SOLACI CACI`17 ARGENTINA
In partnership with tct

HOSPITAL ITALIANO
de Buenos Aires
Instituto de Medicina Cardiovascular

TAVI:
Clinical evidence of long term durability of prosthetic valves and Leaflets Thrombosis

Carla Agatiello, MD
Interventional Cardiology
Hospital Italiano de Buenos Aires

SOLACI CACI

Potencial conflictos de interés

Nombre: Carla Agatiello

- **Proctor para Symetis** (ACURATE TA, Transapical)

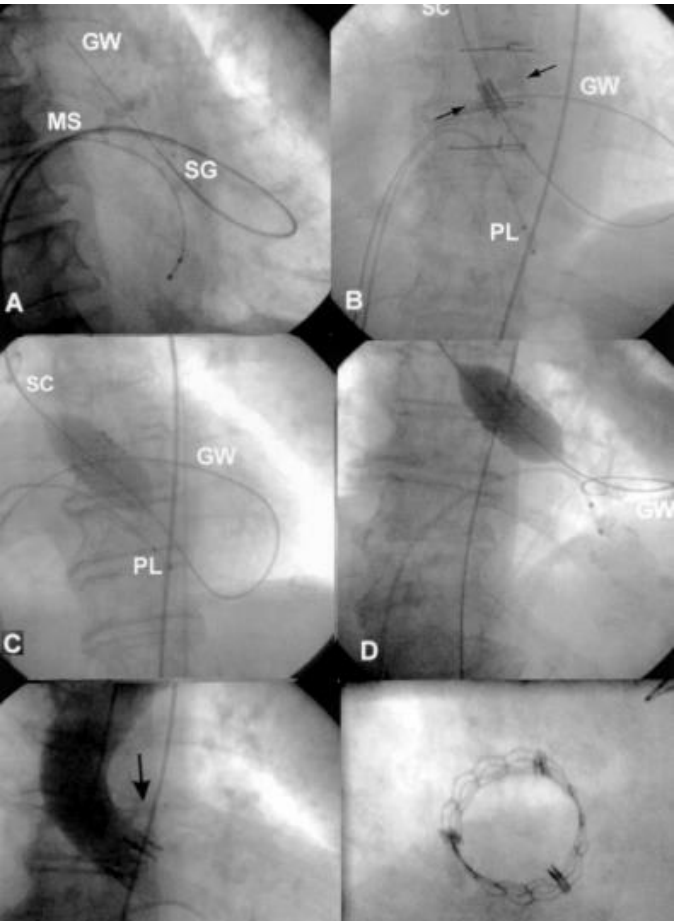
EXPEDITED REVIEW

Treatment of Calcific Aortic Stenosis With the Percutaneous Heart Valve

Mid-Term Follow-Up From the Initial Feasibility Studies: The French Experience

Alain Cribier, MD, FACC,* Helene Eltchaninoff, MD,* Christophe Tron, MD,* Fabrice Bauer, MD,* Carla Agatiello, MD,* Deborah Nercolini, MD,* Sydney Tapiero, MD,* Pierre-Yves Litzler, MD,† Jean-Paul Bessou, MD,† Vasilis Babaliaros, MD*

Rouen, France



J Am Coll Cardiol 2006;47:1214 –23

15años

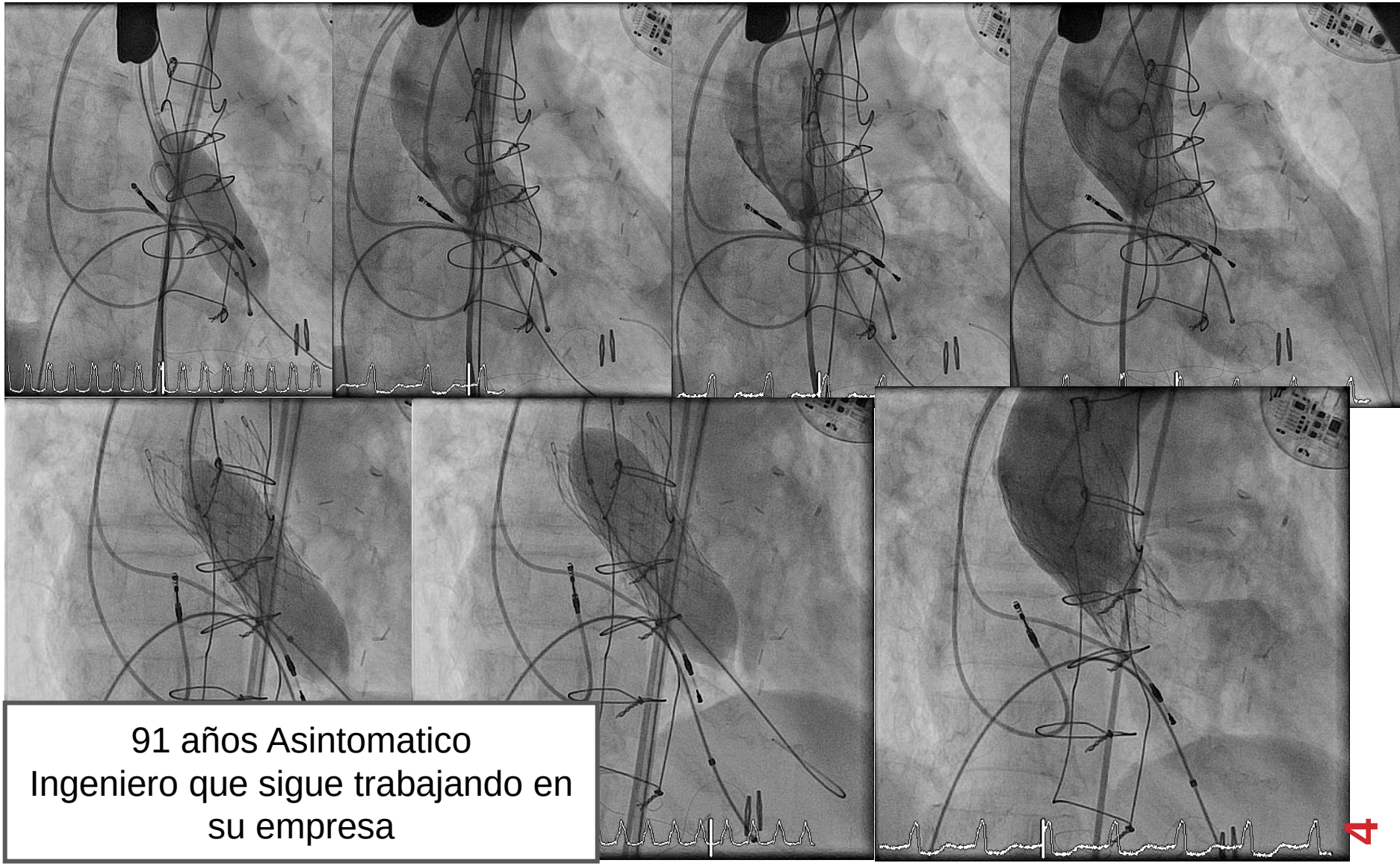
TAVI MINIMALISTA

- Sedación
- Corta estadía hospitalaria
- Ecografia transtoracica
- Descomplejizar TAVI
- Costo efectivo

(J Am Coll Cardiol Intv 2014;7:898–904)

