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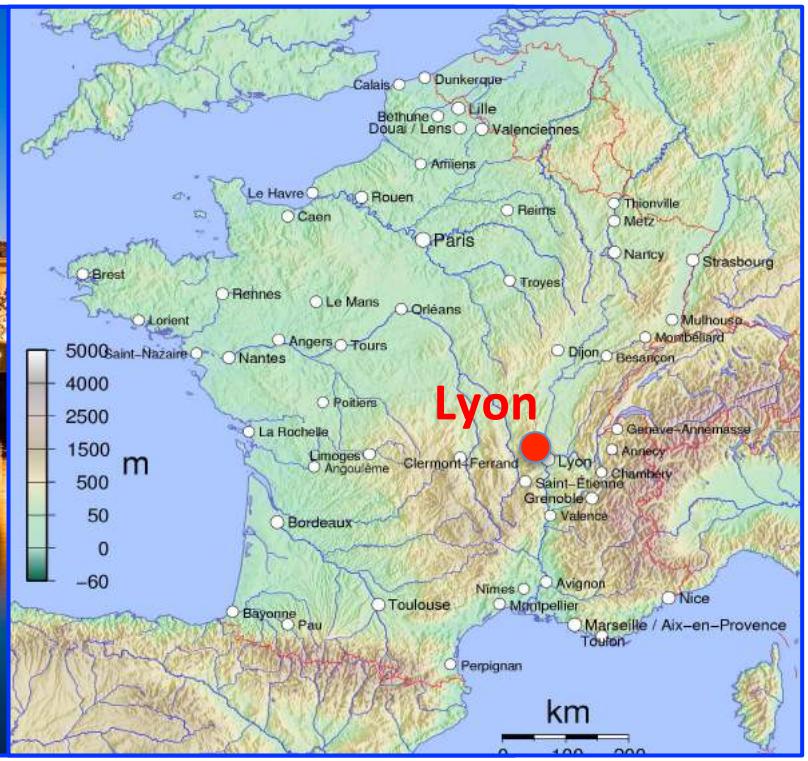
“ TAVI only for High Risk Patients ? ”



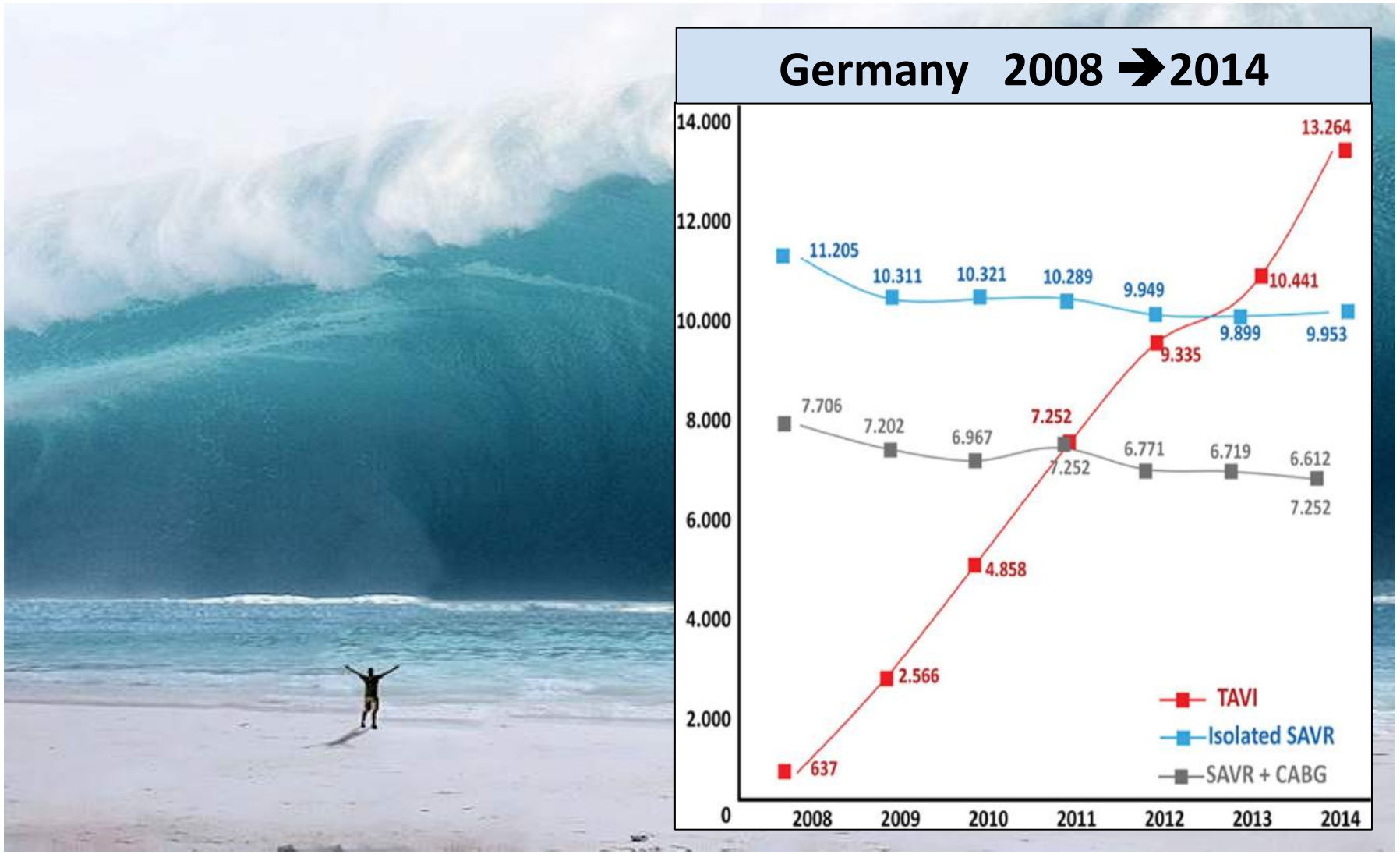
Cardiothoracic and Vascular Surgery Department

Hôpital Louis Pradel

LYON - France

Hospices Civils de Lyon

Disclosure Statement of Financial Interest	List of companies
> Grant/Research Support	Boeringher, Abbott, Medtronic, Edwards
> Consulting Fees/Honoraria	Edwards, Saint Jude Medical, Medtronic, Servier, Novartis
> Major Stock Shareholder/ Equity	
> Royalty Income	Landanger, Delacroix-Chevalier
> Ownership/Founder	
> Intellectual Property Rights	Landanger, Delacroix-Chevalier
> Other Financial Benefit	Sorin, Thoratec, Astra Zeneca



Eggebrecht H, Mehta R EuroIntervention 2016;11:1029-1033

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D.,

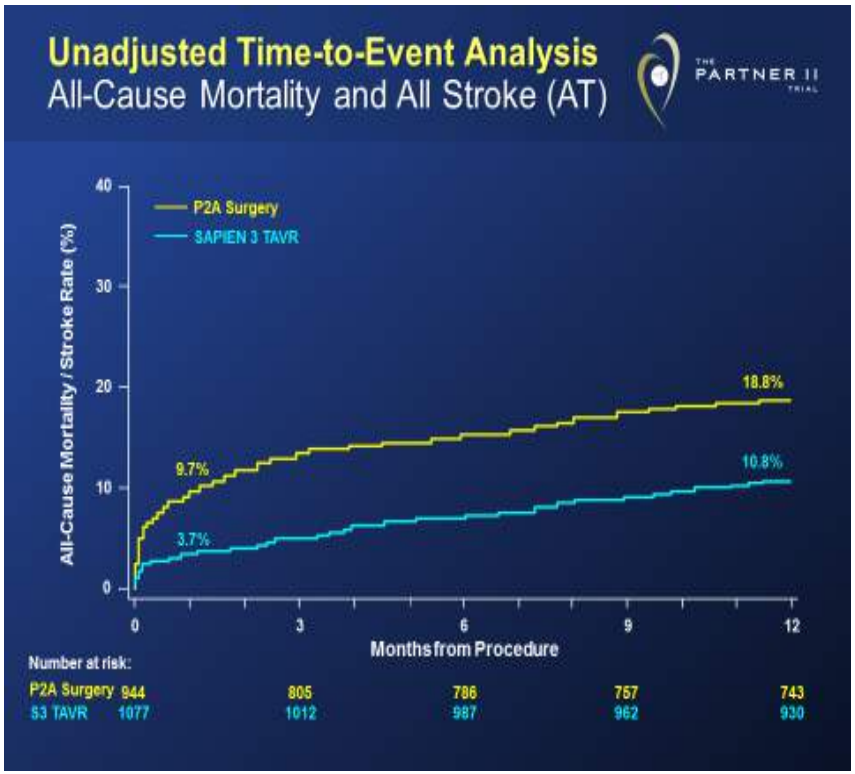
The NEW ENGLAND JOURNAL of MEDICINE

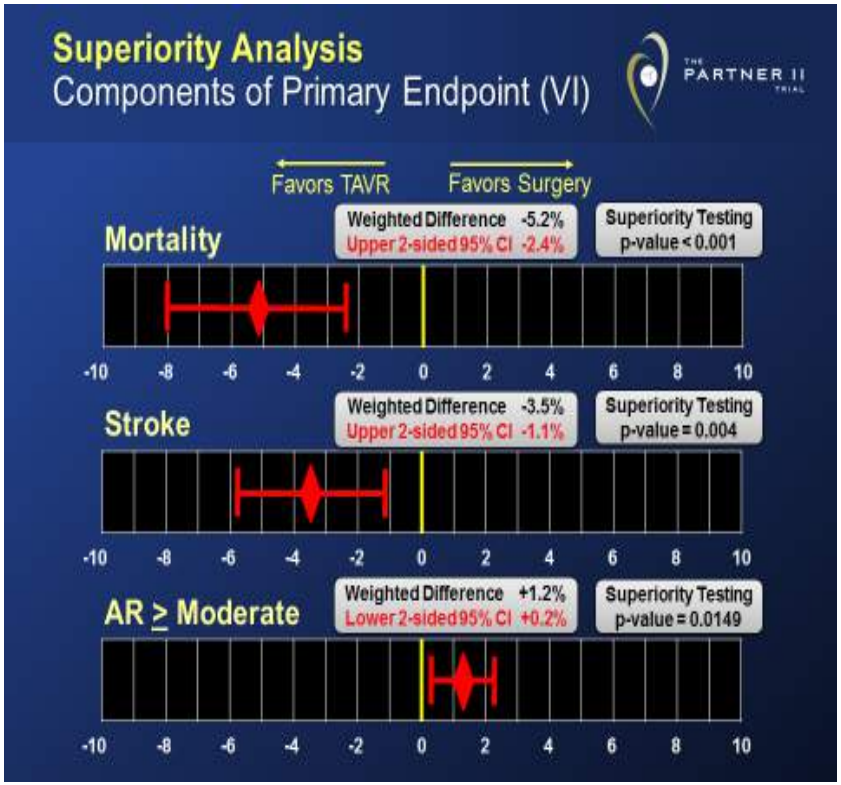
In the transfemoral- access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; P=0.05),

The cohorts defined according to assignment to access route constituted a prespecified subgroup, **but the study was not powered for an analysis of this subgroup**.

We estimated that a sample of 2000 patients would provide the trial with a power of at least 80% to show the **noninferiority of TAVR to surgery** with respect to the primary end point at 2 years, assuming an event rate of 30% in each group.

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis





The Lancet. Volume 387, No. 10034, p2218–2225, 28 May 2016

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Variable	TAVR Sapien 3 *Lancet* 2016; 387: 2218–25	TAVR PARTNER 2A N Engl J Med 2016;374:1609-20.	
	(n=1077)	(n=1011)	
LVEF (%)	58.5 ± 13.4	56.2 ± 10.8	**P < 0.0001**
Moderate-severe MR (%)	91/1033 (9%)	151/899 (16.8%)	**P < 0.0001**
STS score	5.2% (4.3% - 6.3%)	5.8 ± 2.1	**DATA NOT**
Mean gradient (mmHg)	46.1 ± 12.6	44.9 ± 13.4	**P = 0.035**
Gender (%)	665 (62%)	548 (54.2%)	**P = 0.0005**

Comparing apples and oranges

Eugene H. Blackstone, MD J Thorac Cardiovasc Surg 2002;123:8-15

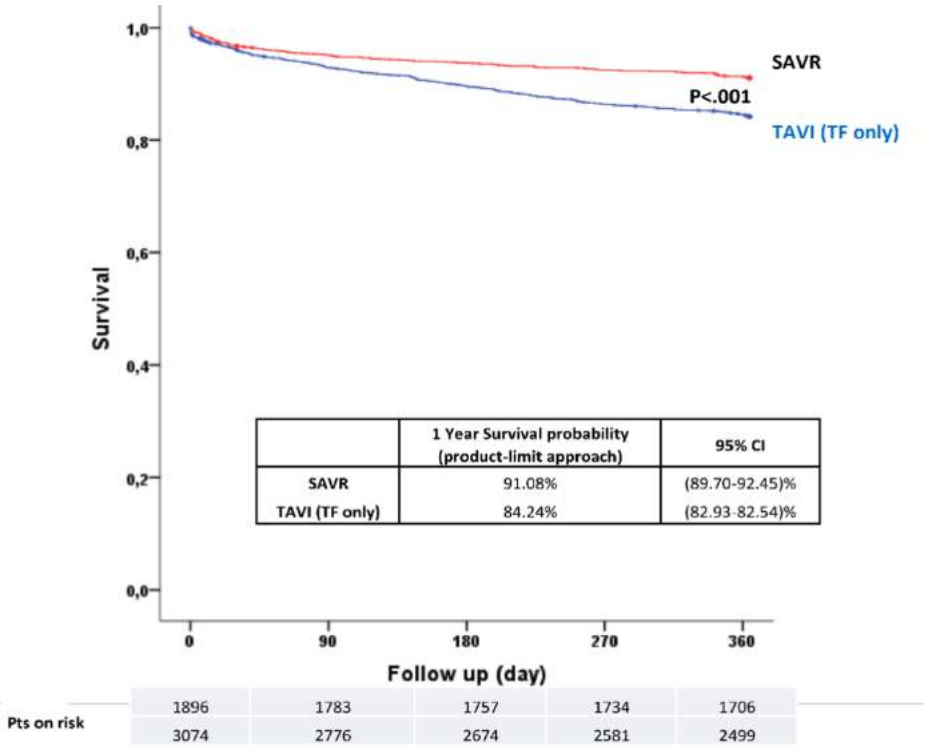
Often, a cursory glance at patient characteristics in each group reveals important differences that lead medical and statistical reviewers and readers alike to scoff, "They're comparing 'apples and oranges!'"

