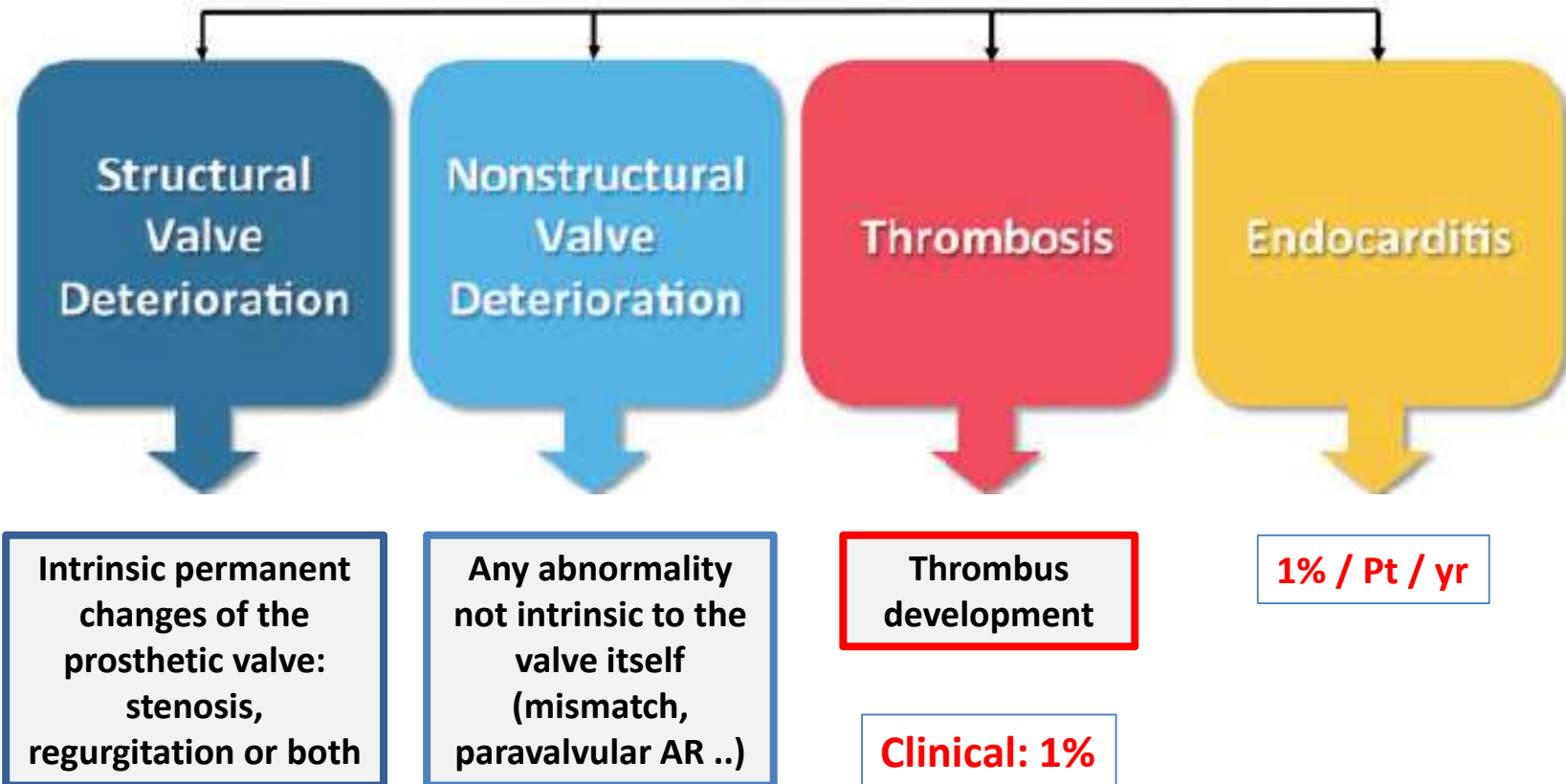# Need for standardized definitions

HOT TOPIC

Bioprosthetic Valve Dysfunction

Structural Valve Deterioration	Nonstructural Valve Deterioration	Thrombosis	Endocarditis
Intrinsic permanent changes of the prosthetic valve: stenosis, regurgitation or both	Any abnormality not intrinsic to the valve itself (mismatch, paravalvular AR ..)	Thrombus development	1% / Pt / yr
		Clinical: 1%	