1ER CASO TAVI ARGENTINA
8 AÑOS

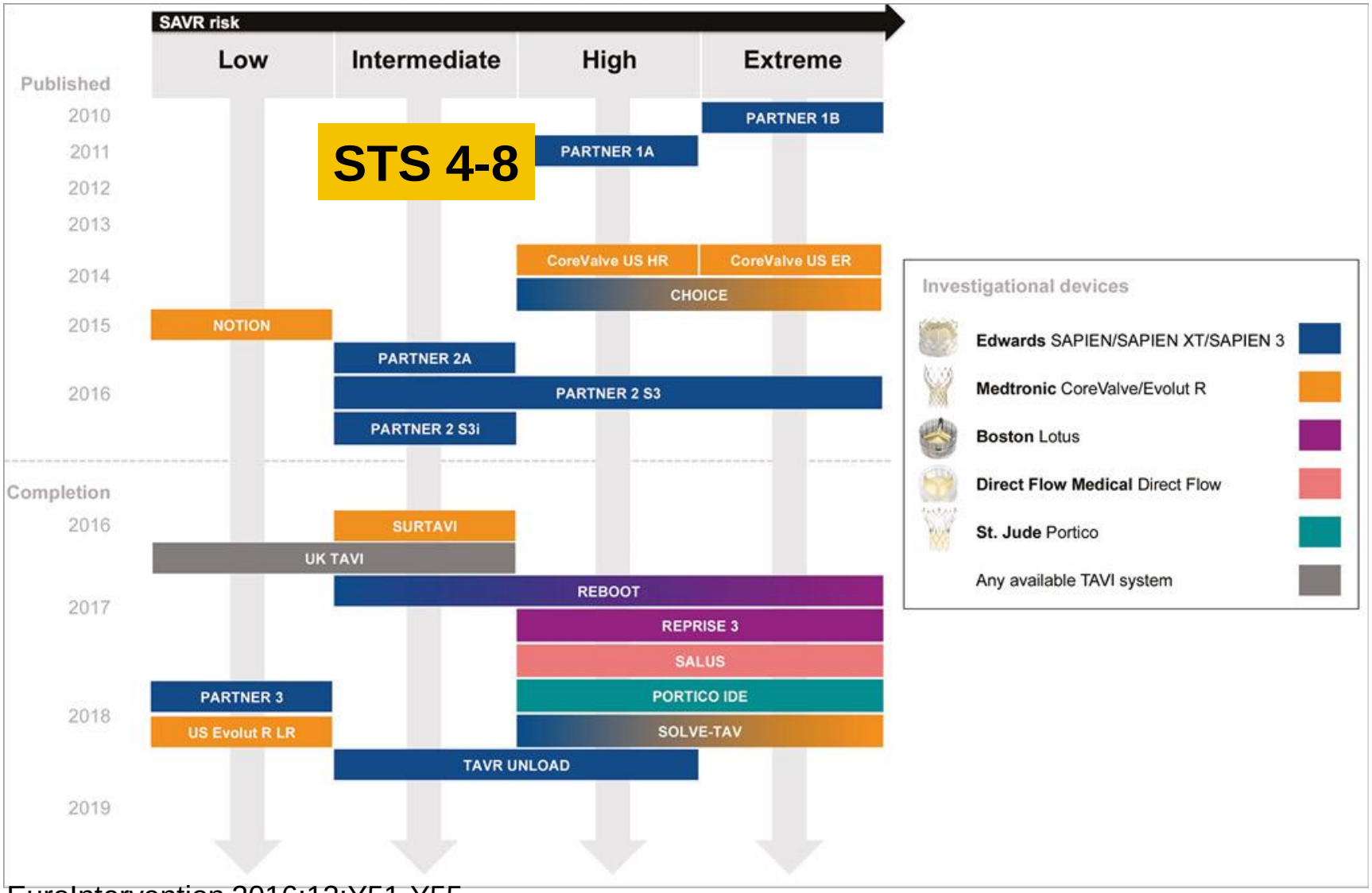
HOSPITAL ITALIANO
de Buenos Aires
Instituto de Medicina Cardiovascular



91 años Asintomatico
Ingeniero que sigue trabajando en su empresa

TAVI EN RIESGO INTERMEDIO: EVIDENCIA

HOSPITAL ITALIANO
de Buenos Aires
Instituto de Medicina Cardiovascular



EuroIntervention 2016;12:Y51-Y55

Upcoming TAVI trials: rationale, design and impact on clinical practice

Seguimiento post TAVI

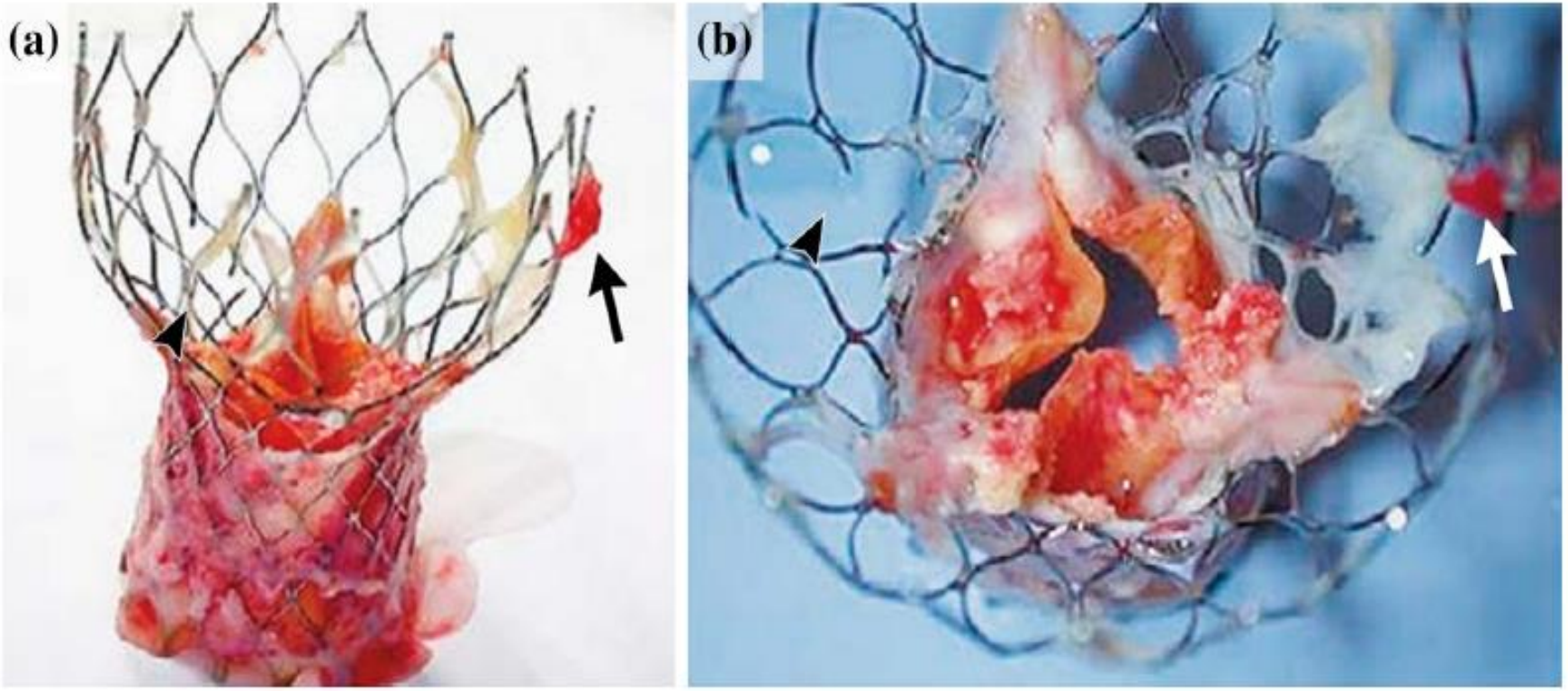
Inoperable

Operable

«Futility»

- **Tiempo de Antigregacion:**
  - 3-6 meses AAS + clopidogrel
  - ACO+ clopidogrel
- **Ecocardiograma Doppler**: deacuerdo guías
- **Clínico**

Deterioro Valvular postTAVI



Falla de bioprotesis : Opción V in V

Wear and tear

Calcification

Pannus

Endocarditis

Thrombus

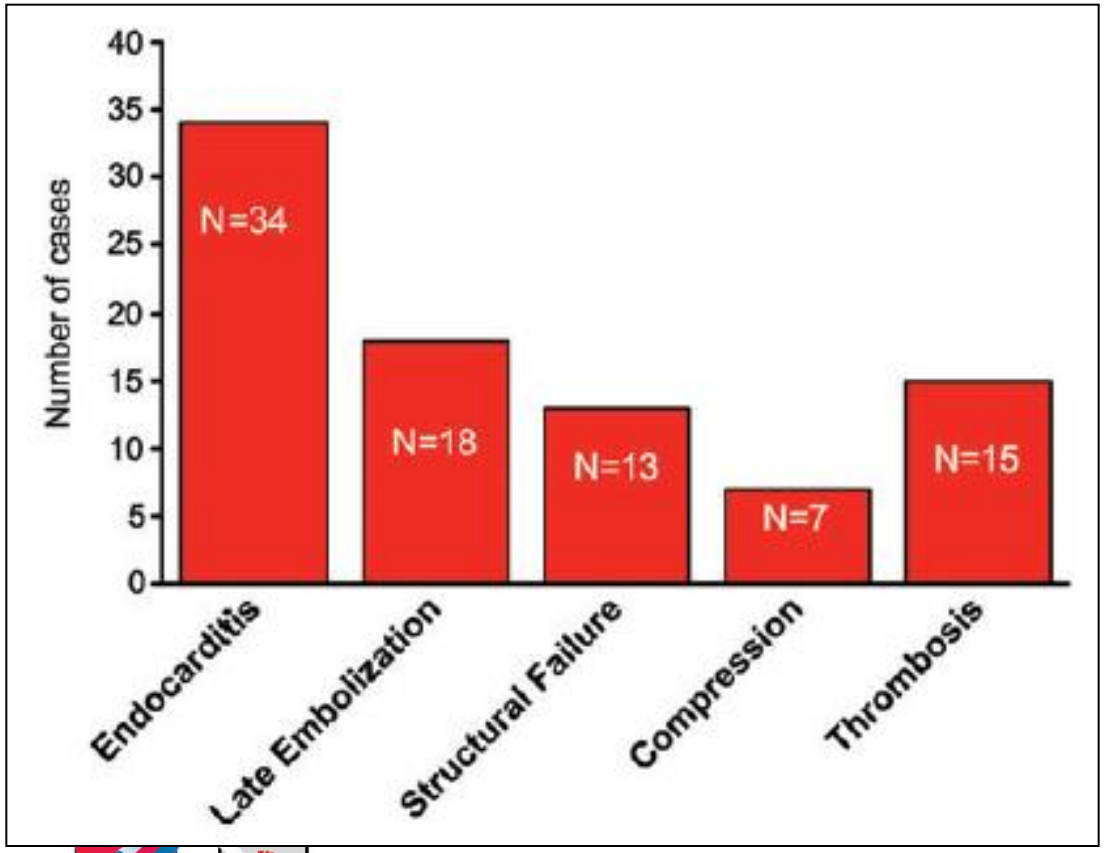
Wear and tear and calcification are the most common reasons for bioprosthetic valve failure