These differences in characteristics between groups are often large, systematic, and statistically significant. They arise from clinically motivated patient selection. (How often does the clinical inferences section of a journal article begin, "In carefully selected patients. . . ?") They arise for undocumented reasons called "treatment variance." They sometimes arise by chance. In whatever way they arise, they invalidate direct comparisons.

The Lancet. Volume 387, No. 10034, p2218–2225, 28 May 2016

Deutsches Aortenklappenregister

German Aortic Valve Registry (GARY)



	1 Year Survival probability (product-limit approach)	95% CI
SAVR	91.08%	(89.70-92.45)%
TAVI (TF only)	84.24%	(82.93-82.54)%

German Aortic Valve Registry (GARY)

	SAVR (n = 1896)	TAVI (n = 4101)	p-value
Age	75.9 ± 6.7	81.8 ± 5.4	< 0.001
Female	54.1%	61.6%	< 0.001
Log. EuroSCORE I	13.4 ± 2.7	14.4 ± 2.9	< 0.001
STS Score	3.7 ± 2.1	5.2 ± 2.8	< 0.001
Body mass index (BMI)	28.2 ± 4.8	27.2 ± 5.0	< 0.001
NYHA III – IV	72.4%	83.7%	< 0.001

Deutsches Aortenklappenregister

	SAVR (n = 1896)	TAVI (n = 4101)	p-value
Major / minor stroke	1.2% / 1.3%	1.5% / 1.2%	0.281/ 0.816
Myocardial infarction	0.5%	0.3%	0.114
New onset pacer / ICD	5.3%	19.1%	< 0.001
Vascular complications	1.1%	7.7%	< 0.001
Aortic valve regurgitation ≥ grade II	0.4%	4.7%	< 0.001
Conversion to open heart surgery	---	1.0%	---
Bleeding ≥ 2 RBC units	51.5%	25.0%	< 0.001

In 2016, 5 issues deserve a particular attention and represent the matter of debate to limit the enlargement of the indications

1) ~~*Neurologic Complications*~~

2) ~~*Vascular Complications*~~

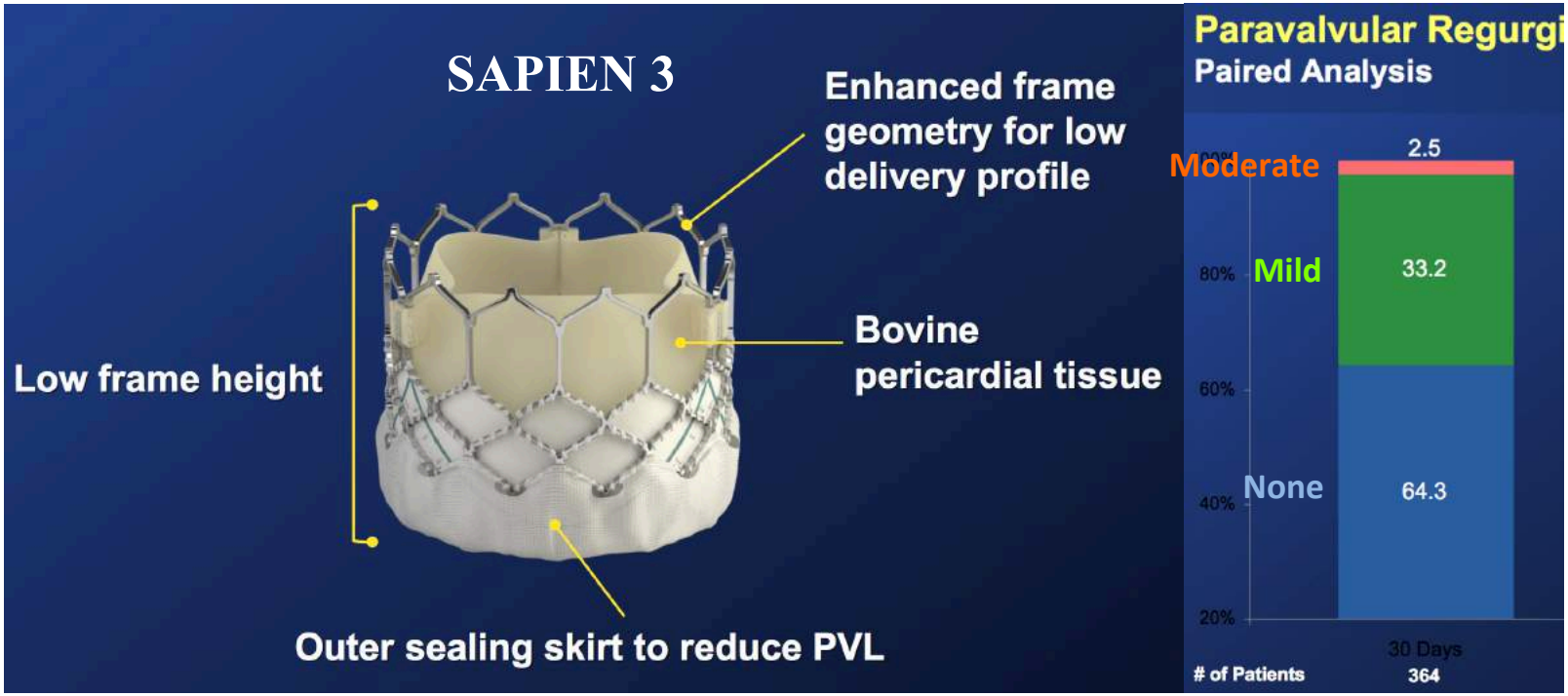
3) ~~*Residual Aortic Regurgitation*~~

4) ***Pacemaker Implantation***

5) ***Durability of the biological prostheses***

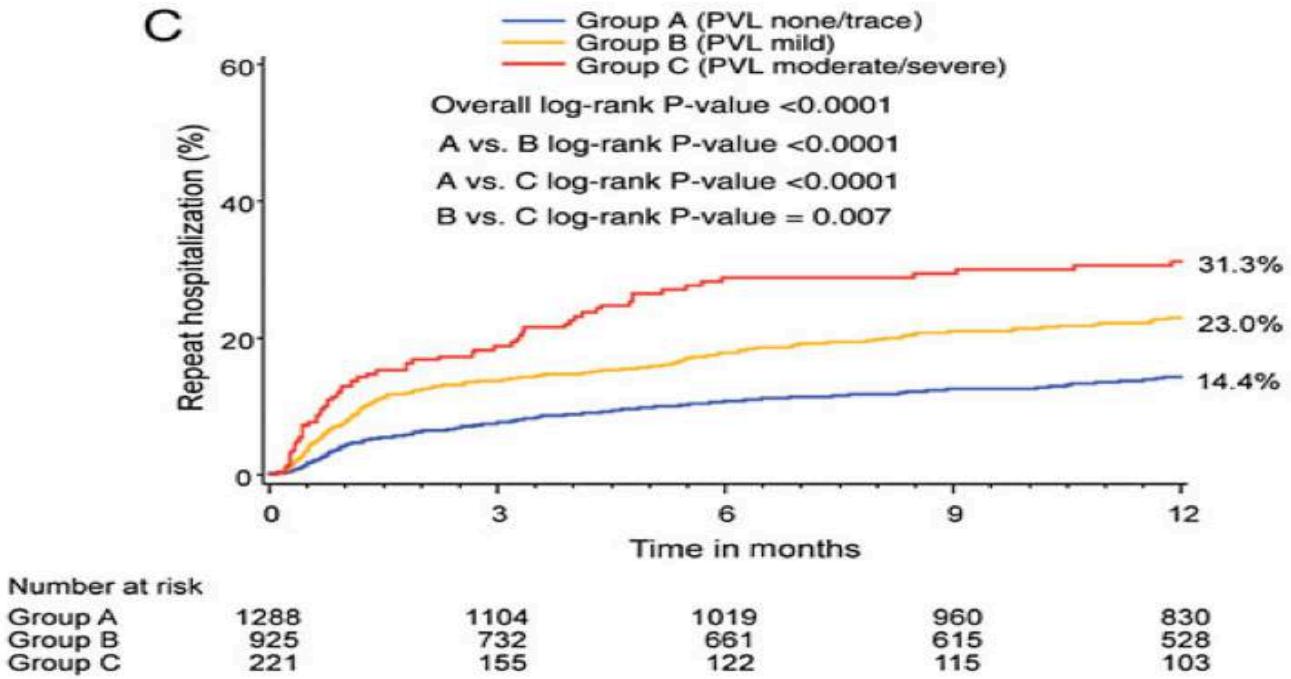
1) RESIDUAL AORTIC REGURG.

Howard C. Herrman on behalf of
The PARTNER II Trial Investigators. *TCT 2015*



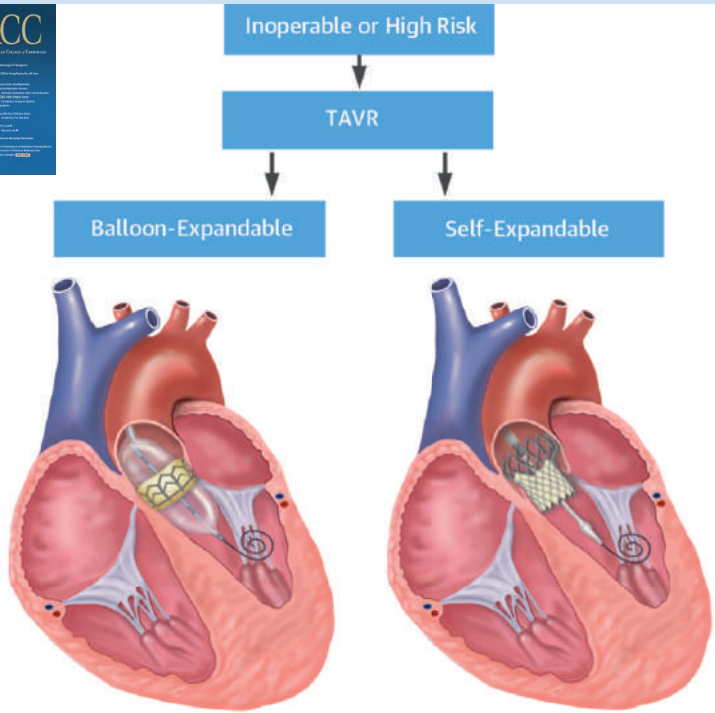
1) RESIDUAL AORTIC REGURGITATION

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



4) PACEMAKER IMPLANTATION

Results From the CHOICE Randomized Clinical Trial
Abdel-Wahab M, JACC VOL. 66, NO. 7, 2015