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SVD: New Standardized Definitions

Moderate haemodynamic SVD (any of the follo...
Mean transprosthetic gradient ≥20...
Mean transprosthetic gradient ≥10 a...
baseline
Moderate intra-prosthetic aortic regurgitatio...
(>1+/4+) from baseline
Severe haemodynamic SVD (any of the followi...
Mean transprosthetic gradient ≥40 mmHg
Mean transprosthetic gradient ≥20...
Severe intra-prosthetic aortic regu...
(>2+/4+) from baseline
Morphological SVD (any of the following)
Leaflet integrity abnormality (i.e. torn or flail...
regurgitation)
Leaflet structure abnormality (i.e. pa...
calcification causing valvular steno...
Leaflet function abnormality (i.e. impaired m...
stenosis and/or central regurgitation)
Strut/frame abnormality (i.e. fracture)
Haemodynamic and morphological SVD

Moderate SVD (any of the following):

Mean gradient ≥ 20 and < 40mmHg
Mean change from baseline ≥ 10 and < 20mm Hg
Moderate central AR, new or worsening > 1

Severe SVD (any of the following):

Mean gradient ≥ 40mmHg
Mean change from baseline ≥ 20mm Hg
Severe central AR, new or worsening > 2

Morphological SVD (any of the following):

Leaflet integrity/function abnormality
Strut/frame abnormality

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Bioprosthetic Valve Failure (BVF) directly patient related

Autopsy findings

Autopsy findings of bioprosthetic valve dysfunction, likely related to the cause of death, or valve-related death (i.e. any death caused by bioprosthetic valve dysfunction or sudden unexplained death following diagnosis of bioprosthetic valve dysfunction)

Repeat intervention

Repeat intervention (i.e. valve-in-valve TAVI, paravalvular leak closure or SAVR) following confirmed diagnosis of bioprosthetic valve dysfunction

Severe hemodynamic SVD

Mean transprosthetic gradient ≥ 40 mmHg

Mean transprosthetic gradient ≥ 20 mmHg change from baseline

Severe intra-prosthetic aortic regurgitation, new or worsening ($>2+/4+$) from baseline

Recent data on durability beyond 5 years 2018-2019 data

ESC/EACTS Standardized definitions except for NOTION

	N°	Period	Valve type
Eltchaninoff *Euro Interv 2018*	378	2002-12	**BE: 100%**
Deutch et al *Euro Interv 2018*	300	2007-09	SE:71% / BE: 29%
Holy et al *Euro Interv 2018*	152	2007-11	SE:100%
Barbanti et al *AHA 2018*	288	2007-12	SE: 83% / BE: 17%
UK Registry *J Am Coll Cardiol 2019*	241	2007-2011	SE:64% / BE 36%
NOTION 2 *J Am Coll Cardiol 2019*	1 45	2009-2013	SE:100%
French Registry *Circulation Intv 2019* **in press**	1403	2002-2011	**SE:16% / BE:84%**