- 20% de deterioro estructural post cirugia valvular, a 10 años evidenciado por seguimiento por ETE
- Reoperaciones del 30-50% a 15 años

Piazza et al.JACC:Vol4;N7, 2011

Transcatheter heart valve failure: a systematic review

Darren Mylotte[1,2], Ali Andalib[1], Pascal Thériault-Lauzier[1], Magdalena Dorfmeister[3], Mina Girgis[1], Waleed Alharbi[1], Michael Chetrit[1], Christos Galatas[1], Samuel Mamane[1], Igal Sebag[4], Jean Buithieu[1], Luc Bilodeau[1], Benoit de Varennes[5], Kevin Lachapelle[5], Ruediger Lange[3], Giuseppe Martucci[1], Renu Virmani[6], and Nicolo Piazza[1,3]*

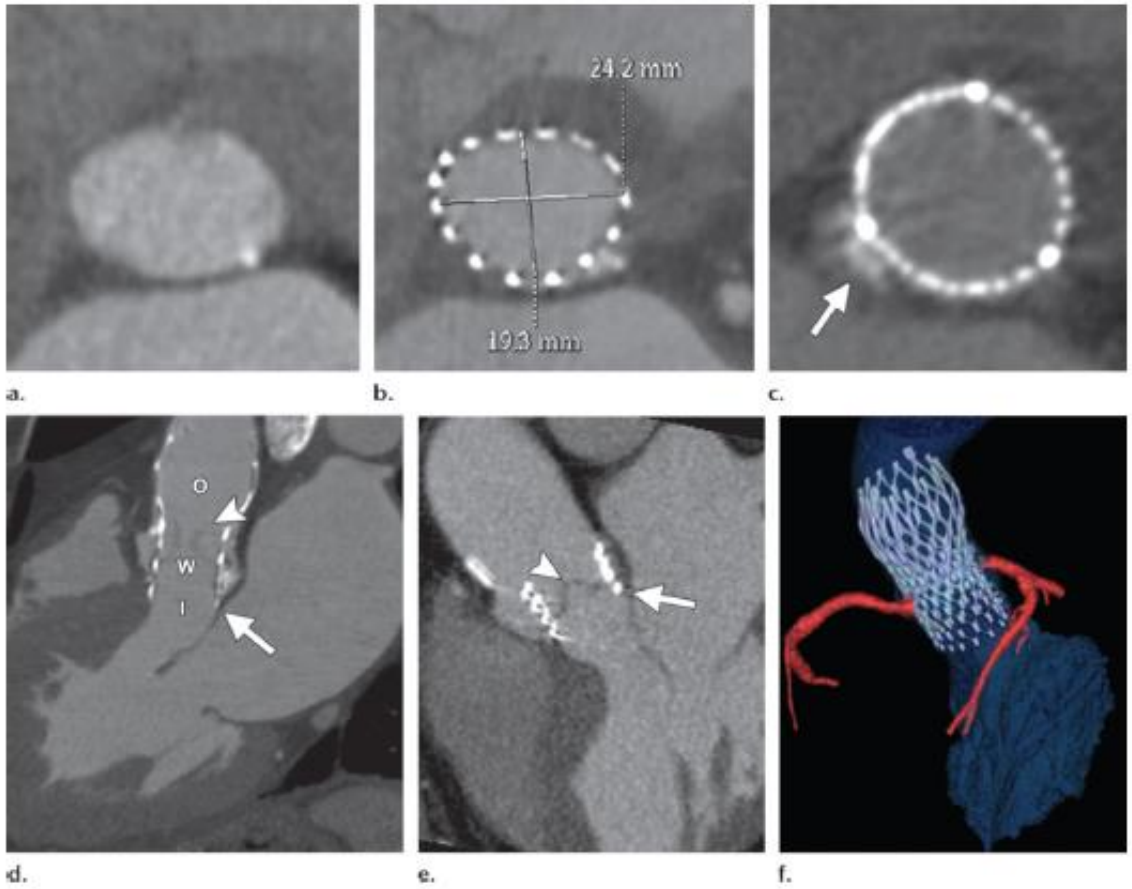


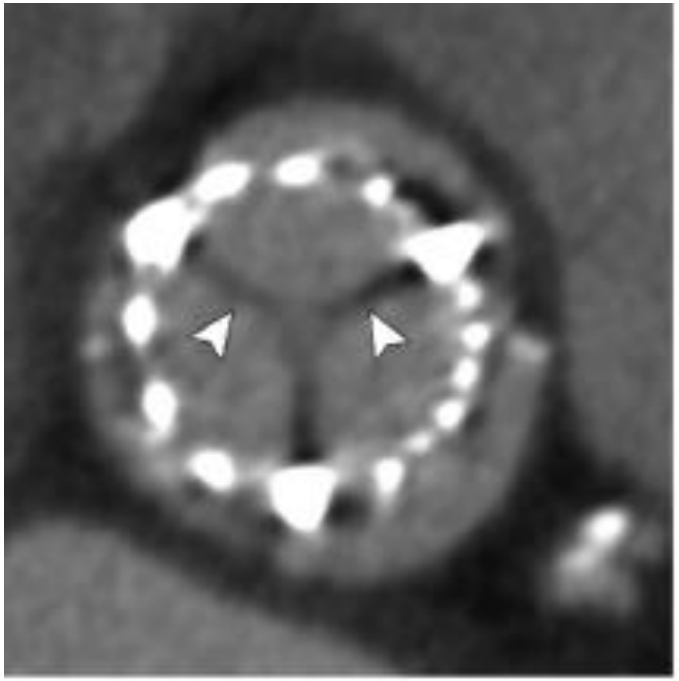
15 cases of TAVR valve thrombosis reported from 12/02-03/14

14 symptomatic
1 subclinical

Mylotte D. et al. European Heart Journal 2015

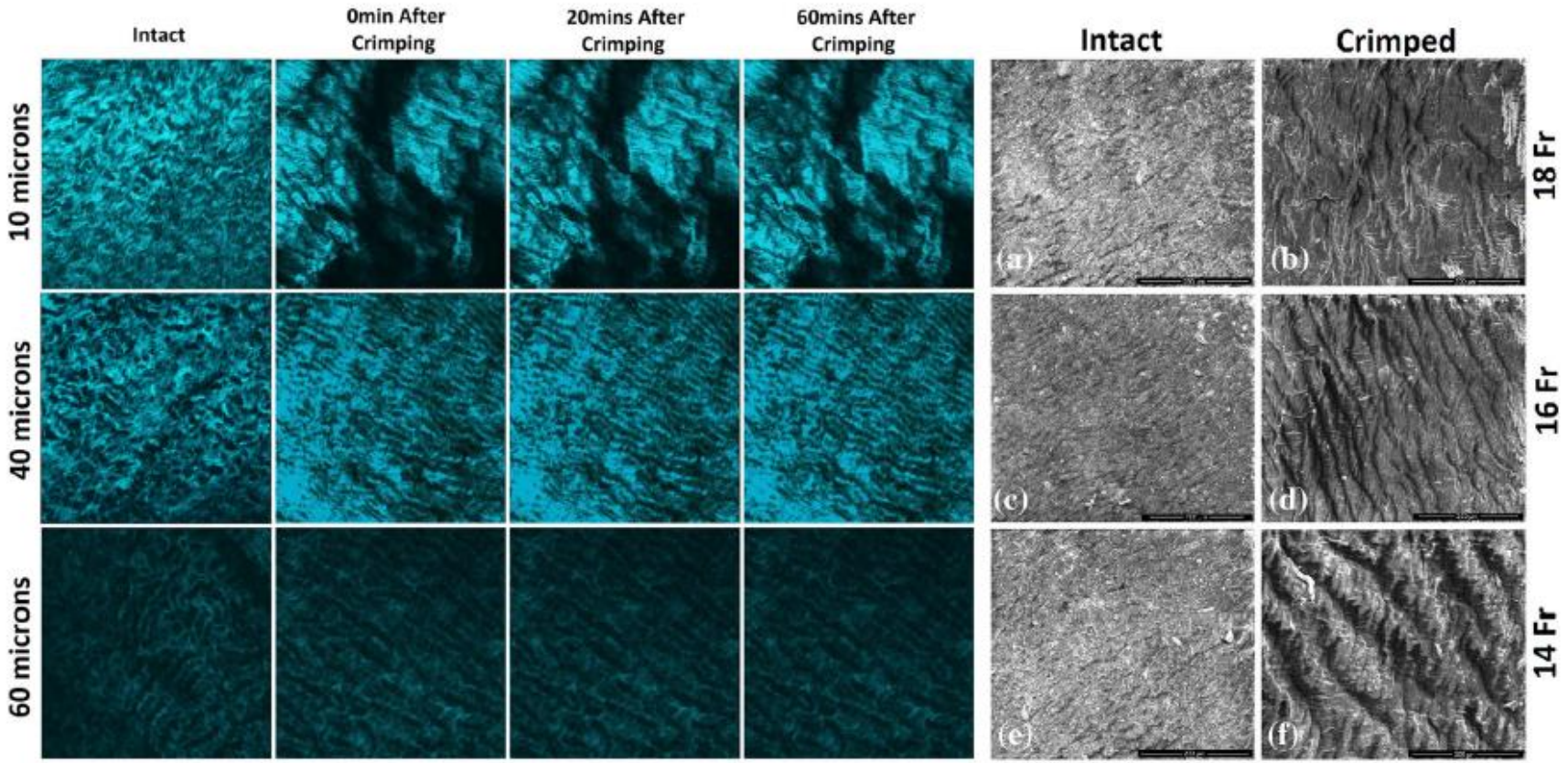
Estructura by CT post TAVI Follow up





Transcatheter Aortic Valve Replacement: Postoperative CT Findings of Sapien and CoreValve Transcatheter Heart Valves[1]