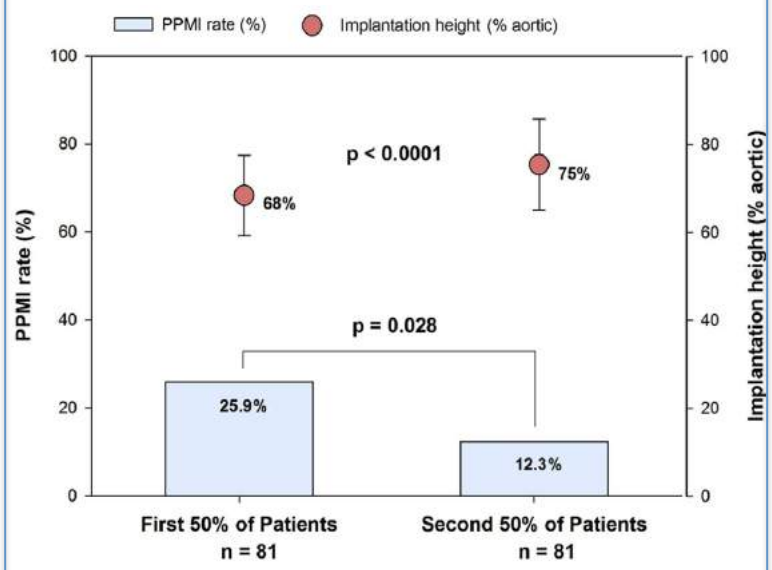


New Pace Maker

23% **38%**

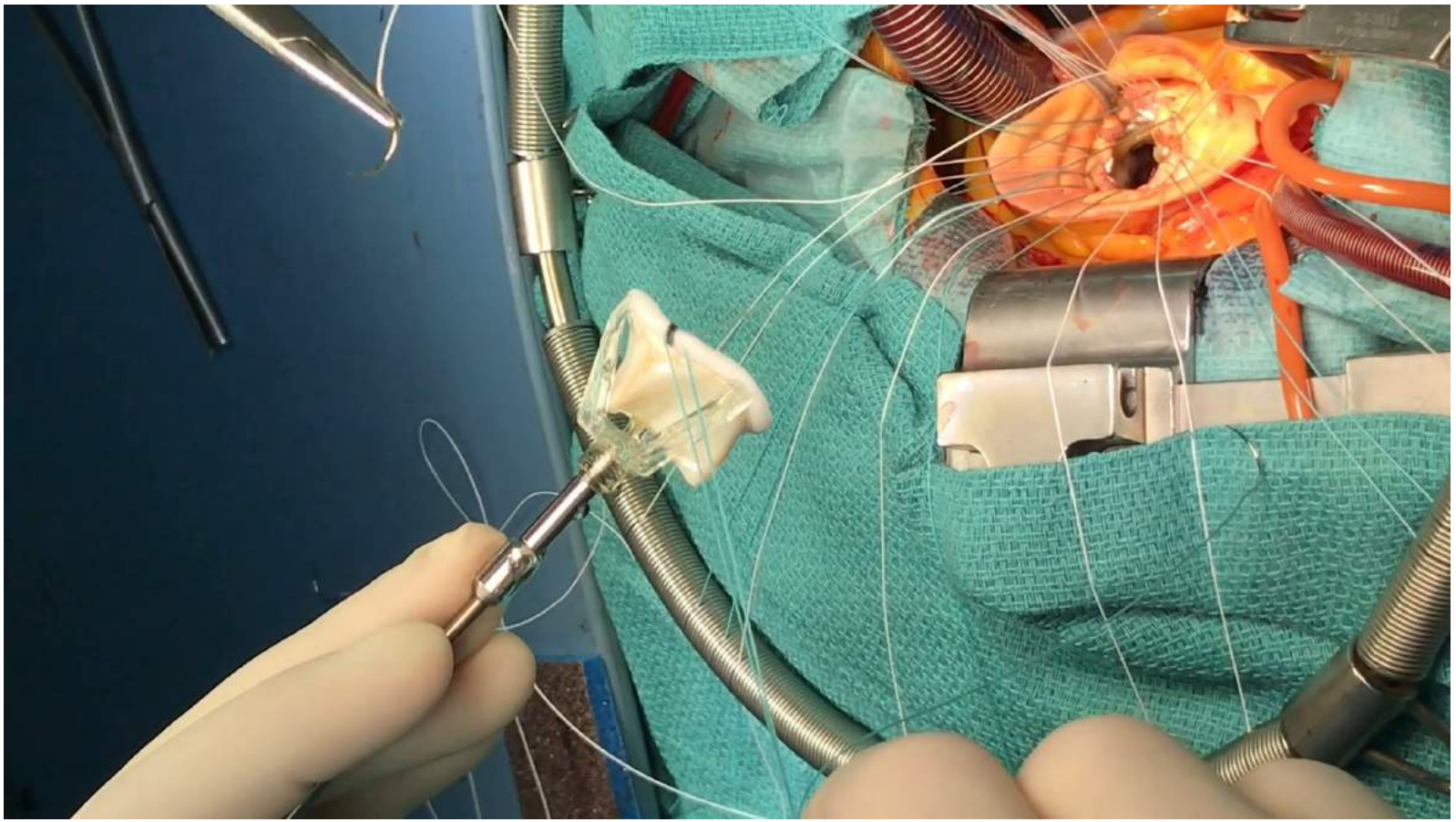
Changes in the Pacemaker Rate After Transition From Edwards SAPIEN XT to SAPIEN 3 Transcatheter Aortic Valve Implantation

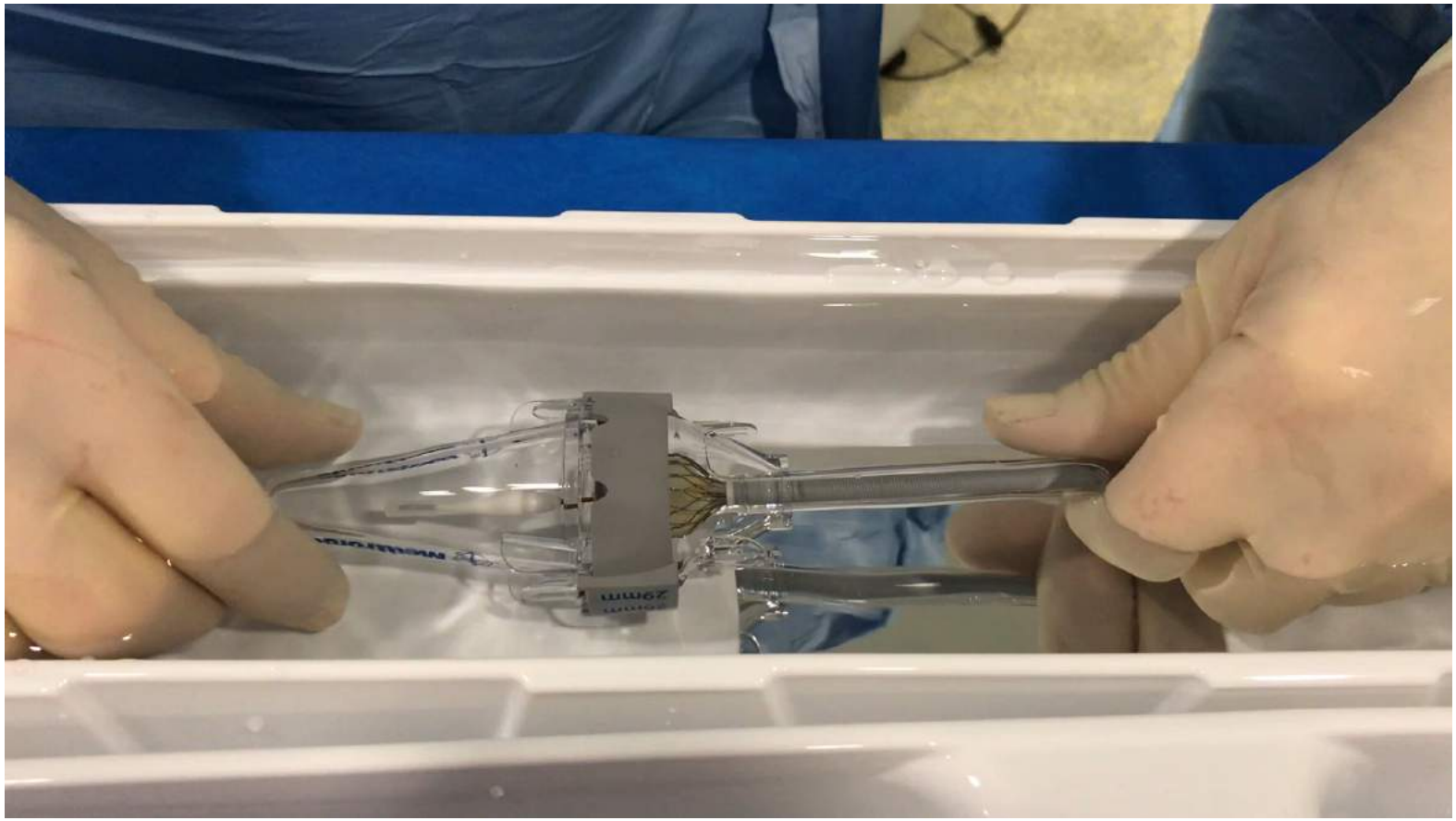
JACC Intv 2016



New Pace Maker

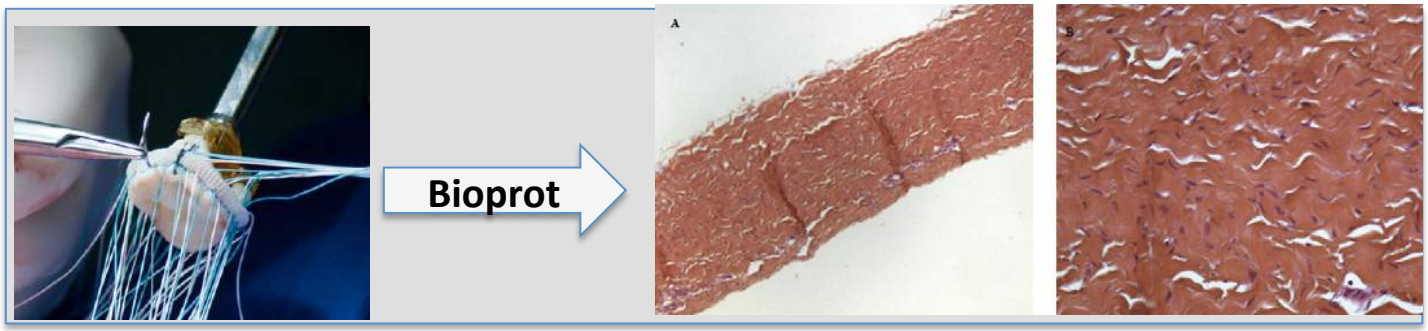
26% **12%**

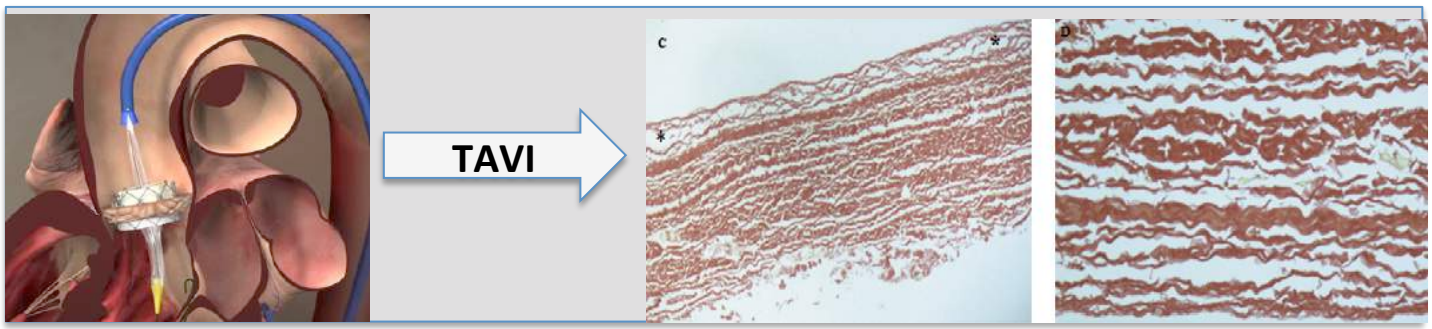



29mm

5) LONGEVITY OF BIOLOGICAL PROSTHESES

Evidence of leaflet injury during TAVI deployment
Zegdi et al. Eur J Cardiothorac Surg 2011;40:257-9