Recent data on durability beyond 5 years 2018-2019 data

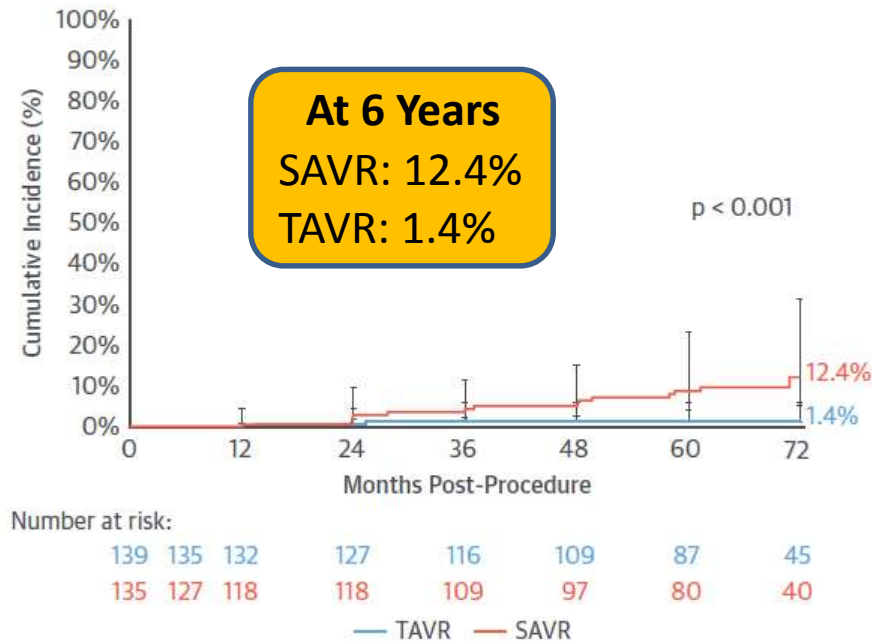## ESC/EACTS Standardized definitions except for NOTION

	7-y survival (KM)	7-y/8-y Total SVD	7/8-y Severe SVD	7-y/8-y Re-intervention
Eltchaninoff *Euro Interv 2018*	18%	**3.2%**	**1%**	**0.6%**
Deutch et al *Euro Interv 2018*	23.2%	14.9%		4 Pts (%?)
Holy et al *Euro Interv 2018*	35%		0%	3.3% (not for SVD)
Barbanti et al *AHA 2018*		8.2%	2.4%	0.7%
UK Registry* *6 yrs *JACC 2019*		8.7%	0.4%	0%
NOTION 2* *JACC 2019*	58%	4.3%	0.7%	2.2%
French Registry *Circulation Interv 2019*	18%	**11.2%**	**4.2%**	**1%**

Re-intervention: 0.7 – 1%

NOTION 2 randomized trial
SVD with a modified definition

FIGURE 2 Cumulative Incidence of SVD Defined as a Mean Gradient of ≥20 mm Hg and an Increase in Mean Gradient ≥10 mm Hg After 3 Months Post-Procedure

At 6 Years
SAVR: 12.4%
TAVR: 1.4%

$p < 0.001$

Number at risk:

139	135	132	127	116	109	87	45
135	127	118	118	109	97	80	40

— TAVR — SAVR

Mean gradient ≥ 20 mm Hg
AND
Increase ≥ 10 mm Hg from baseline

TABLE 4 Structural Valve Deterioration and Its Components Through 6 Years

	TAVR (n = 139)*	SAVR (n = 135)*	p Value
Baseline hemodynamic parameters*			
3-month mean gradient	8.33 ± 3.93	12.15 ± 4.45	<0.0001
3-month central AR			
None/trace	99.2	98.2	
Mild	0.8	1.8	
Moderate	0.0	0.0	
Severe	0.0	0.0	
SVD	4.8	24.0	<0.001
Moderate hemodynamic SVD	3.6	23.7	
Mean gradient ≥20 mm Hg	2.9	22.2	
Mean gradient ≥10 and <20 mm Hg change from 3 months	1.4	11.1	
Moderate central AR	0.0	0.0	
Severe hemodynamic SVD	0.7	3.0	
Mean gradient ≥40 mm Hg	0.0	1.5	

According to this definition, the rate of SVD at 6 years after SAVR is lower but remains greater than after TAVR

Assessment of Structural Valve Deterioration of Transcatheter Aortic Bioprosthesic Balloon-Expandable Valves Using the New Consensus Definition. The Rouen Study