Tejido post crimping

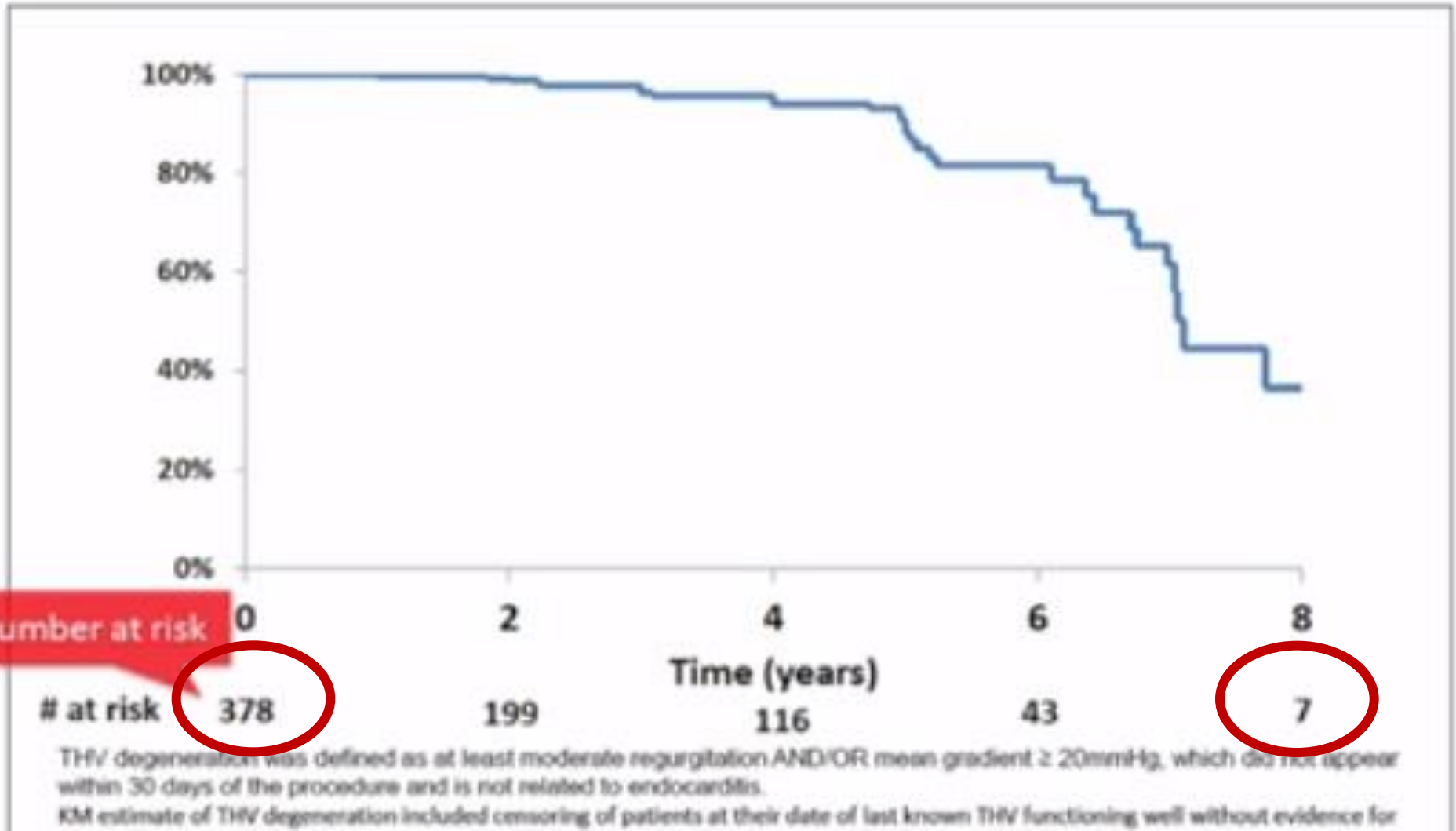


Ruptura de elastina en superficie y profundidad de leaflet post crimping

Lashkmi Dasi et al. On the mechanism of TAVR.Annals of Biomedical Engineering 2017;45:310-331

Rouen Vancouver Experience

Combined Vancouver-Rouen Experience



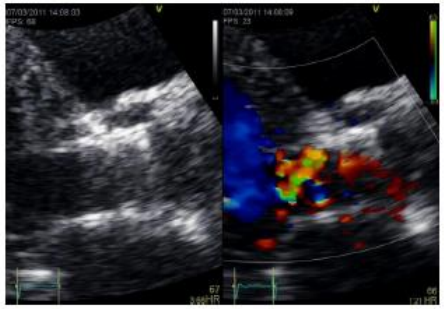
THV degeneration was defined as at least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.

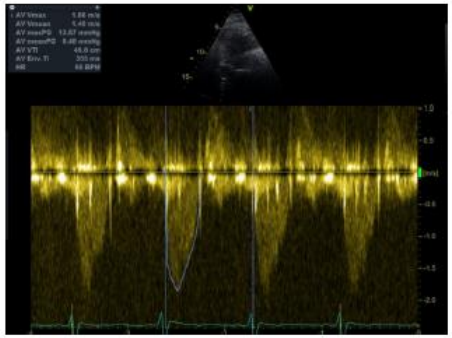
KM estimate of THV degeneration included censoring of patients at their date of last known THV functioning well without evidence for

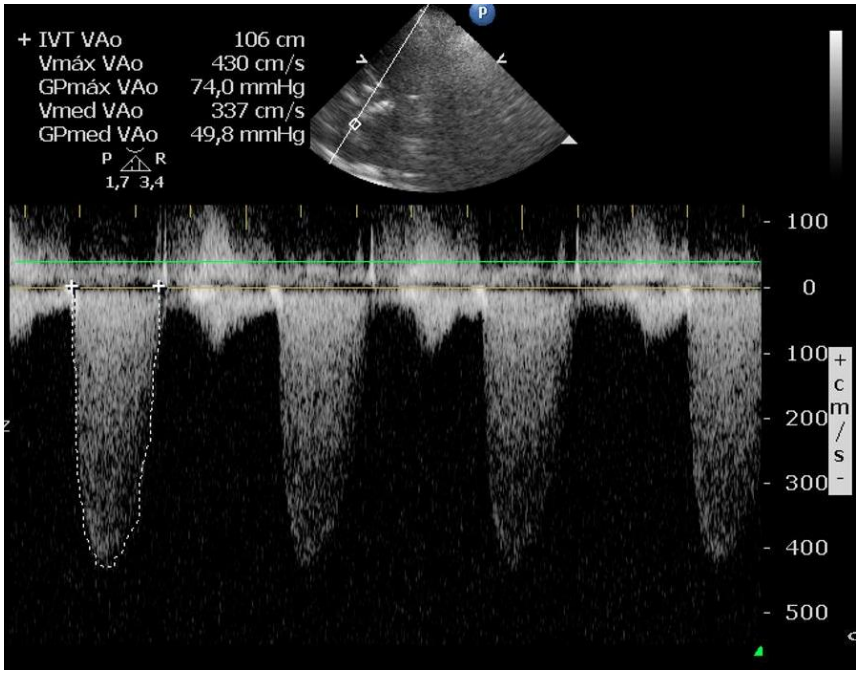
Disfunción TAVI(VHD)

Definicion :

Incremento de >10mmhg en gradiente medio transprotesico dentro de primer año con respecto al alta