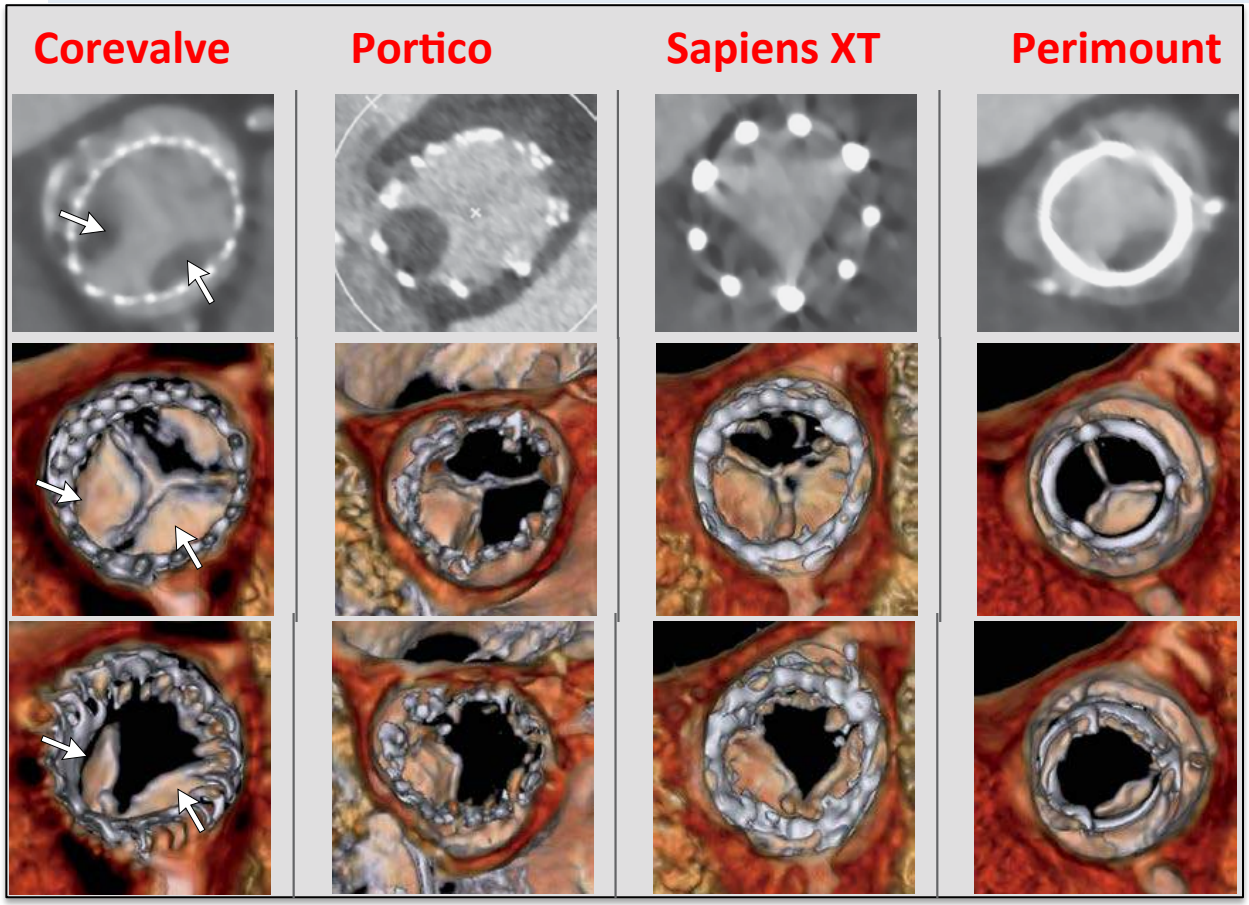


Collagen fiber fragmentation and disruption

5) LONGEVITY OF BIOLOGICAL PROSTHESES

Possible Subclinical Leaflet Thrombosis in *TAVI*

Makkar et al. N Engl J Med 2015;373:2015-24



Clinical Trial
55 pts → 40%

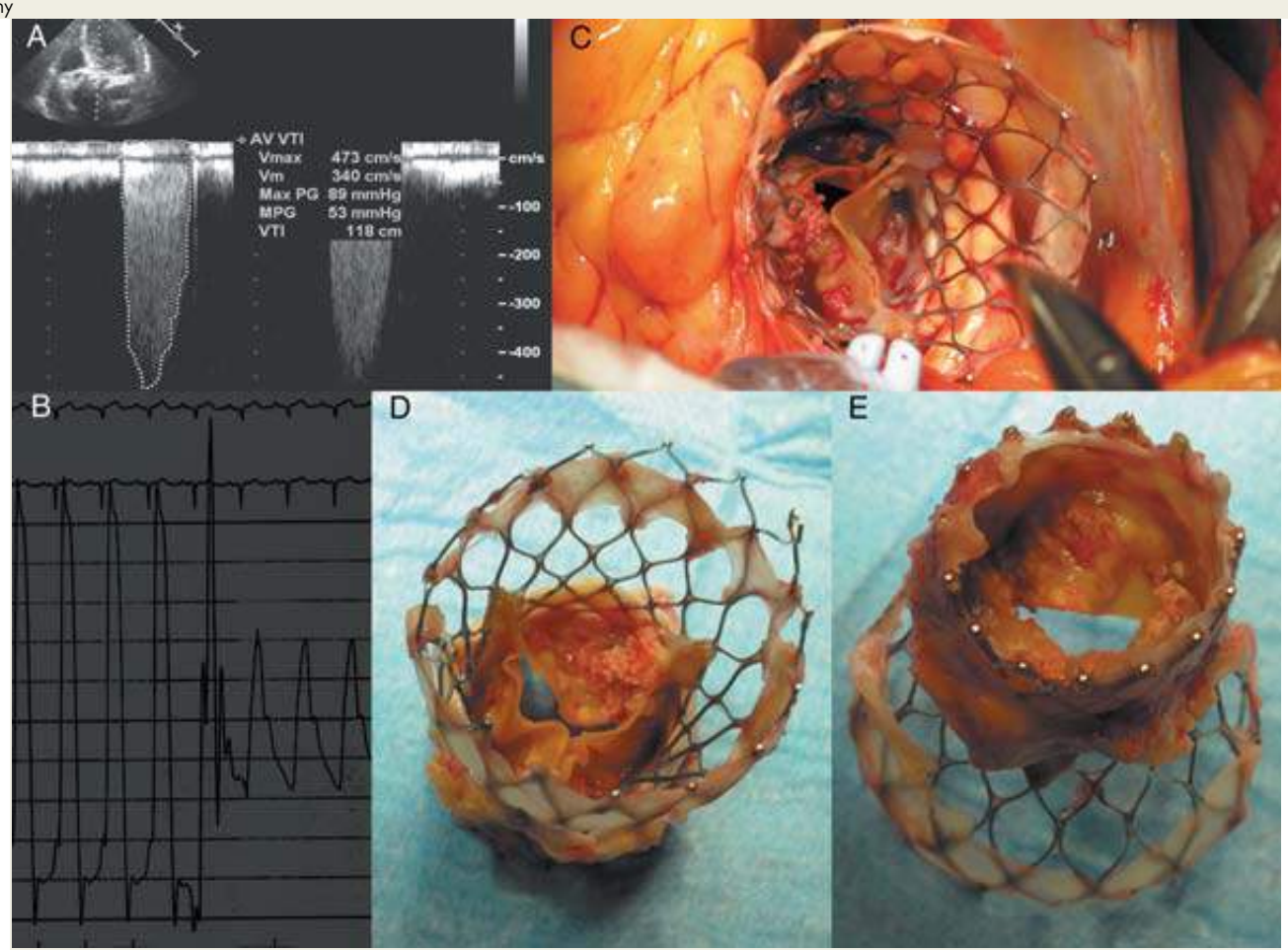
Resolve/Savory
132 pts →13 %

VKA related
VKA sensible

Early calcific degeneration of a CoreValve transcatheter aortic bioprosthesis

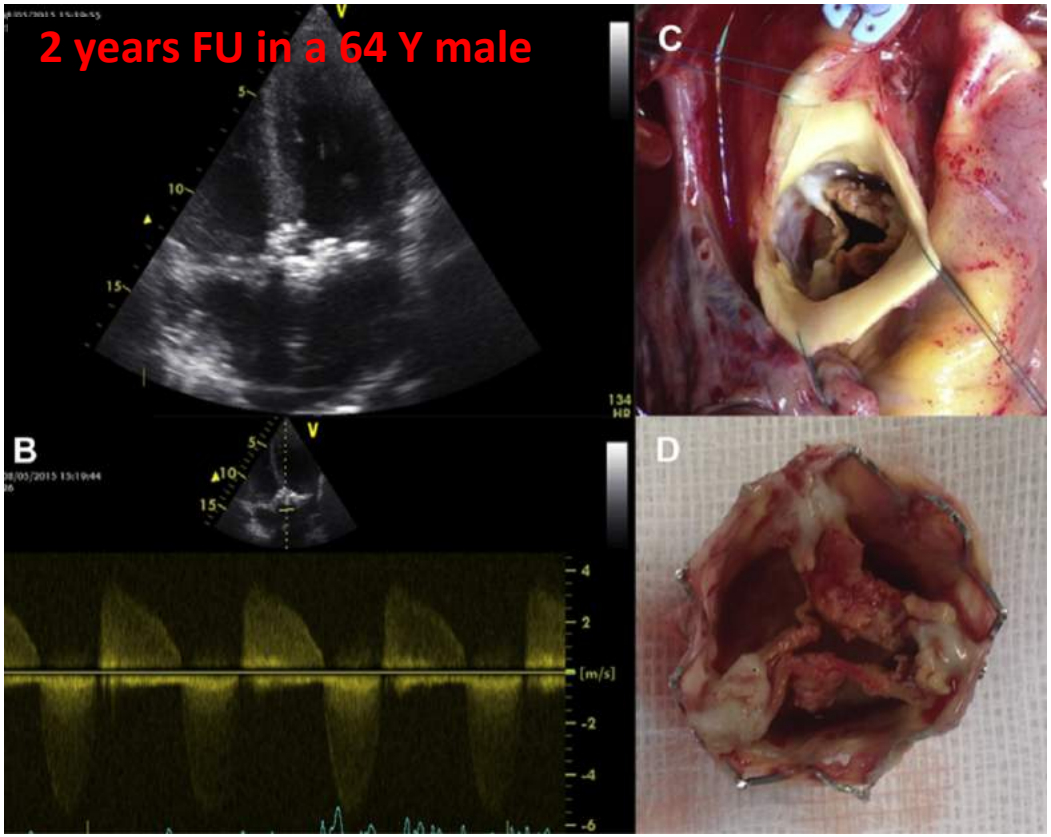
Sea Hing Ong[1]*, Ralf Mueller[1], and Stein Iversen[2] **5 years FU in a female aged 74**

[1]Department of Cardiology/Angiology, HELIOS Klinikum Siegburg, Siegburg, Germany and [2]Department of Cardiovascular Surgery, HELIOS Klinikum Siegburg, Siegburg, Germany



Early Edwards SAPIEN Valve Degeneration After TAVR

Brahim Harbaoui, MD, MSC,*y Pierre-Yves Courand, MD, MSC,*y Zoé Schmitt, MD,z Fadi Farhat, MD, PHD,x Raphael Dauphin, MD,* Pierre Lantelme, MD, PHD*y **JACC Cardiovasc Interv. 2016**



Early transcatheter aortic valve degeneration in the young

Mathieu van Steenberghe [a,*], Chun-Yi de Vasconcelos [b], Dominique Delay [a], Lars Niclauss [a], Matthias Kirsch [a]

[a] *Cardiac Surgery Unit, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland*
[b] *Pathology Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland*

43 years old male BMI = 40.4 ➔ TAVI → **3 years later ➔ Euroscore = 1.19%**
Discharged on Day 10

2016 euroPCR

Methods

- The a … an 5 years ago:
  April
- **Sites**
  - S
  - H
- **Inclu**
  - P
  - B … SAPIEN XT).
- **Exclu**
  - M
  - Tl
  - D … urgitation).
  - P
  - In

Cardiovascular News

The international newspaper for cardiovascular specialists — August 2016 Issue 42

Olaf Wendler: TAVI for lower risk — Page 10

Philip Urban: Profile — Page 16

Adam Hartley: Patients and the web — Page 23

Study indicates signal for valve degeneration in TAVI patients by eight years

Speaking at EuroPCR (17–20 May, Paris, France), Danny Dvir reported that there is a significant increase in valve degeneration between five and seven years after a transcatheter aortic valve implantation (TAVI) device is deployed. Although stressing that this was a "preliminary analysis" using early-generation devices and, therefore, "we must be cautious", he estimated that, based on these findings, about half of patients who undergo TAVI may show early signs of valve degeneration within eight years of implantation.

Dvir (St Paul's Hospital, Vancouver, Canada), who was presenting the data on behalf of the teams in Vancouver Canada and Rouen France, commented that as a result of TAVI being "increasingly being performed" in younger and lower-risk cohorts, more patients are expected to survive "long after" transcatheter heart valve implantation. However, he noted that durability of TAVI devices has "only been assessed over the

degeneration with the average time to degeneration being 61 months. Of these, 23 showed signs of aortic regurgitation and 12 showed signs of aortic stenosis/mixed regurgitation. Dvir commented that the "vast majority" of patients with aortic regurgitation had intravalvular regurgitation and that among patients with stenosis, "stenosis indices appeared only in long-term follow-up". In terms of valves that degenerated, three were a Cribier-Edwards device, 19

Absorb now available in the USA following FDA approval

Five years after receiving the CE mark, Abbott Vascular's bioresorbable vascular scaffold (Absorb) has been granted FDA approval—making it the first fully dissolving scaffold to be commercially available in the USA. The Absorb GT1 system, which is gradually absorbed by the body in approximately three years, is now approved for use in percutaneous coronary intervention (PCI) in patients with coronary artery disease.

The approval was based on data from the ABSORB III trial, which showed that patients who received the Absorb GT1 system had a similar rate of target lesion failure (the trial's primary endpoint) at one year as those who received an everolimus-eluting stent with a permanent polymer (Xience, Abbott Vascular): 7.8% vs. 6.1%, respectively (p=0.007 for non-inferiority). This study also showed that there were no significant differences between devices in the rates of cardiac death, target-vessel myocardial revascularisation or device thrombosis.

However while there was not a significant

2016 euro PCR

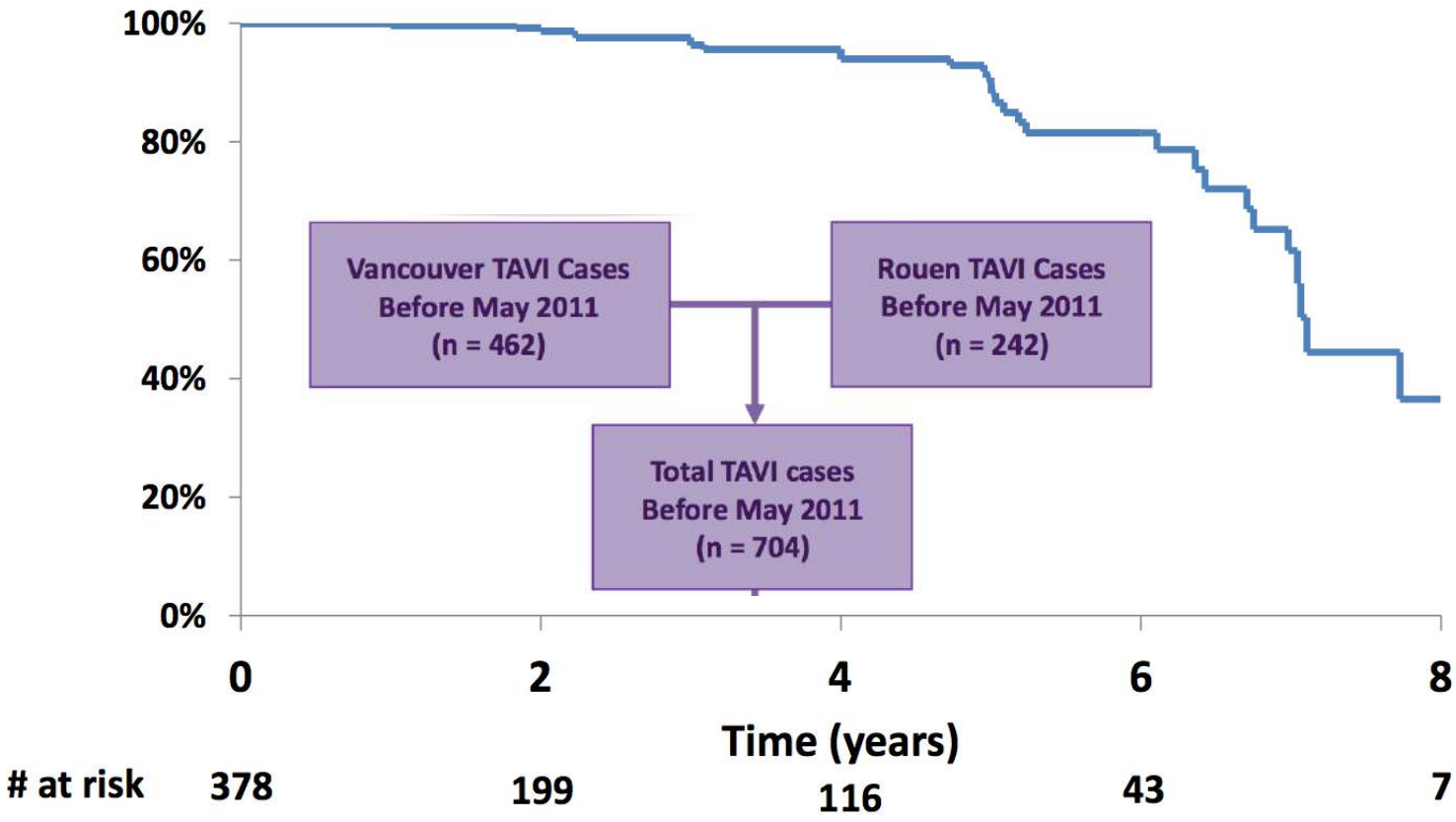
Methods

- **Degeneration definition** in the current analysis:

  At least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.