Hélène Eltchaninoff[1,2*], MD; Eric Durand[1,2], MD, PhD; Guillaume Avinée[1,2], MD; Christophe Tron[1], MD; Pierre-Yves Litzler[2,3], MD; Fabrice Bauer[1,2], MD; Jean-Nicolas Dacher[2,4], MD; Camille Werhlin[1], MD; Najime Bouhzam[1], MD; Nicolas Bettinger[1], MD; Pascal Candolfi[5], PhD; Alain Cribier[1], MD
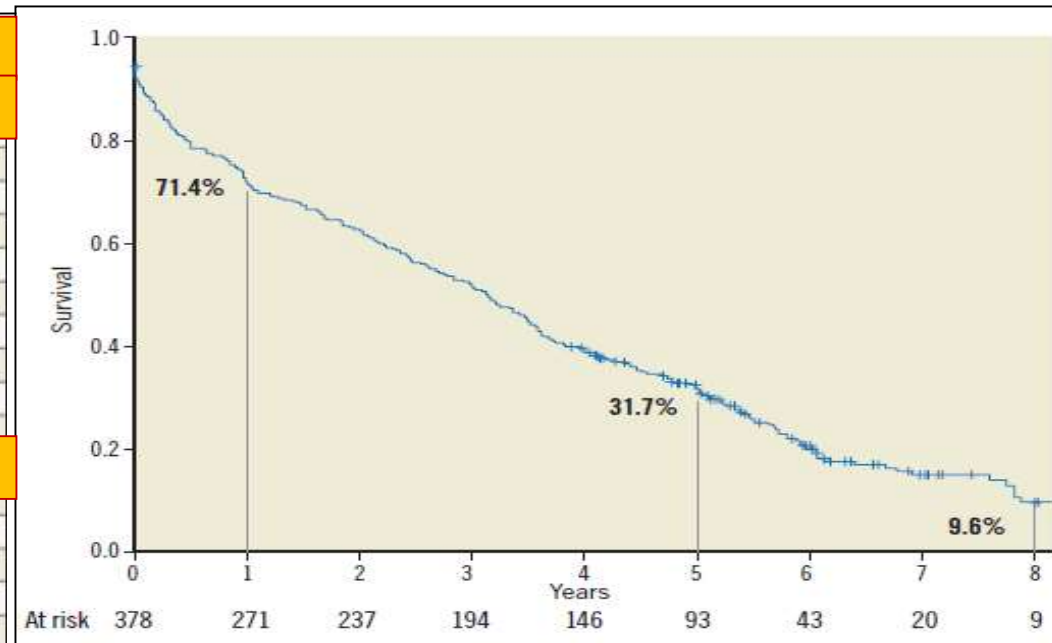
100%

378 Pts: From 2002 to 2012
## Compassionate / Inoperable / High-risk

Baseline characteristics

Age, years	**83.3±6.8**
NYHA Class III-IV	**75.1%**
Hypertension, n (%)	253 (65.5%)
PVD, n (%)	82 (21.2%)
Renal failure, n (%)	289 (74.9%)
MI, n (%)	91 (23.6%)
AF, n (%)	148 (38.3%)
Stroke, n (%)	23 (6.0%)
Pacemaker, n (%)	48 (12.4%)
PCI, n (%)	105 (27.2%)
CABG, n (%)	71 (18.4%)
Logistic Euroscore	**22.8±13.1%**
STS, %	10.6±8.5
EOA, cm²	0.68±0.19
Mean gradient, mmHg	49.8±16.6
Moderate/severe AR, n (%)	12 (3.1%)
LVEF, %	55.0±16.3

SURVIVAL (KM)

Kaplan-Meier survival curve: Survival vs Years. 71.4% at 1 year, 31.7% at ~4.5 years, 9.6% at 8 years.

At risk: 378 (0), 271 (1), 237 (2), 194 (3), 146 (4), 93 (5), 43 (6), 20 (7), 9 (8)