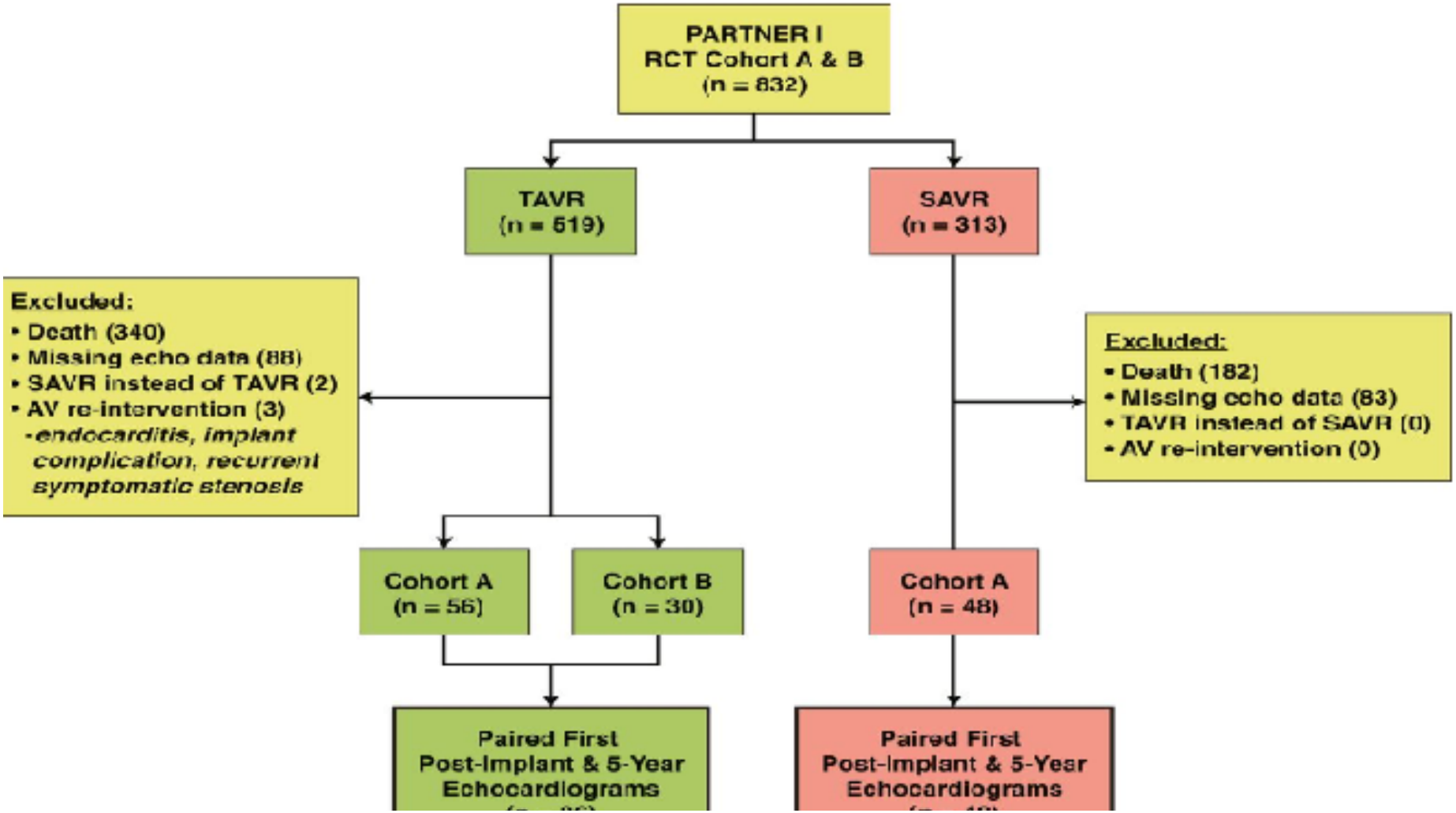




Valor normal: 8-10mmHg

Valor VHD: 34mmHg

PARTNER 5añosF/U



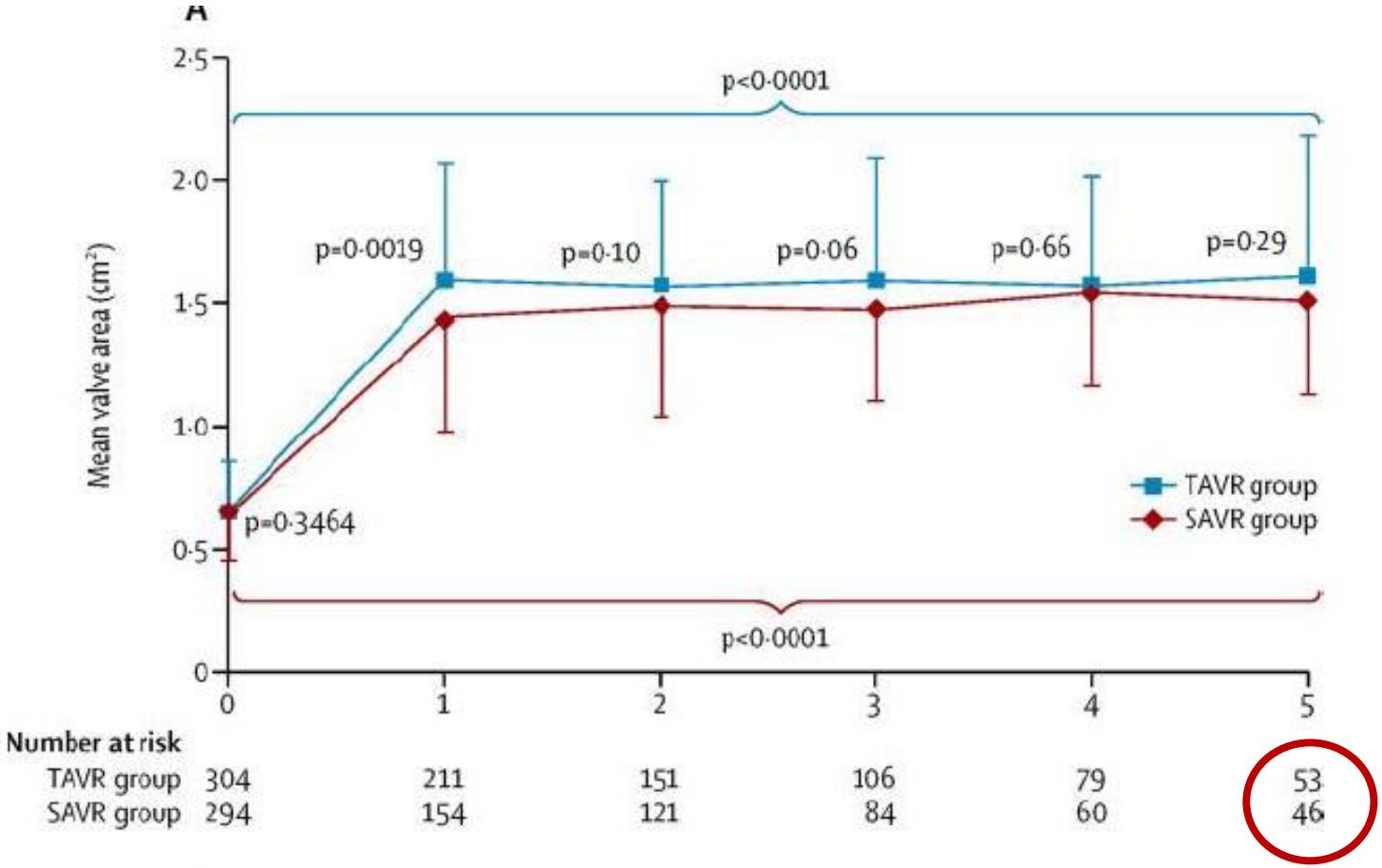
Long-Term Valve Performance of TAVR and SAVR

A Report From the PARTNER I Trial

JACC 2017

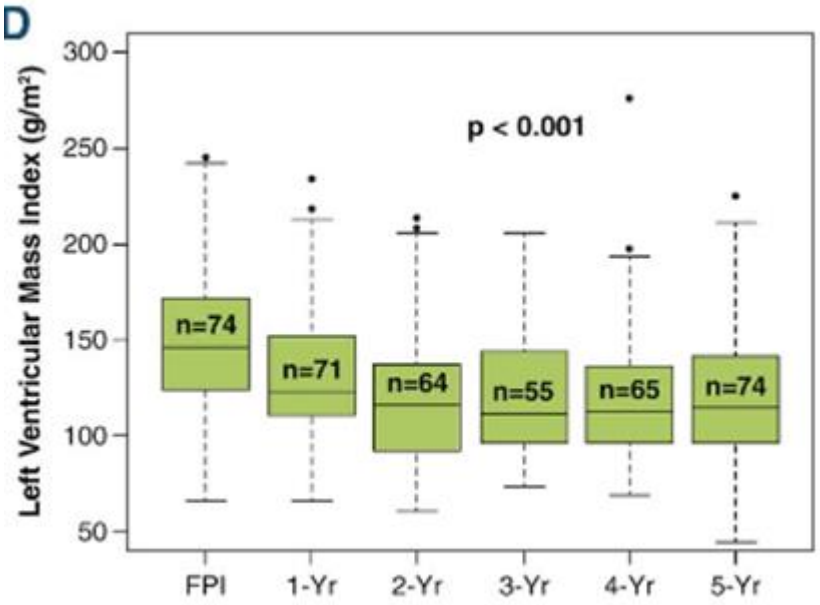
Melissa A. Daubert, Neil J. Weissman, Rebecca T. Hahn, Philippe Pibarot, Rupa Parvataneni, Michael J. Mack, Lars