- Long-term echocardiographic exams performed during house visits.

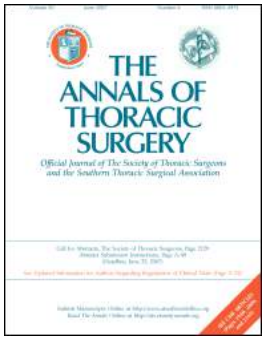
Freedom from THV degeneration



2016 euro PCR

Summary

- The current analysis includes a first look at long-term durability after TAVI, evaluating cases performed 5-14 years ago with early-generation balloon-expandable THV devices.
- In this preliminary report, a significant increase in degeneration rate was observed between 5-7 years after TAVI.
- Estimate of THV degeneration (resulting in at least moderate stenosis AND/OR regurgitation) was ~50% within 8 years.
- Renal failure was the strongest correlate of THV degeneration.



Very Long-Term Outcomes of the Carpentier-Edwards Perimount Valve in Aortic Position

Thierry Bourguignon, MD, Anne-Lorra
Alain Mirza, MD, Claudia Loardi, MD
Michel Marchand, MD, and Michel Au

Structural Valve Deterioration (SVD) and Reoperation for SVD ***Echographic evaluation 97.7%***

The bioprosthesis was considered to have deteriorated on strict echocardiographic assessment whenever severe aortic stenosis (mean transvalvular gradient > 40 mm Hg) or severe aortic regurgitation (effective regurgitant orifice area > 0.30 cm^2, vena contracta > 0.6 cm) was observed, even if the patient was asymptomatic.

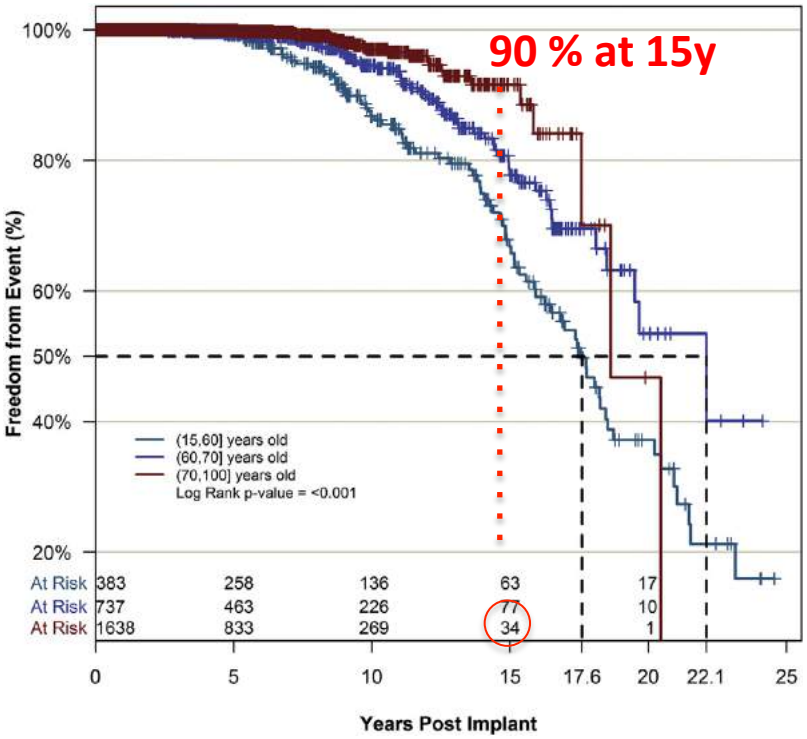


Fig 3. Kaplan-Meier freedom from structural valve deterioration (SVD) by age groups. The expected valve durability (median survival time without SVD) was 17.6 and 22.1 years for the younger (≤ 60) and the 60 to 70 years group, respectively.

Hancock II Bioprosthesis for Aortic Valve Replacement: The Gold Standard of Bioprosthetic Valves Durability?

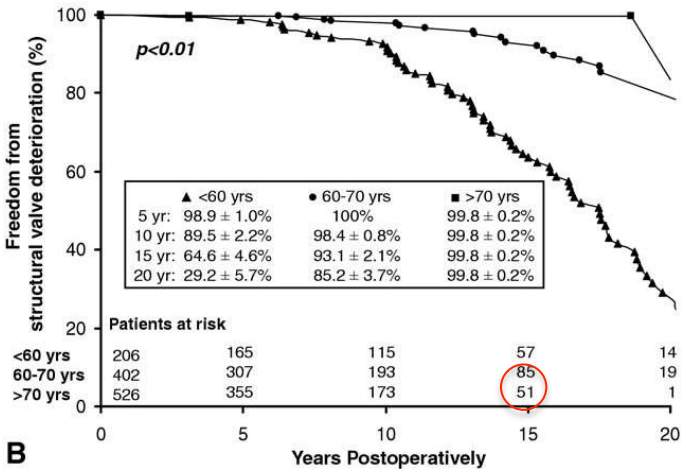
Tirone E. David, MD, Susan Armstrong, MS, and Manjula Maganti, MS

From September 1982 to December 2004, **1134 consecutive patients**... monitored prospectively **every second year**. Most patients **(94%)** had multiple echocardiographic studies to assess valve and heart function.

Structural Valve Deterioration

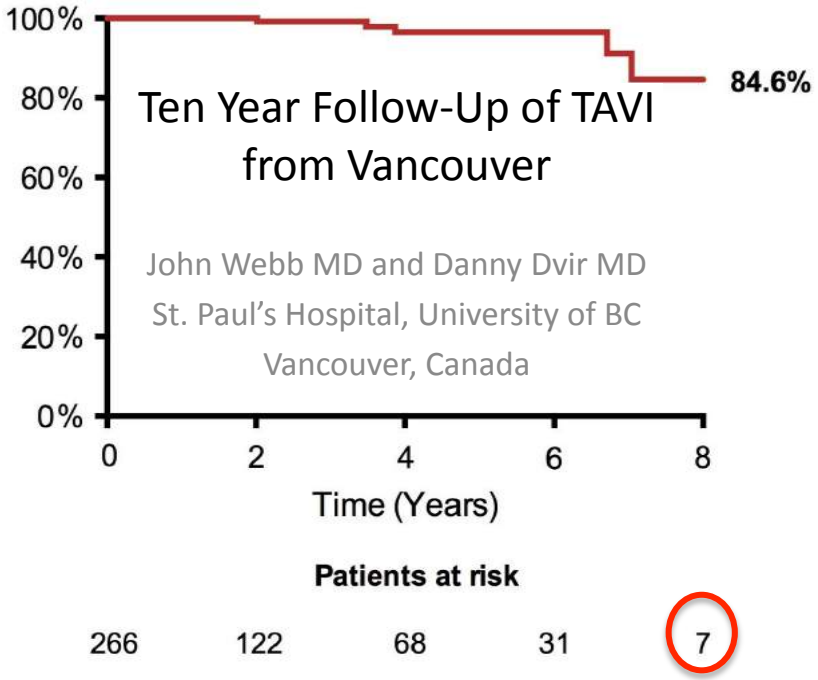
Structural valve failure (SVD) was documented in 87 patients by echocardiography or operati or both. Repeat AVR was performed in 74 pati 13 patients were believed to be inoperab 0 age group and 7 in ≥60 years group) T only 2 valve failures in patients older th , 18 in patients aged 60 to 70 years, and 67 in pa nts younger than 60 years. Age was the only independent predictor of SVD. Freedom of SVD

87 SVD → 2 < 70Y



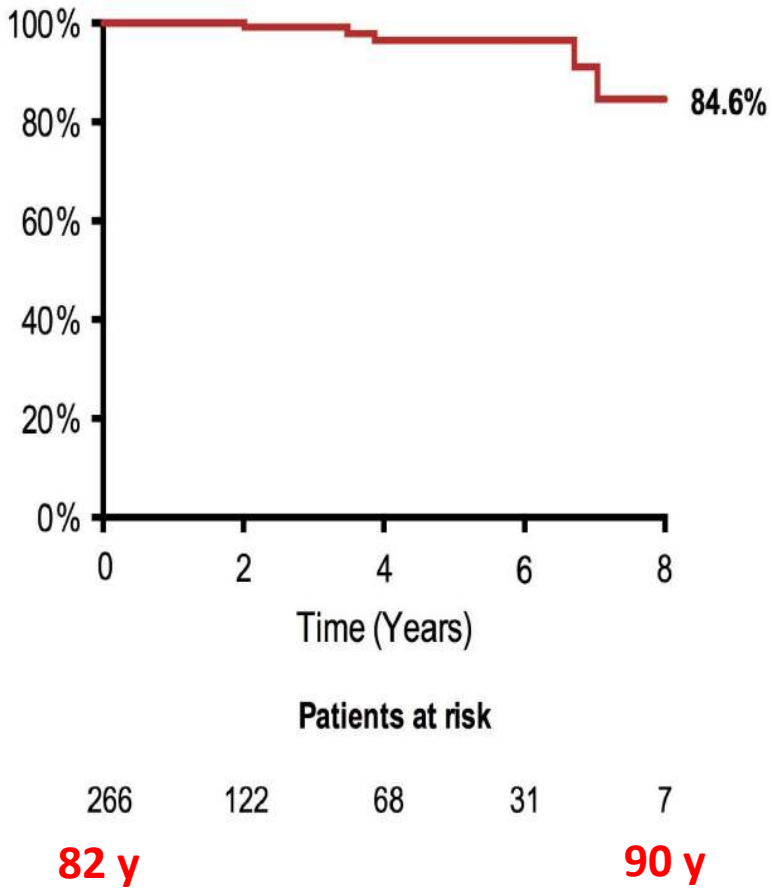
SVD definition	# of cases	% of cases
Severe Stenosis and/or Regurgitation[1,]	5	1.9%
Re-intervention (SAVR or TAVR)[3]	3	1.1%
Severe AS, severe AR, or Re-intervention	5	1.9%

Freedom from severe stenosis, regurgitation, or re-intervention



THV severe failure was defined severe AS AND/OR severe AR. KM estimate of THV degeneration included censoring of patients at their date of last known THV functioning well without evidence for failure per study definition.