The Rouen Study
100% Balloon Expandable Valves

Exhaustive Echocardiographic Follow-up Obtained in 98 % of Pts
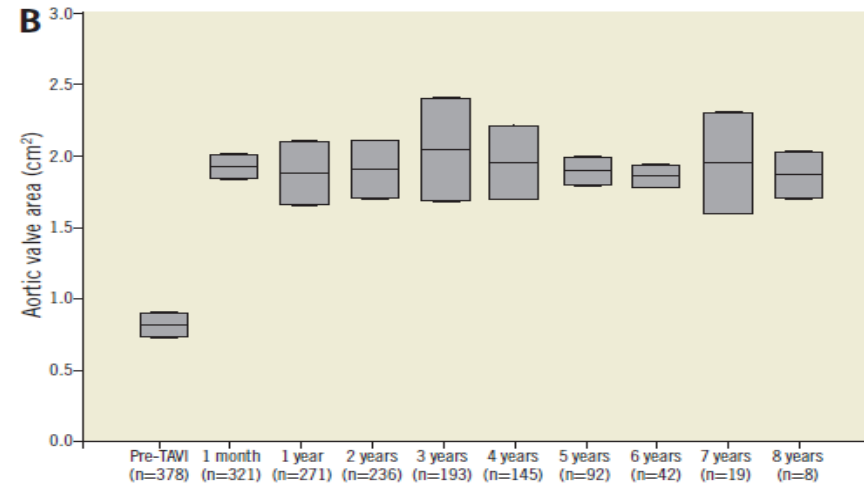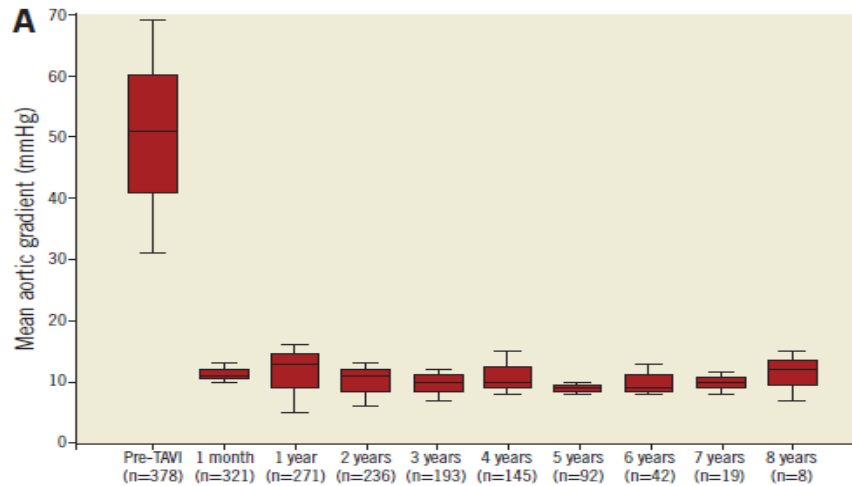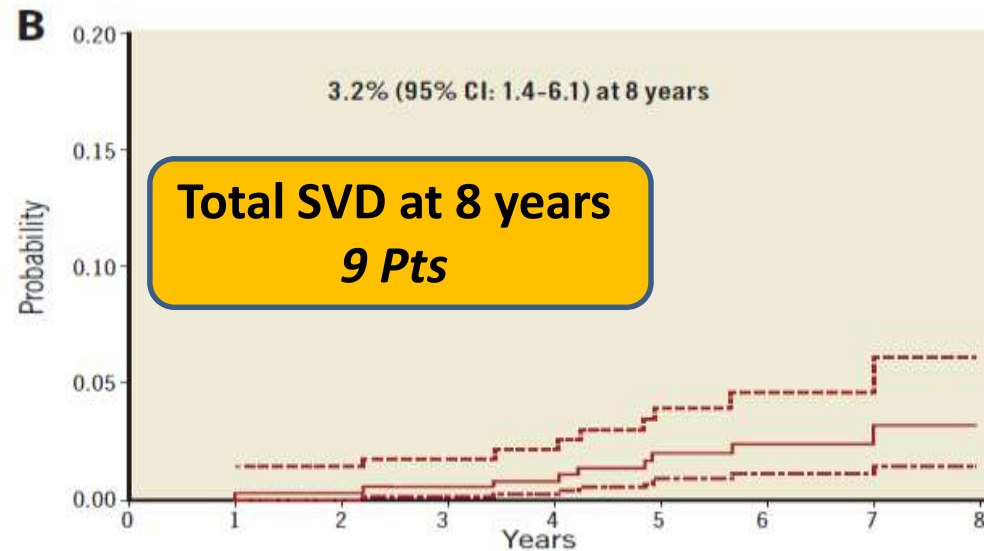

Unchanged mean gradient and valve area

The Rouen Study
100% Balloon Expandable Valves

« Structural Valve Deterioration »