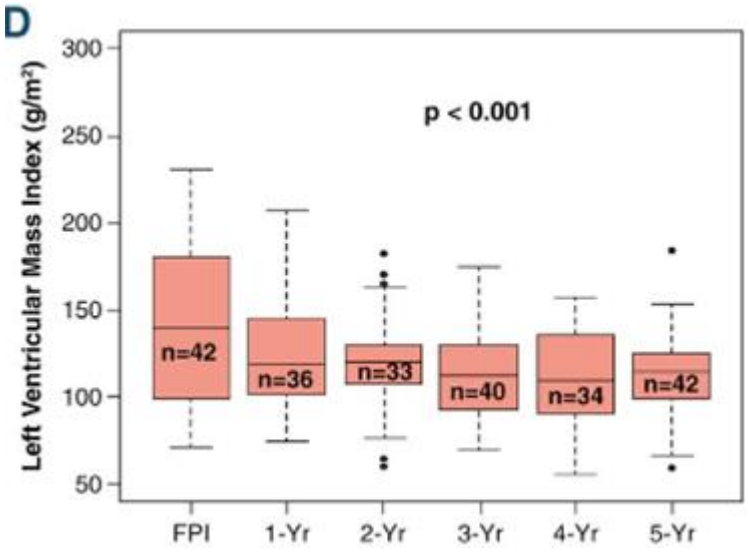
Hemodinamia post TAVI



PARTNER 1-cohort A Mack et al Lancet et al 2015

PARTNER 5añosF/U





Cohorte TAVI **Cohorte SAVR**

Remodelado ventricular

Long-Term Outcomes After Transcatheter Aortic Valve Replacement in High-Risk Patients With Severe Aortic Stenosis

The U.K. Transcatheter Aortic Valve Implantation Registry

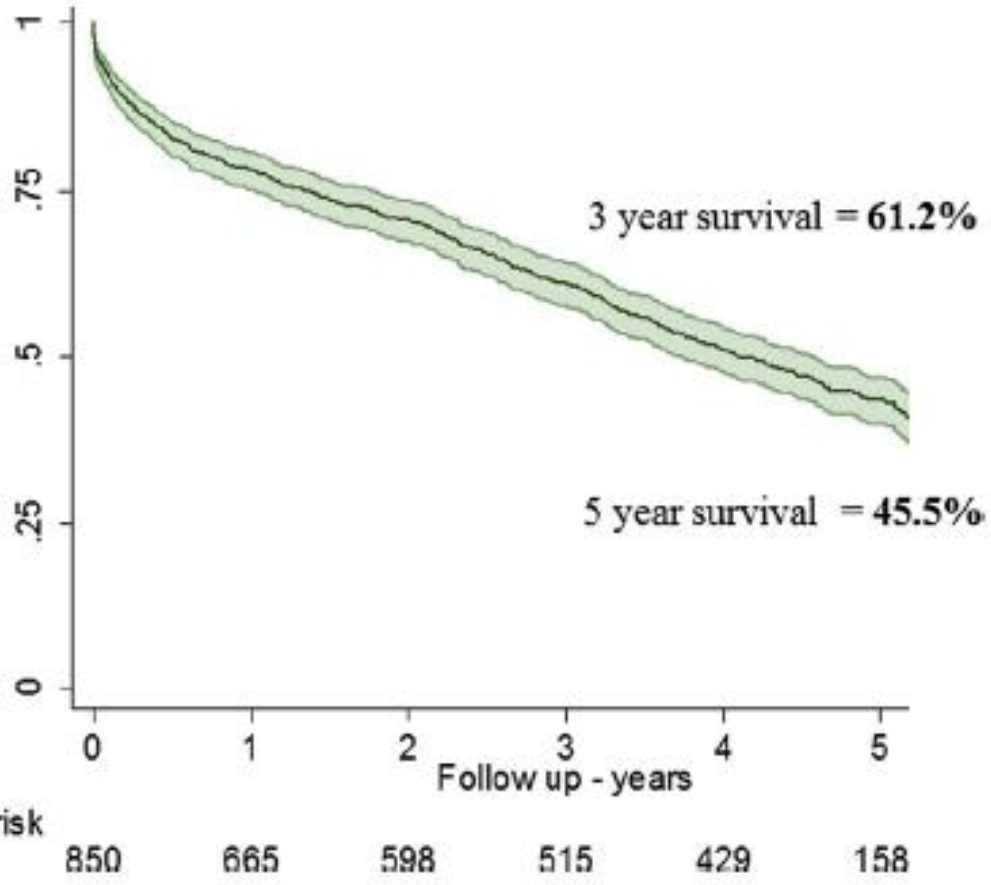
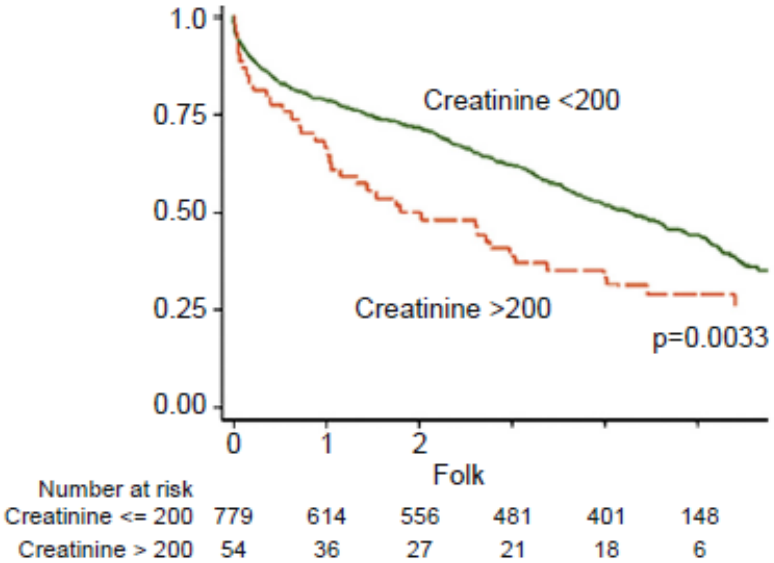
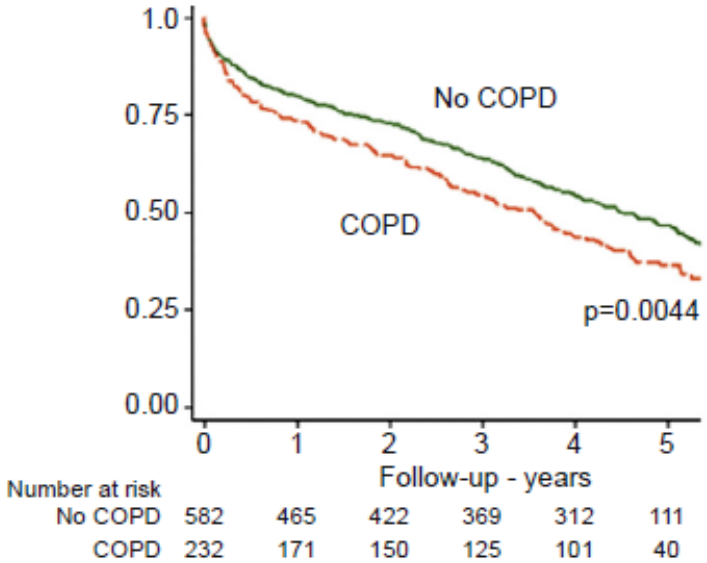


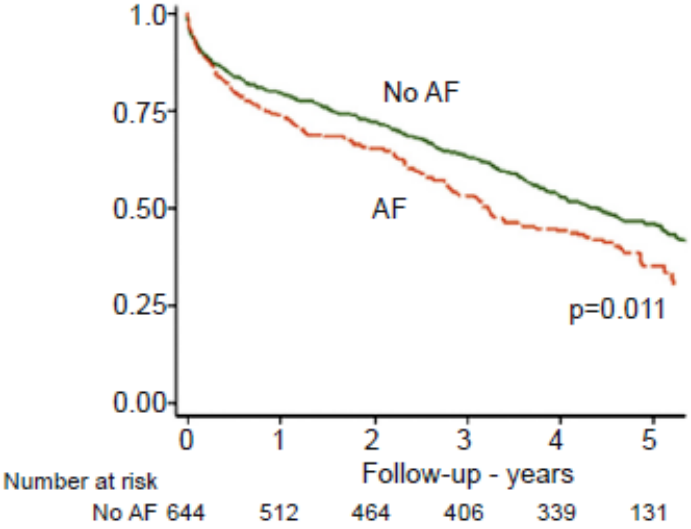
TABLE 1 Baseline Demographics and TAVR Procedure (N = 850)

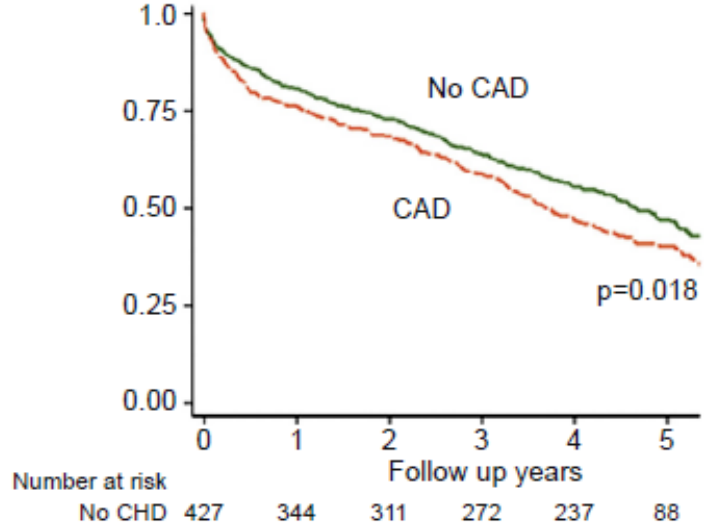
Age, yrs	82 ± 7
Male	442/850 (52.0)
Coronary artery disease	381/808 (47.2)
Previous cardiac surgery	248/833 (30.4)
Peripheral vascular disease	238/812 (29.8)
COPD	232/814 (28.5)
Atrial fibrillation	202/846 (23.9)
Diabetes	193/841 (22.9)
Creatinine >200 μg/mmol	54/833 (6.5)
NYHA functional class I/II	197/846 (23.3)
NYHA functional class III/IV	649/846 (76.7)
LVEF ≥50%	549/845 (65.0)
LVEF 30%–49%	223/845 (26.4)
LVEF <30%	73/845 (8.6)
Aortic valve peak gradient, mm Hg	81 ± 27
CoreValve*	442/843 (52.5)
SAPIEN valve†	401/846 (47.5)
Transfemoral route	581/850 (68.4)
Nontransfemoral route	269/850 (31.6)