Ten Year Follow-Up of TAVI from Vancouver



Very Long-Term Outcomes of the Carpentier-Edwards Perimount Valve in Aortic Position

Thierry Bourguignon, MD, Anne-Lorraine Bouquiaux-Stablo, MD, Pascal Candolfi, PhD, Alain Mirza, MD, Claudia Loardi, MD, Marc-Antoine May, MD, Rym El-Khoury, MD, Michel Marchand, MD, and Michel Aupart, MD

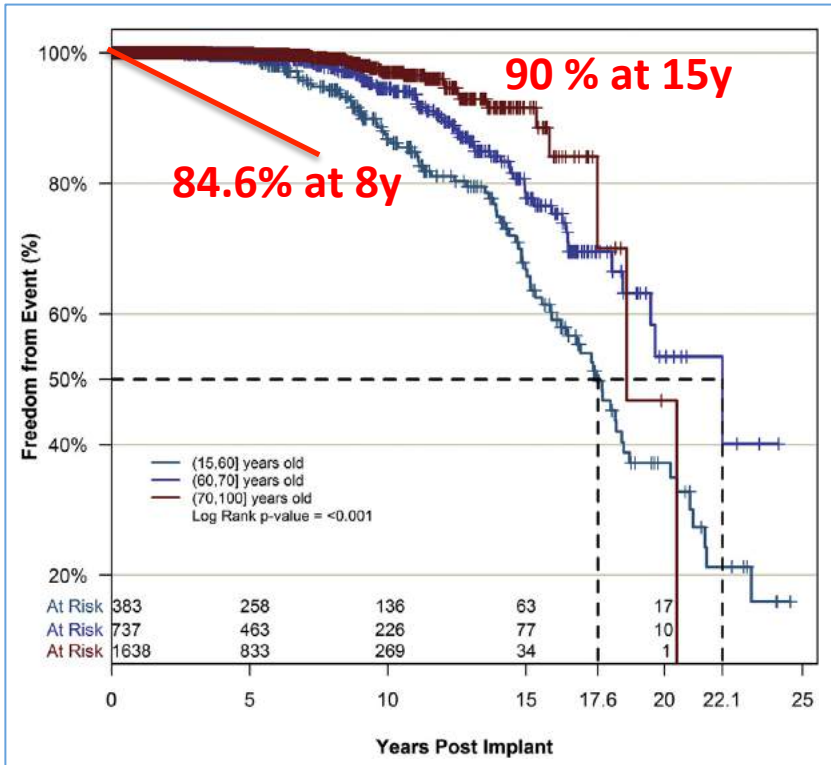
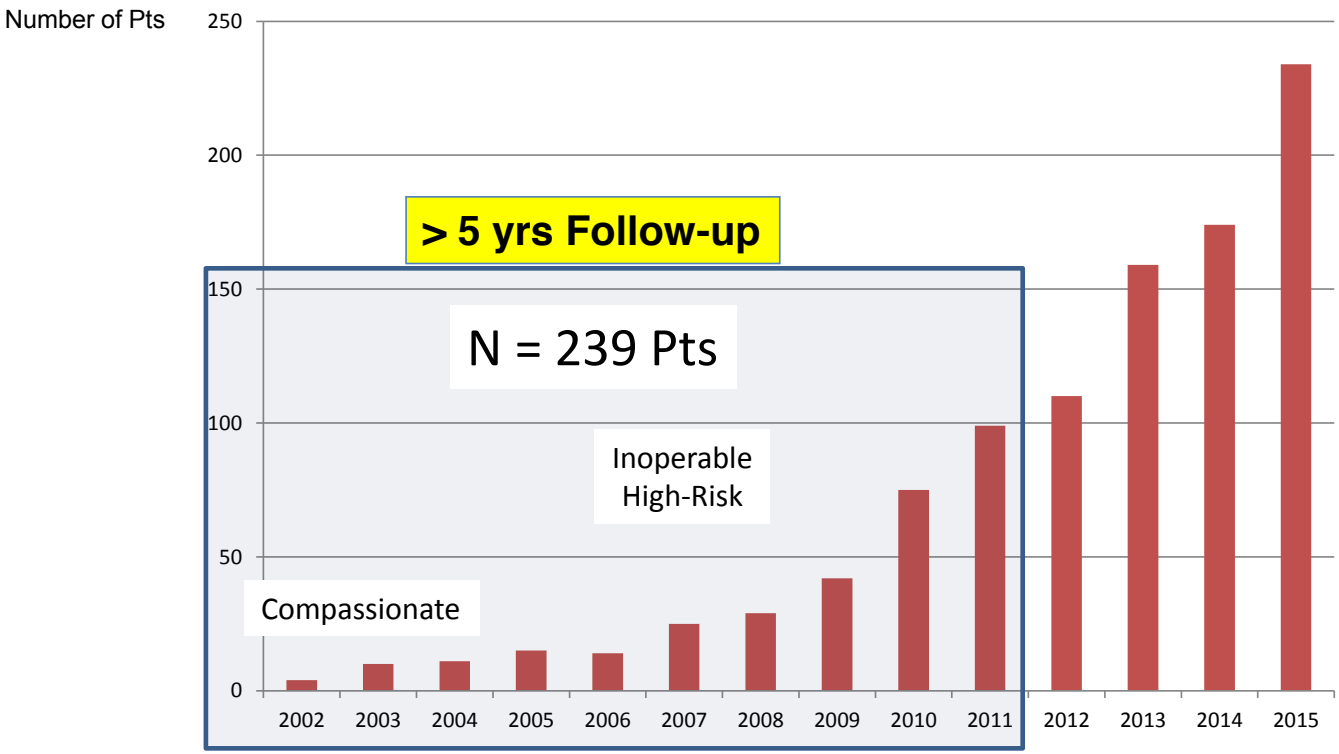


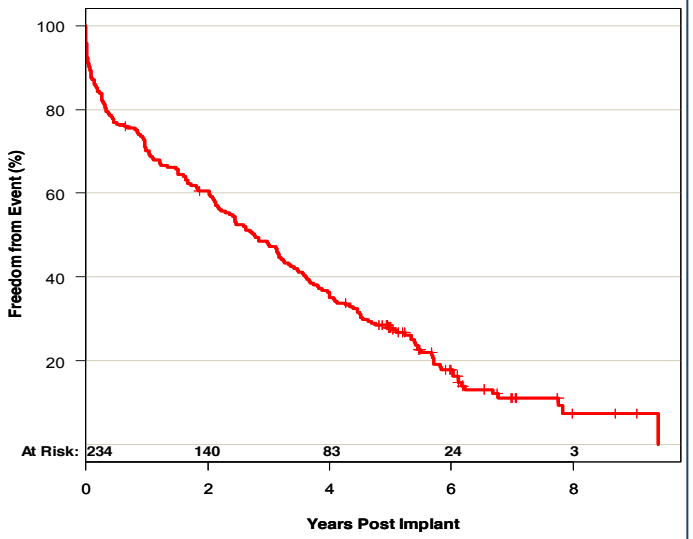
Fig 3. Kaplan-Meier freedom from structural valve deterioration (SVD) by age groups. The expected valve durability (median survival time without SVD) was 17.6 and 22.1 years for the younger (≤ 60) and the 60 to 70 years group, respectively.

TAVR in Rouen since 2002



Actuarial Analysis – Freedom from Mortality

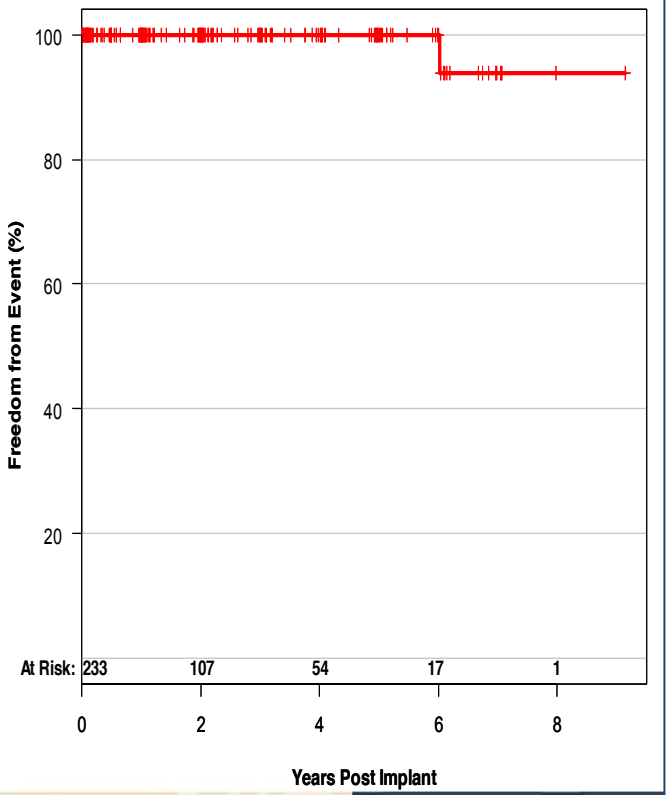
- 5 patients (2%) excluded (lost FU)
- 194 patients died
- Total FU: 686.3 patient-years
- Maximum FU: 9.4 years
- Patients still alive were censored to the latest visit or echo date available



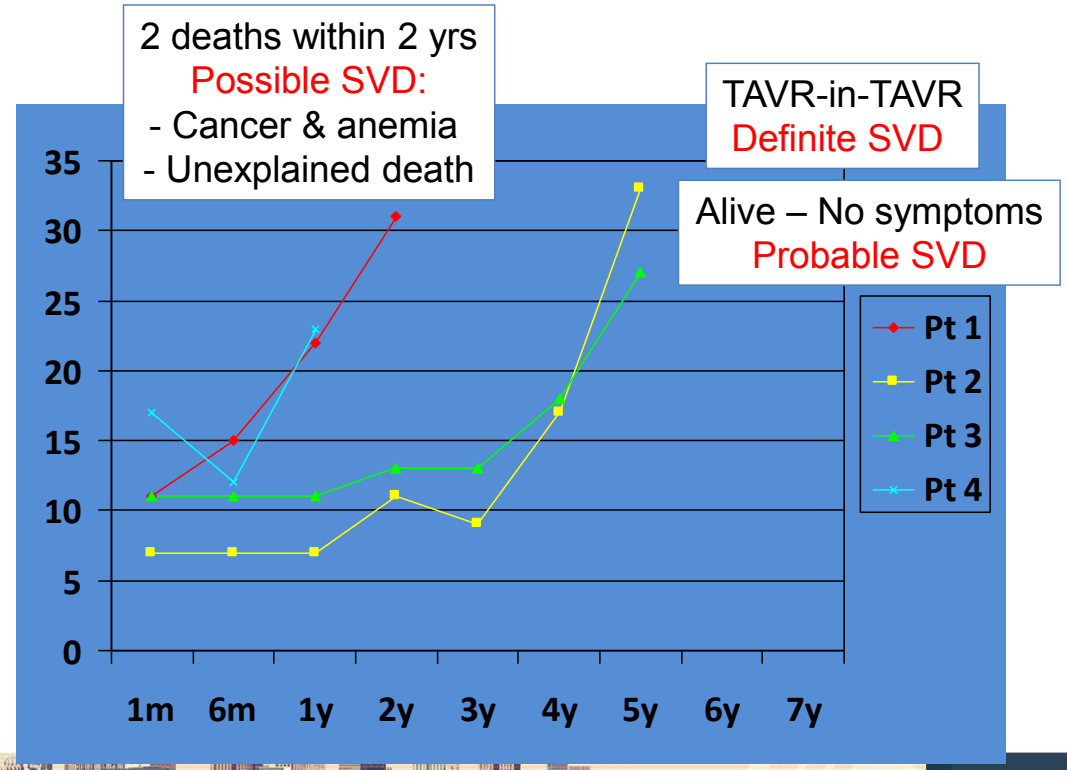
Freedom from SVD in Rouen - Using cardiac surgeon's definition

- 6 patients were excluded (lost FU)
- Last available echo date was used in this actuarial analysis

- No patient with mean GR > 40mmHg
- Only 1 patient had definite SVD: severe AR + elevated gradient, leading to re-intervention (TF-TAVR in TA-TAVR)



Our 4 cases according to this definition



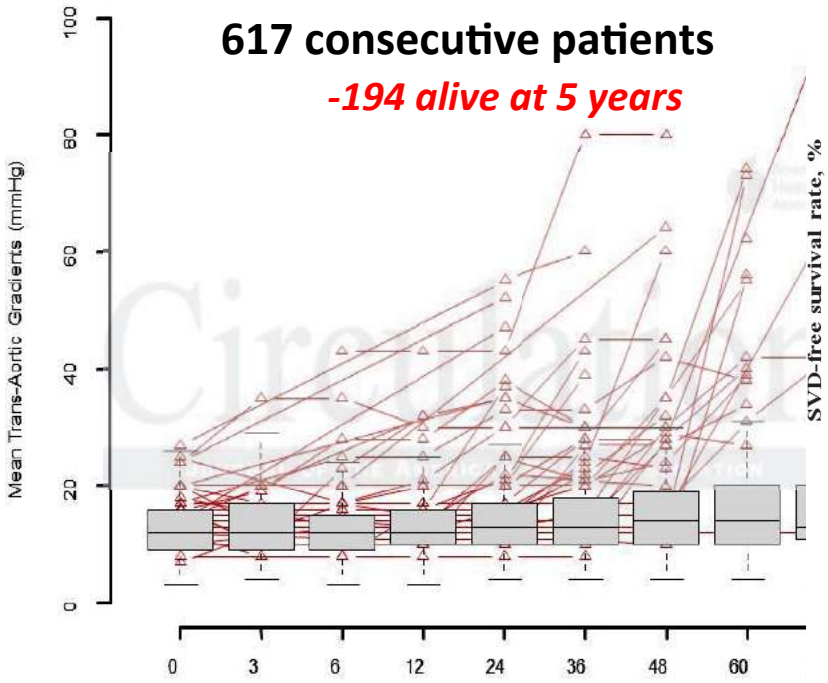
Early Structural Valve Deterioration of Mitroflow Aortic Bioprosthesis: Mode, Incidence and Impact on Outcome in a Large Cohort of Patients