Free from SVD 87% at 8 years

87.2% (95% CI: 76.2-99.2) at 8 years

t risk 378   271   236   193   145   92   42   19   8

Kaplan Meyer Analysis

3.2% (95% CI: 1.4-6.1) at 8 years

Total SVD at 8 years _9 Pts_

Death-competing risk analysis

Moderate SVD:
Mean gradient ≥ 20 and < 40mmHg, or
Mean change from baseline ≥ 10 and < 20mm Hg
Moderate central AR, new or worsening > 1

At 8 years:
Severe SVD in 3 Pts only
Re-intervention in 2: 0.58%

Severe SVD:
Mean gradient ≥40mmHg, or
Mean change from baseline ≥ 20mm Hg
Severe central AR, new or worsening > 2

What about SVD post-SAVR ?

Very Long-Term Outcomes of the Carpentier-Edwards Perimount Aortic Valve in Patients Aged 60 or Younger

Thierry Bourguignon, MD, Rym El Khoury, MD, Pascal Candolfi, PhD, Claudia Loardi, MD, Alain Mirza, MD, Julie Boulanger-Lothion, MD, Anne-Lorraine Bouquiaux-Stablo-Duncan, MD, Fabien Espitalier, MD, Michel Marchand, MD, and Michel Aupart, MD