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 8, NO. 5, 2015
APRIL 27, 2015:645–53









Duncan *et al.*
Long-Term Outcome After TAVR: The U.K.-TAVI Registry

SOLACI CACI`17 ARGENTINA
In partnership with tct

Long-Term Outcomes After Transcatheter Aortic Valve Implantation

Insights on Prognostic Factors and Valve Durability From the Canadian Multicenter Experience

Causas de Muerte F/U

Table 2 Causes of Death During Follow-Up Period

Cardiac	35 (23.0)
Cardiac failure	23 (15.1)
Sudden death	4 (2.6)
Myocardial infarction	6 (3.9)
Endocarditis	1 (0.7)
Post-mitral replacement	1 (0.7)
Noncardiac	90 (59.2)
Pulmonary failure	41 (26.9)
Kidney failure	12 (7.9)
Stroke	9 (5.9)
Major bleeding	7 (4.6)
Cancer	8 (5.3)
Other*	13 (8.6)
Unknown	27 (17.8)

23% CARDIACA

60% NO CARDIACA

CACI

- Rodés-Cabau et al. JACC 2012:1864 –75

Predictores de Muerte post TAVI

Table 3 Univariate and Multivariate Predictors of Cumulative Late Mortality

	Univariate		Multivariate Model	
Variables	HR (95% CI)	p Value	HR (95% CI)	p Value
Chronic atrial fibrillation	1.53 (1.14–2.06)	0.005	1.39 (1.03–1.89)	0.031
Cerebrovascular disease	1.32 (0.95–1.84)	0.098	—	—
COPD	1.72 (1.27–2.34)	0.0004	1.84 (1.35–2.51)	0.0001
eGFR	1.10 (1.01–1.21)*	0.037	1.12 (1.02–1.23)*	0.024
Frailty	1.37 (0.99–1.88)	0.052	1.41 (1.02–1.96)	0.034
Pulmonary hypertension	1.54 (1.12–2.11)	0.007	—	—

*For each decrease of 10 ml/min. N = 339.
CI = confidence interval; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; HR = hazard ratio.

Table 4 Univariate and Multivariate Predictors of Cumulative Cardiac Mortality

	Univariate		Multivariate Model	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Cerebrovascular disease	1.57 (0.94–2.62)	0.084	—	—
Pulmonary hypertension	2.04 (1.26–3.32)	0.004	1.98 (1.19–3.27)	0.008
eGFR	1.15 (1.02–1.29)*	0.019	1.17 (1.05–1.33)*	0.040
STS-PROM score	1.04 (1.01–1.07)	0.013	—	—

*For each decrease of 10 ml/min.
Abbreviations as in Tables 1 and 3.

Rodés-Cabau et al. JACC 2012:1864 –75

Predictores de Muerte Tardía en TAVI TF

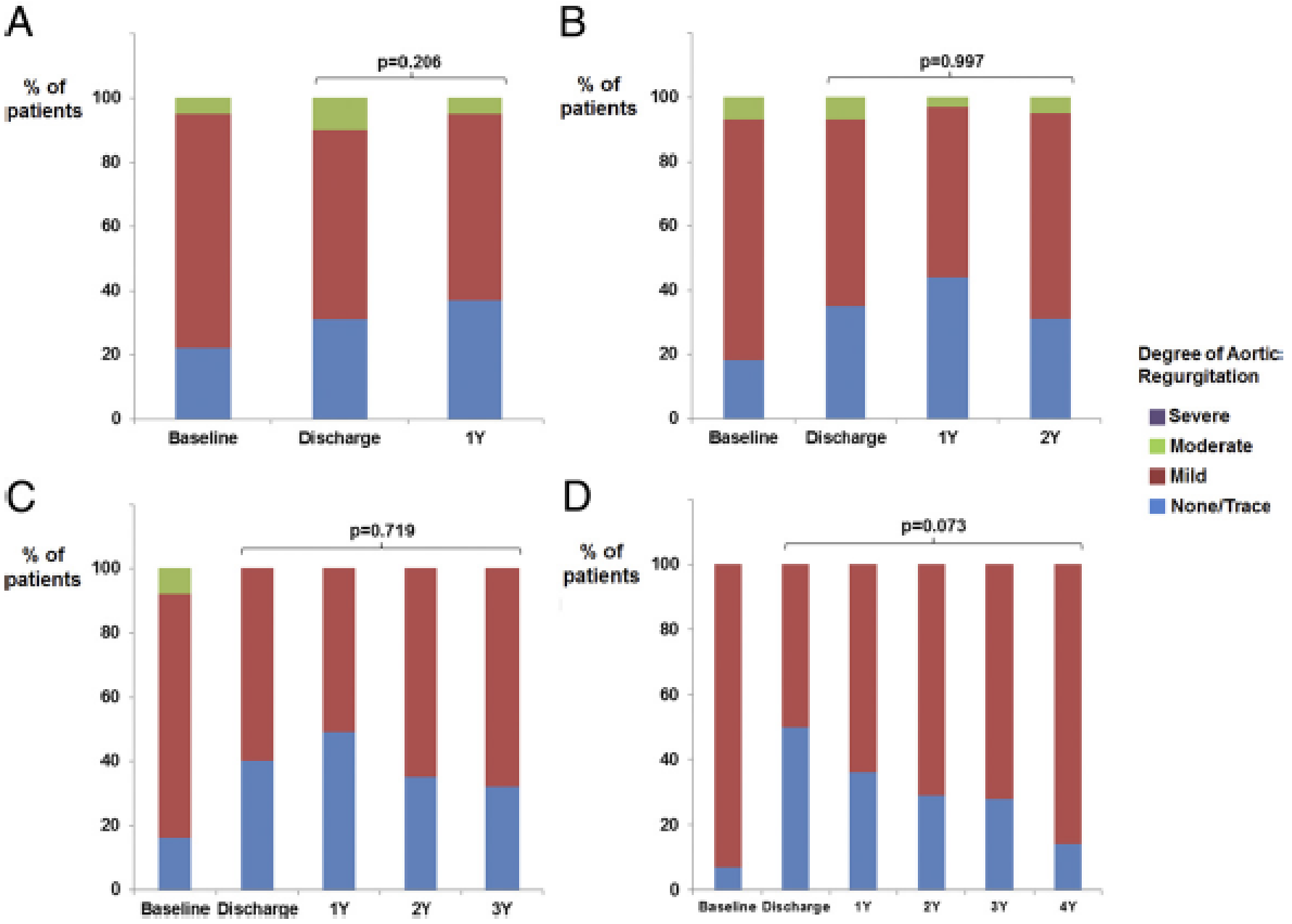
Table 6 Baseline Univariate and Multivariate Predictors of Cumulative Late Mortality in TF Approach Patients

	Univariate		Multivariate Model	
Variables	HR (95% CI)	p Value	HR (95% CI)	p Value
Chronic atrial fibrillation	1.68 (1.09–2.58)	0.018	—	—
Coronary artery disease	1.43 (0.90–2.26)	0.098	—	—
COPD	1.71 (1.09–2.70)	0.021	—	—
Pulmonary hypertension	1.81 (1.13–2.91)	0.014	1.63 (1.01–2.64)	0.043

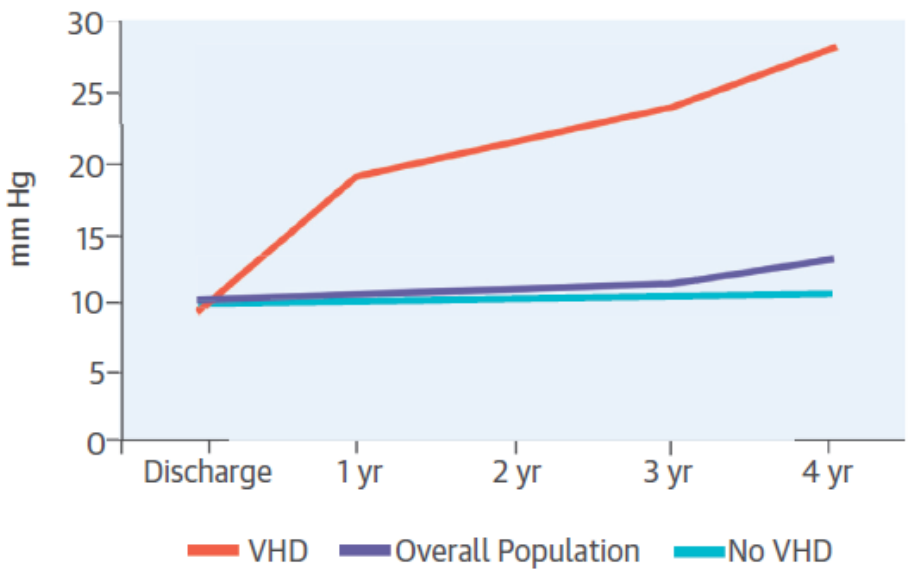
N = 162.