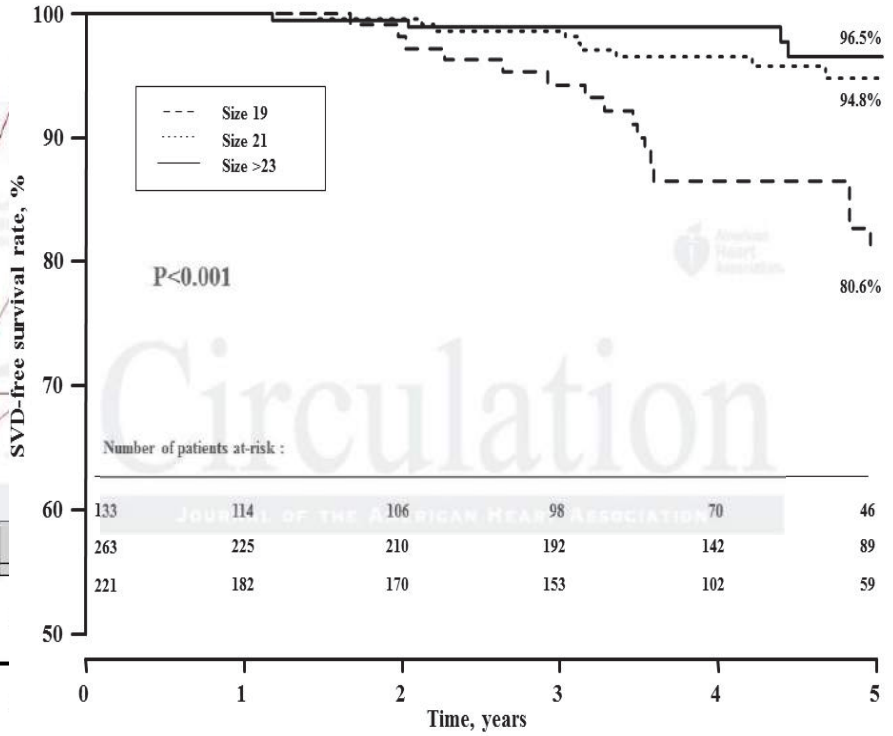
Thomas Sénage, Thierry Le Tourneau, Yohann Foucher, Sabine Pattier, Caroline Cueff, Magali Michel, Jean-Michel Serfaty, Hubert François Carton, Christian Perigaud, Antoine Mugniot, Ousama Al Habash, Olivier Baron and Jean Christian Roussel

Circulation 2014

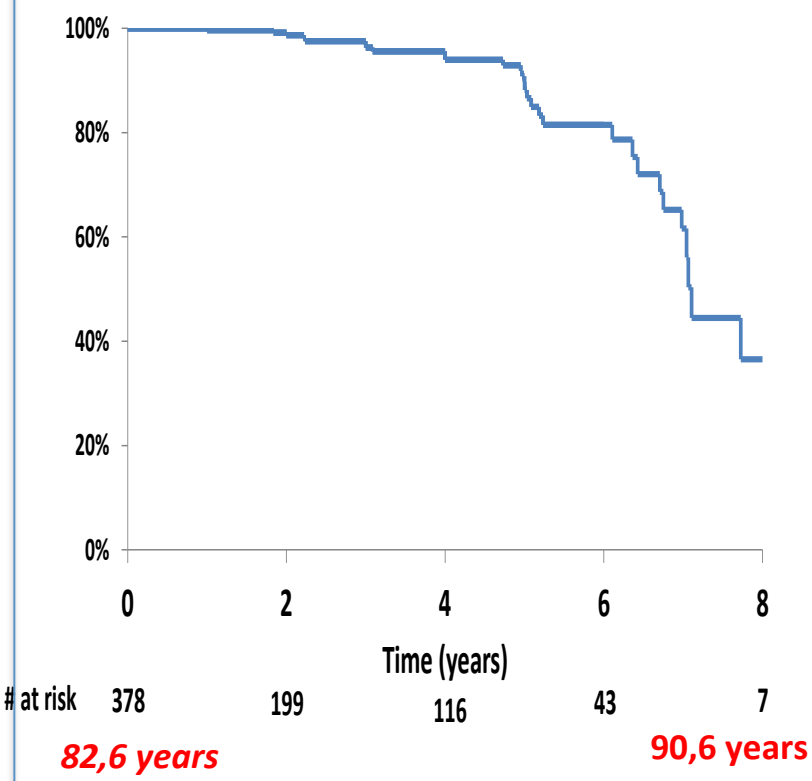
617 consecutive patients

-194 alive at 5 years





2016 euroPCR Freedom from THV degeneration



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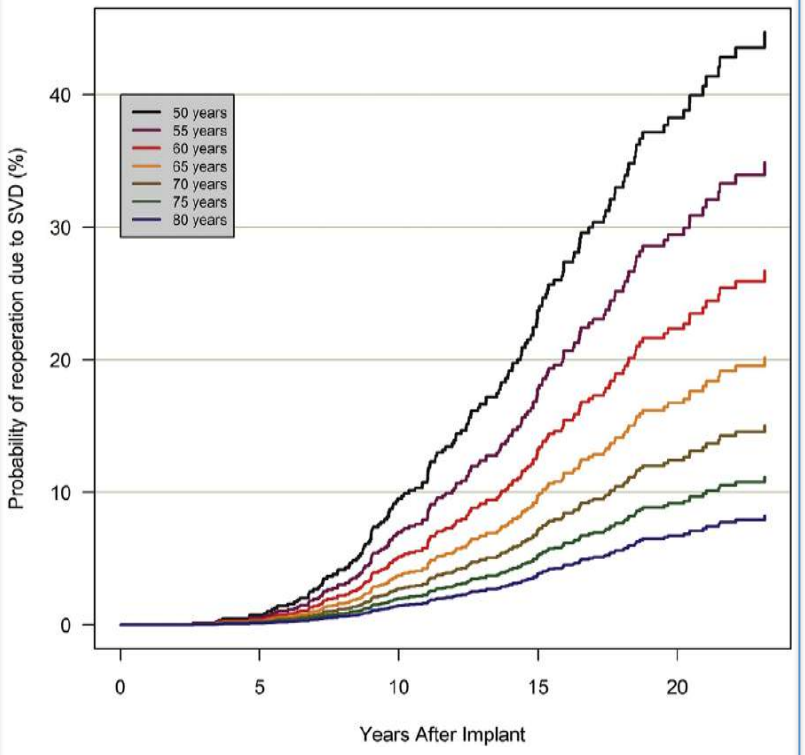
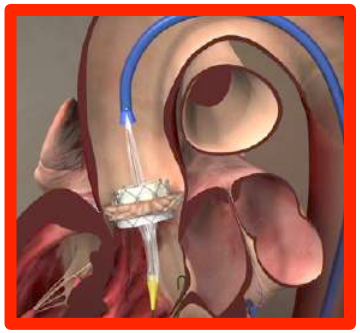


Weak Follow-up ➔ Real Signal on Durability



~~TAVI only for High Risk Patients ?~~

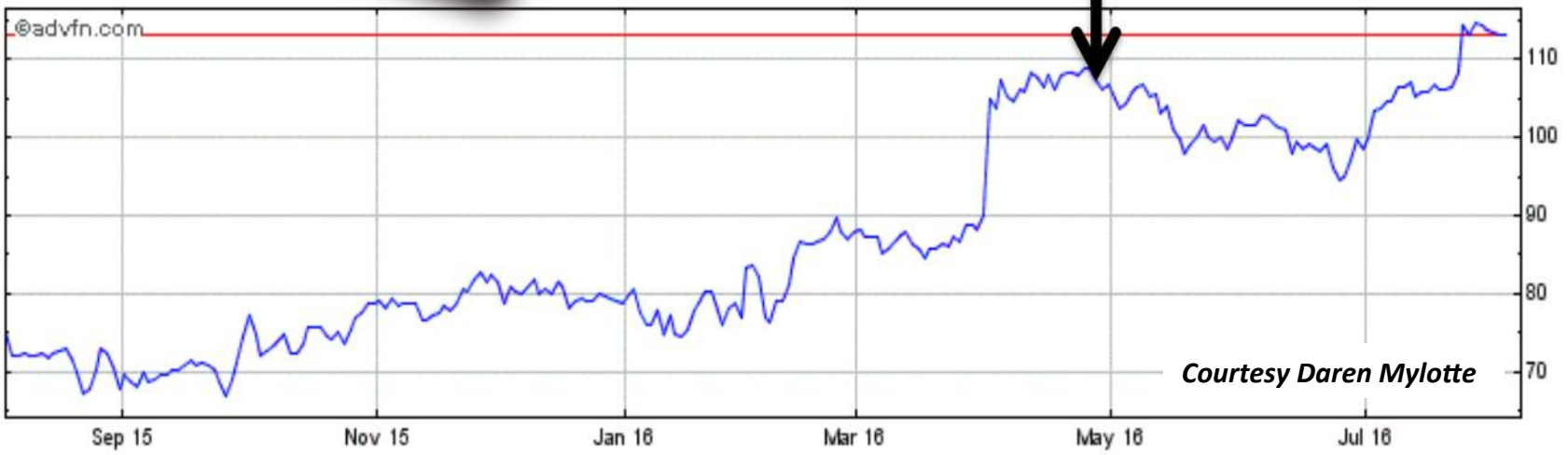
~~TAVI only for elderly Patients ?~~

life expectancy above 5 years ? 10 years ?

L'espérance de vie d'un homme de 87 ans est de 5 ans (5,03).
L'espérance de vie d'une femme de 87 ans est de 6 ans et 4 mois (6,3).

Edwards Lifesciences Stock Price

EuroPCR 2016



LONGEVITY

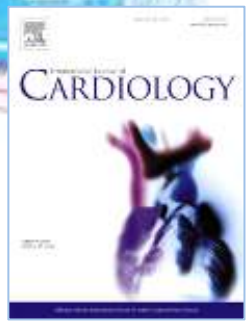
5 years

LIFE Expectancy

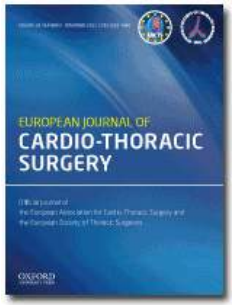
13 years

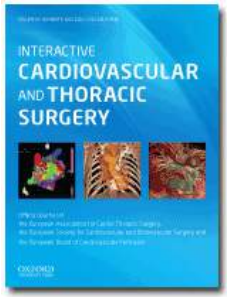
Source: Insee 2013

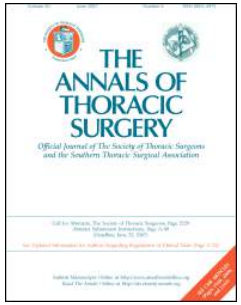
75. L'espérance de vie d'un homme de 75 ans est de 11 ans et 4 mois (11,35).
L'espérance de vie d'une femme de 75 ans est de 14 ans et 3 mois (14,28).



Société Française de Cardiologie







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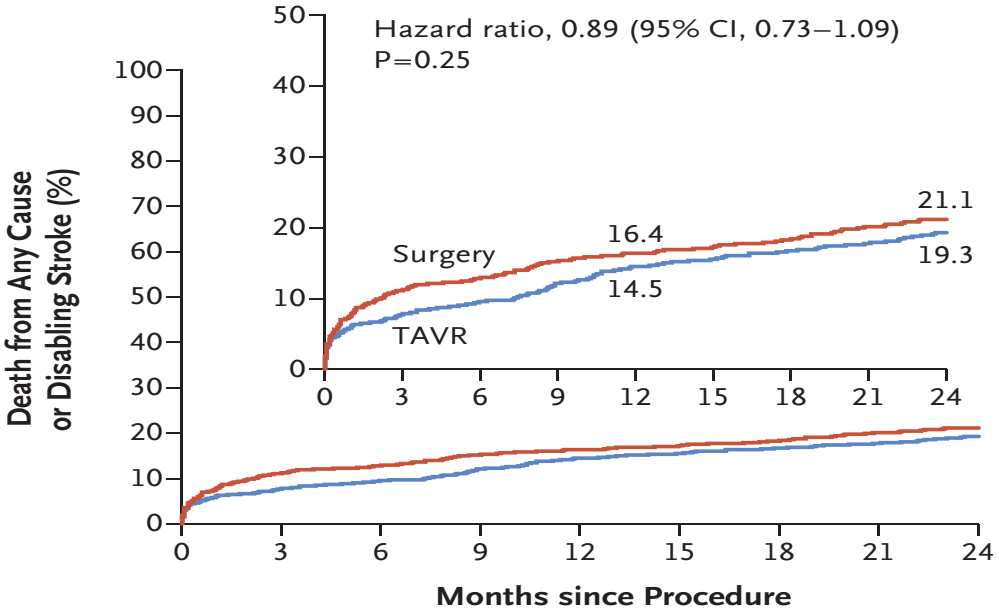
Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D.,



No. at Risk									
TAVR	1011	918	901	870	842	825	811	801	774
Surgery	1021	838	812	783	770	747	735	717	695