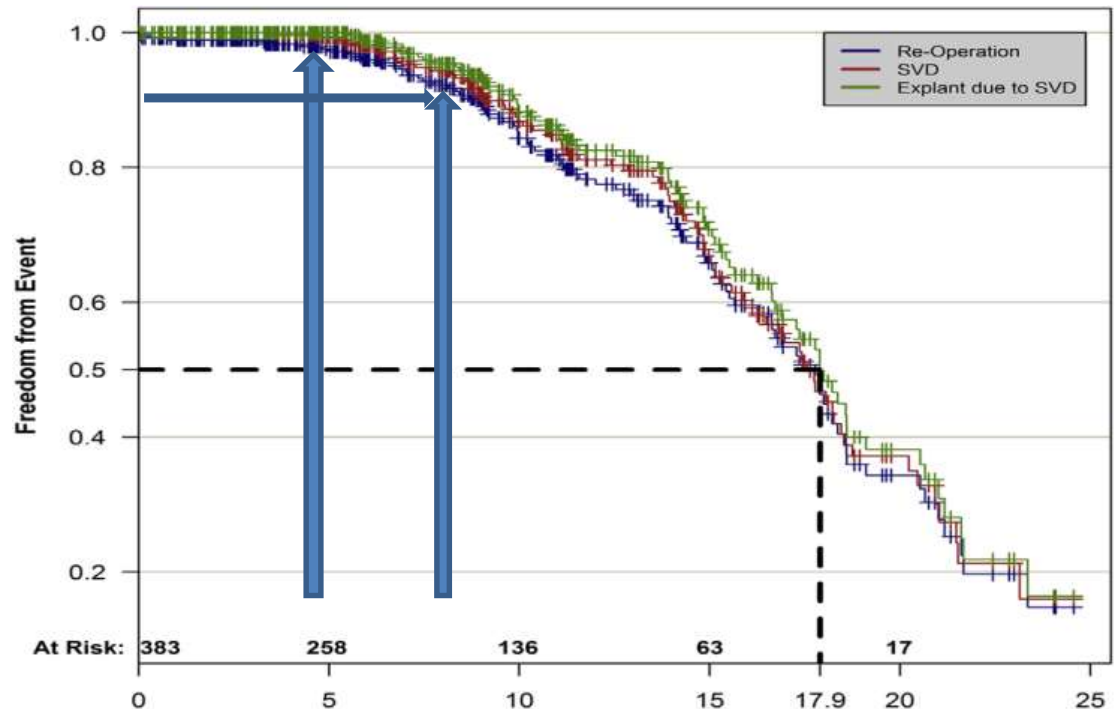**Ann Thorac Surg 2015; 100:853-9**

1984-2003
373 Pts
CE Perimount
Mean FU = 8.6±5.9 yrs

Actuarial freedom from reintervention

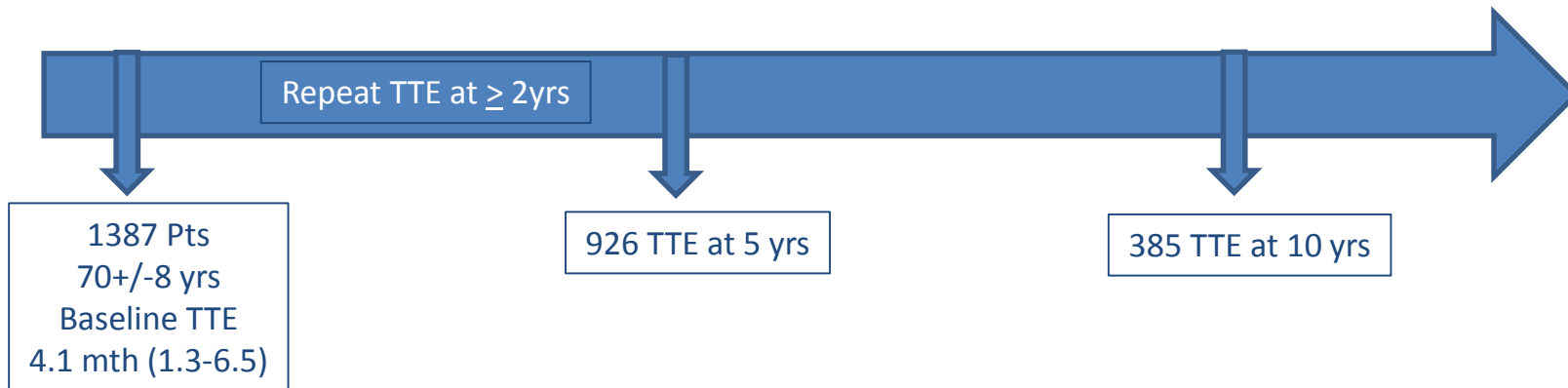|	
10 yrs:	88±2%
15 yrs:	71±4%
20 yrs:	38±6%

Recent data with SAVR using echocardiographic assessment

Rate, Timing, Correlates, and Outcomes of Hemodynamic Valve Deterioration After Bioprosthetic Surgical Aortic Valve Replacement
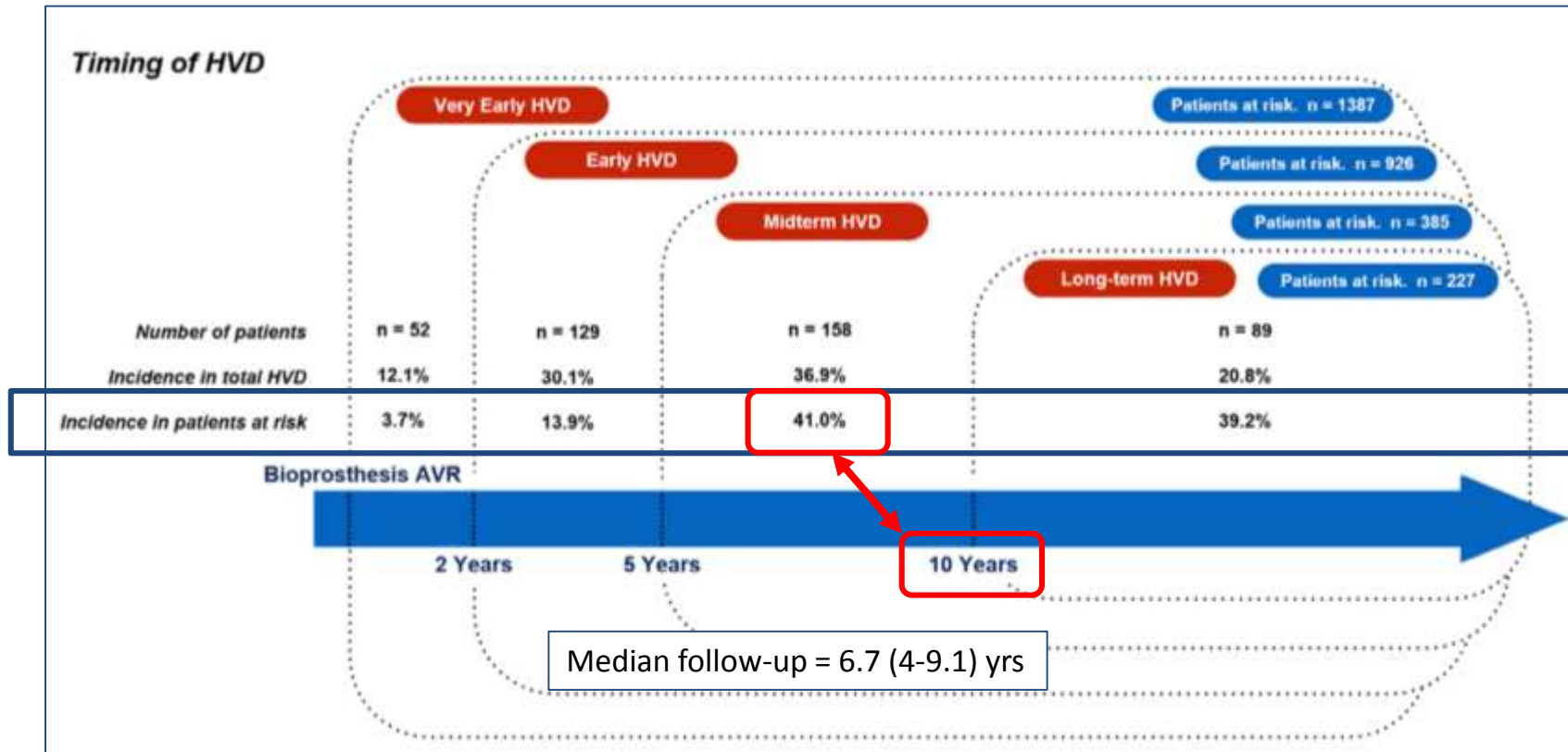
Circulation. 2018;138:971-985

Erwan Salaun, MD
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Josep Rodés-Cabau, MD
Patrick Mathieu, MD, MSc
Marie-Annick Clavel, DVM, PhD
Philippe Pibarot, DVM, PhD

Repeat TTE at ≥ 2yrs

1387 Pts
70+/-8 yrs
Baseline TTE
4.1 mth (1.3-6.5)

926 TTE at 5 yrs

385 TTE at 10 yrs

Hemodynamic valve deterioration defined by:

1) an increase in mean gradient ≥ 10 mm Hg with a decrease in EOA or worsening of trans-prosthetic aortic regurgitation ≥1/3 and at least moderate on FU and;
2) abnormalities of leaflets morphology and motion

Recent data with SAVR using echocardiographic assessment

Timing of HVD

	Very Early HVD	Early HVD	Midterm HVD	Long-term HVD
			Patients at risk. n = 1387	
			Patients at risk. n = 926	
			Patients at risk. n = 385	
			Patients at risk. n = 227	
Number of patients	n = 52	n = 129	n = 158	n = 89
Incidence in total HVD	12.1%	30.1%	36.9%	20.8%
Incidence in patients at risk	3.7%	13.9%	41.0%	39.2%

Bioprosthesis AVR

2 Years   5 Years   10 Years

Median follow-up = 6.7 (4-9.1) yrs

HVD during the total echo follow-up = 30.9% (428 Pts)

Among Pts with HVD, only 37% (159 Pts) underwent re-intervention

Conclusions

- Severe structural valve deterioration after TAVI is rare in an elderly population and the need for re-intervention is very low (< 1 %) at 7-8 y

- This is particularly true with the first generations of Balloon Expandable Valve as shown in the Rouen series (0.5% reintervention at 8 years)

- Sub-clinical SVD is more frequent and exists in both surgical and percutaneous bioprosthetic valves

- Recent data and extension of TAVI emphasize the need for annual assesment of all bioprosthetic valves using echo (and CT +/-PET-Scan when necessary to eliminate thrombus or endocarditis) using standardized definitions

- The incidence of SVD with TAVI Valves in a lower-risk and younger population remains unkown.

- The incidence of SVD with the new generation (SAPIEN 3) Balloon Expandable valve will deserve further assessment on long-term