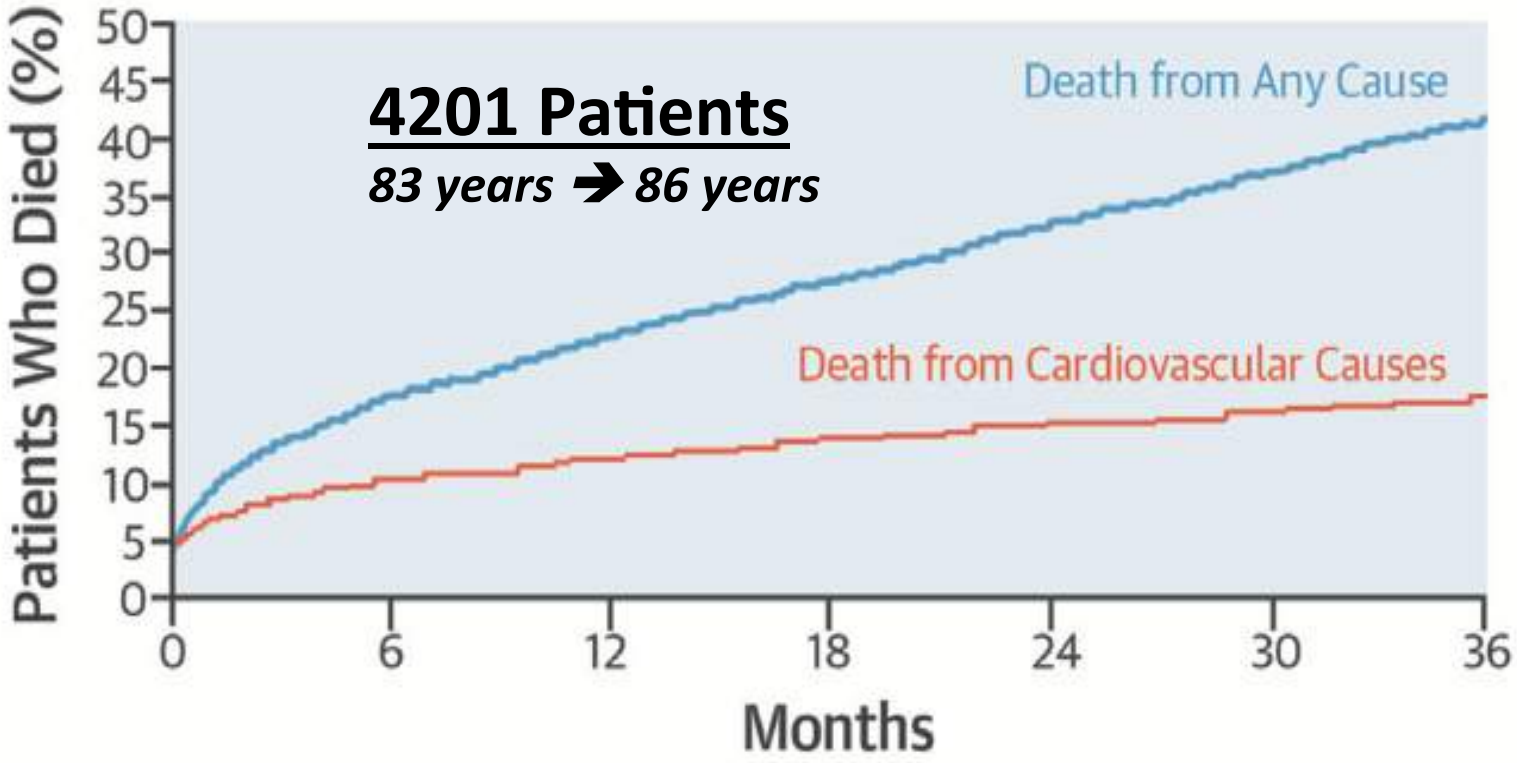
2016 euroPCR

Methods

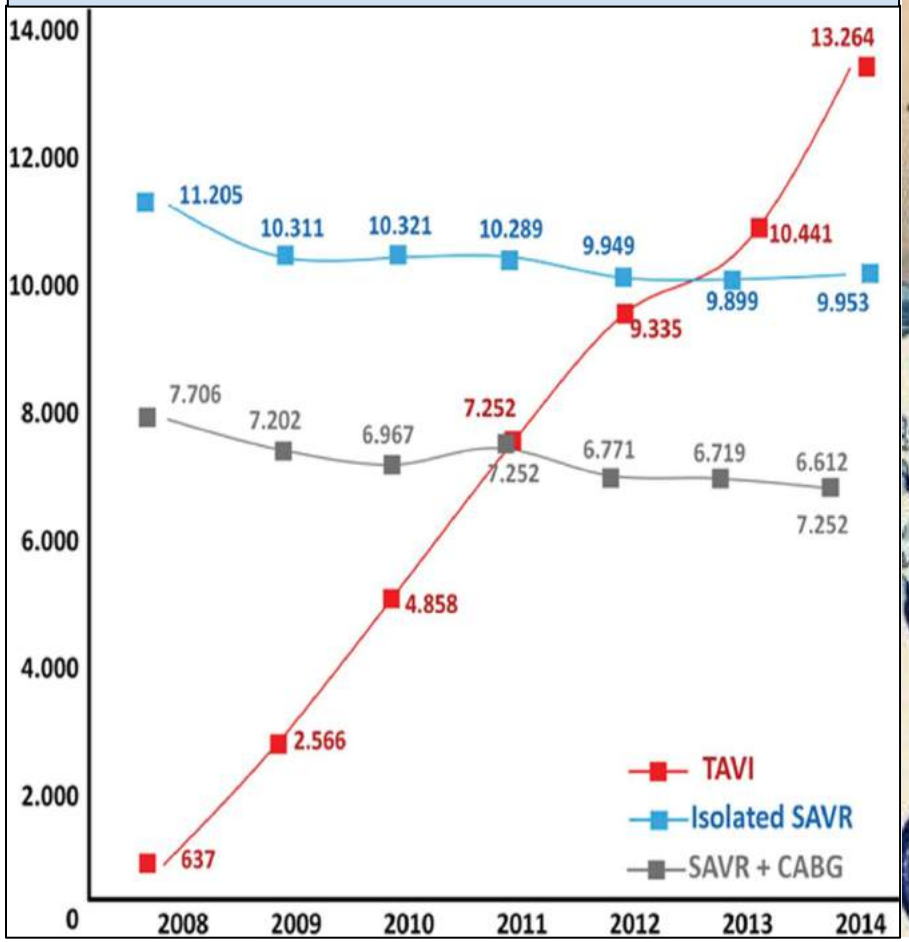
- The analysis consisted of patients that underwent TAVI more than 5 years ago: April 2002- April 2011 (range of time since TAVI: 5-14 years).
- **Sites**:
  - St. Paul's Hospital. Vancouver, Canada
  - Hôpital Charles Nicolle. Rouen, France
- **Inclusion Criteria:**
  - Patients that underwent TAVI before May 2011.
  - Balloon-expandable devices (Cribier Edwards, Edwards SAPIEN, SAPIEN XT).
- **Exclusion criteria:**
  - More than one THV implanted in the aortic position.
  - THV used to treat a failed surgical valve (valve-in-valve).
  - Device failure ≤ 30 days after TAVI (≥ moderate stenosis OR regurgitation).
  - Patient mortality within ≤ 30 days after TAVI.
  - Infective endocarditis in the aortic position after TAVI.

Late Outcomes of Transcatheter Aortic Valve Replacement in High-Risk Patients

The FRANCE-2 Registry

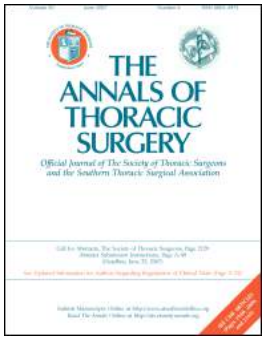


Germany 2008 → 2014



Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

The Lancet. Volume 387, No. 10034, p2218–2225, 28 May 2016



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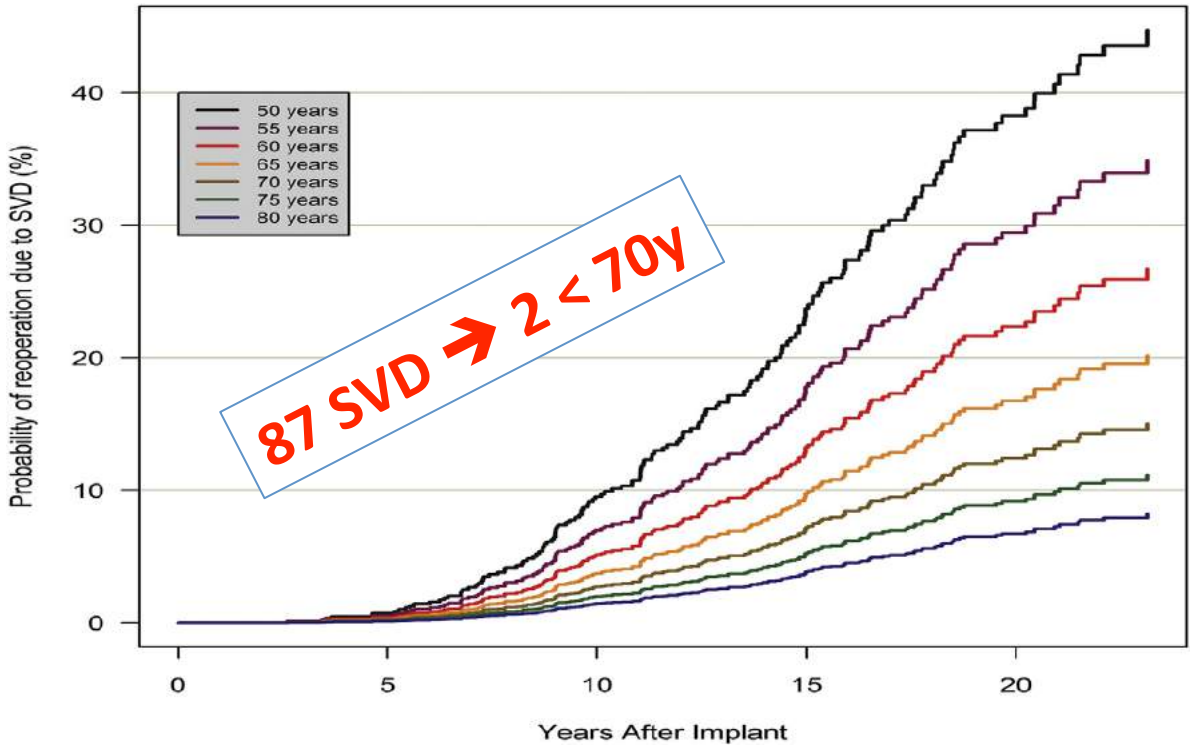
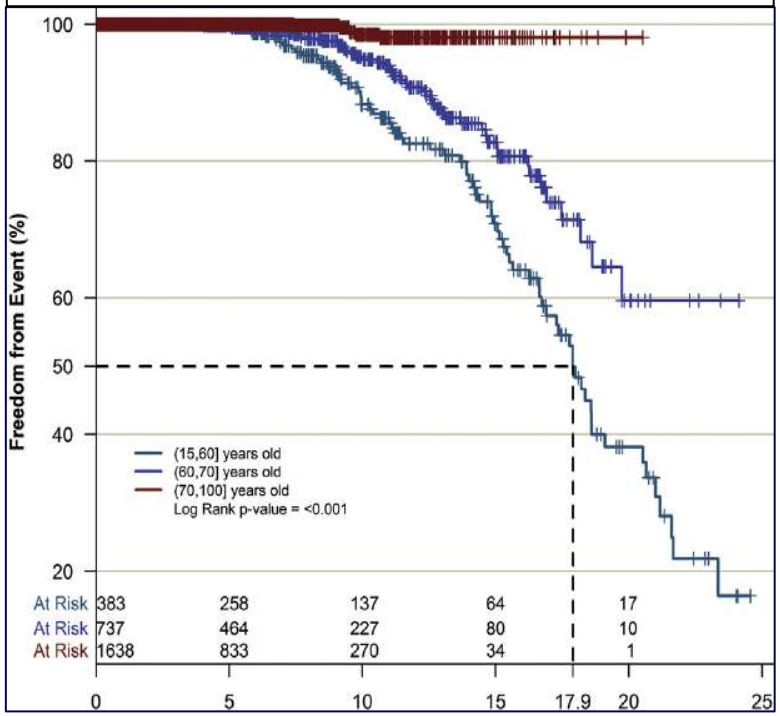


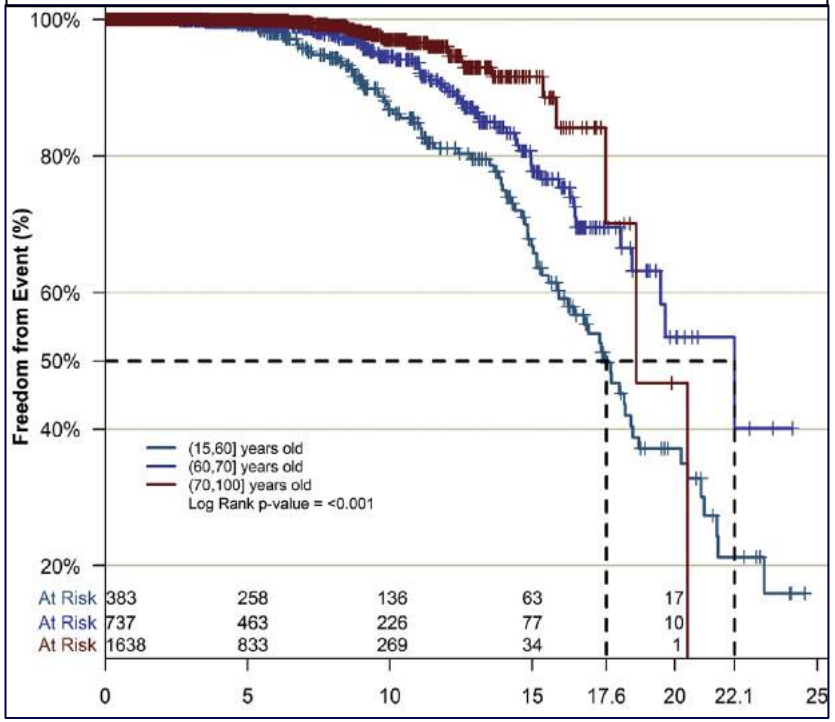
5) LONGEVITY OF BIOLOGICAL PROSTHESES

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

Freedom from reoperation



Freedom from SV Deterioration



Structural valve deterioration is the Achille's heel of bioprostheses

In 2016, 5 issues deserve a particular attention and represent the matter of debate to limit the enlargement of the indications

1) ~~Neurologic Complications~~

2) ~~Vascular Complications~~

3) ~~Residual Aortic Regurgitation~~

4) Pacemaker Implantation

5) Durability of the biological prostheses


IMPAIR