TF = transfemoral; other abbreviations as in Table 3.

Rodés-Cabau et al. JACC 2012:1864 –75


A
% of patients
p=0.206
100
80
60
40
20
0
Baseline
Discharge
1Y
B
% of patients
p=0.997
100
80
60
40
20
0
Baseline
Discharge
1Y
2Y
Degree of Aortic Regurgitation
Severe
Moderate
Mild
None/Trace
C
% of patients
p=0.719
100
80
60
40
20
0
Baseline
Discharge
1Y
2Y
3Y
D
% of patients
p=0.073
100
80
60
40
20
0
Baseline
Discharge
1Y
2Y
3Y
4Y

Gradientes post TAVI



Incremento de gradiente transvalvular medio de >10mmhg
Gradiente medio al alta : **9.5±5.0mmHg** Gradiente medio F/U: **26.1±11.0mmHg**
En 4.5% población estudiada (68pts/1521pts)

Incidence, Timing, and Predictors of Valve Hemodynamic Deterioration After Transcatheter Aortic Valve Replacement Multicenter Registry Am Coll Cardiol 2016;67:644–55)

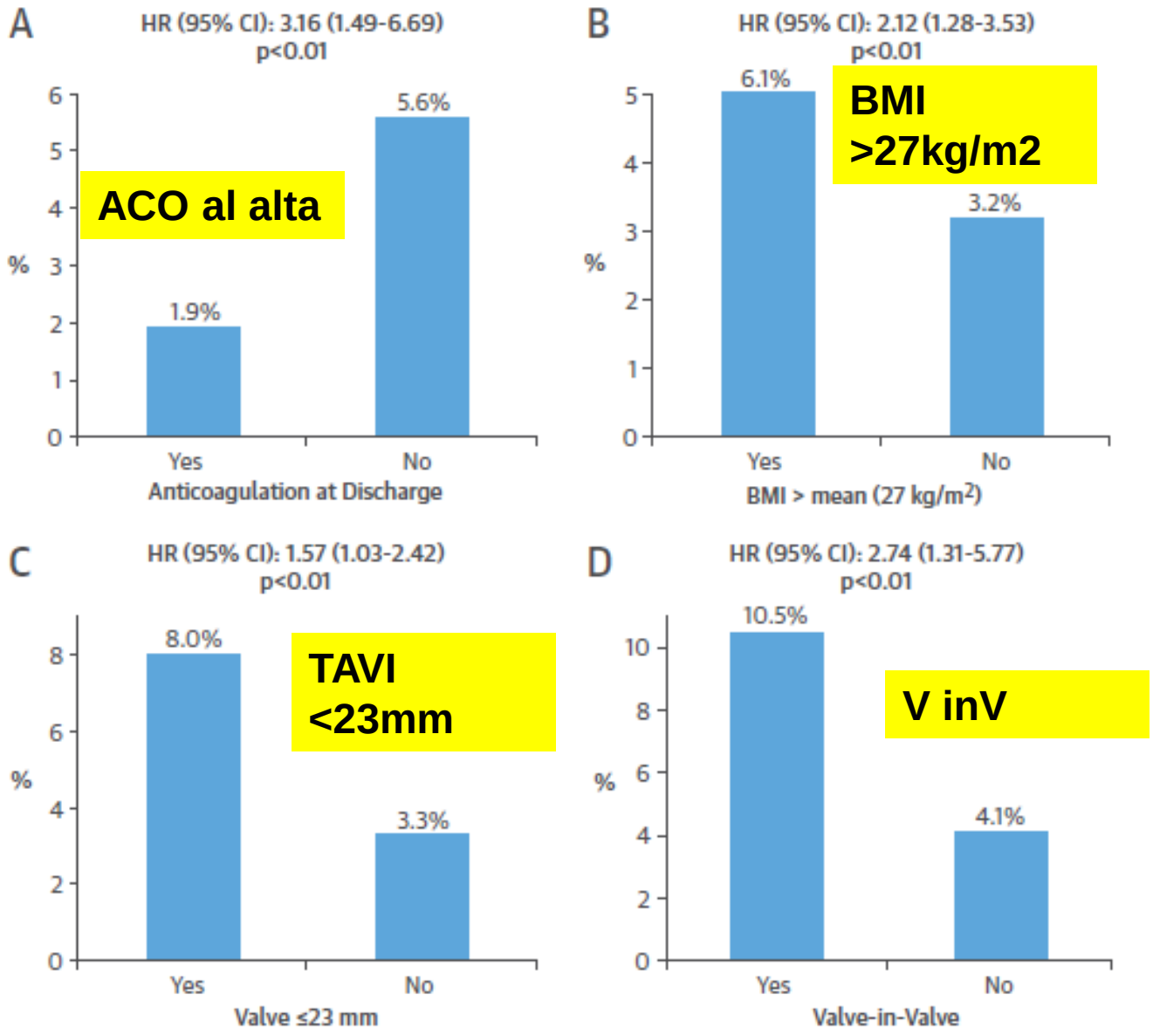
Predictores
de deterioro hemodinamico post TAVI

Predictors of Transcatheter Valve Hemodynamic Deterioration Post-TAVR

- Absence of Anticoagulation Therapy at Discharge
- Valve-in-Valve Procedure (TAVR in a Surgical Valve)
- ≤23 mm Transcatheter Heart Valve
- Greater Body Mass Index

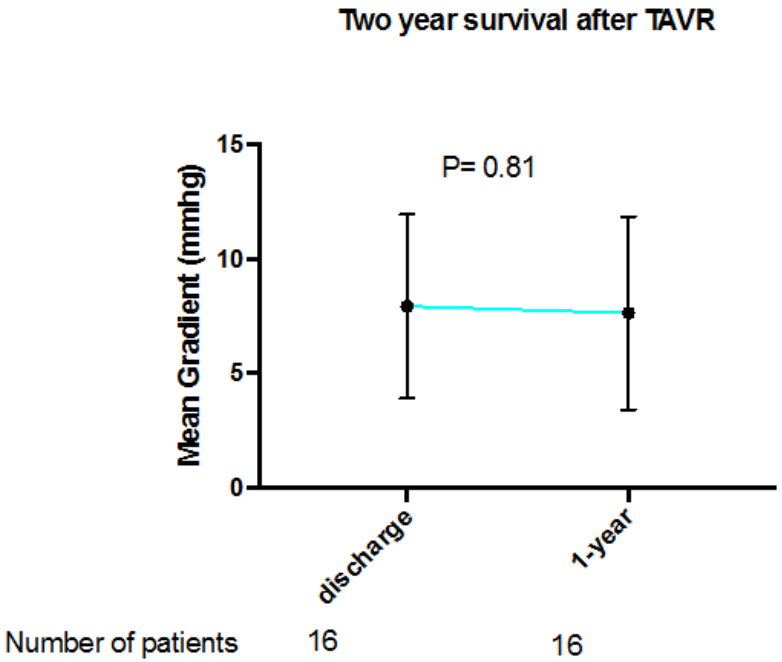
JIncidence, Timing, and Predictors of Valve Hemodynamic Deterioration After Transcatheter Aortic Valve Replacement Multicenter Registry Am Coll Cardiol 2016;67:644–55)

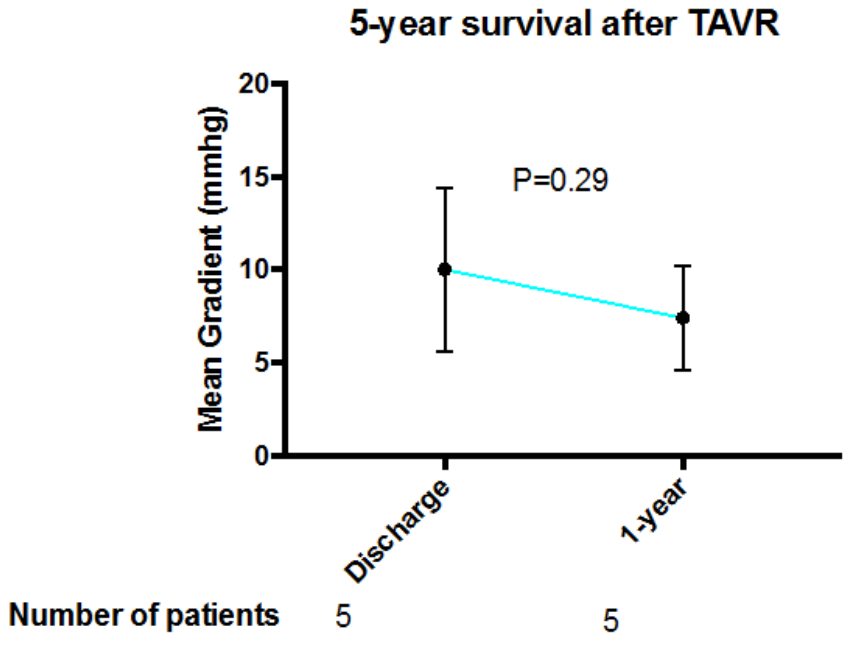
Predictores de VHD



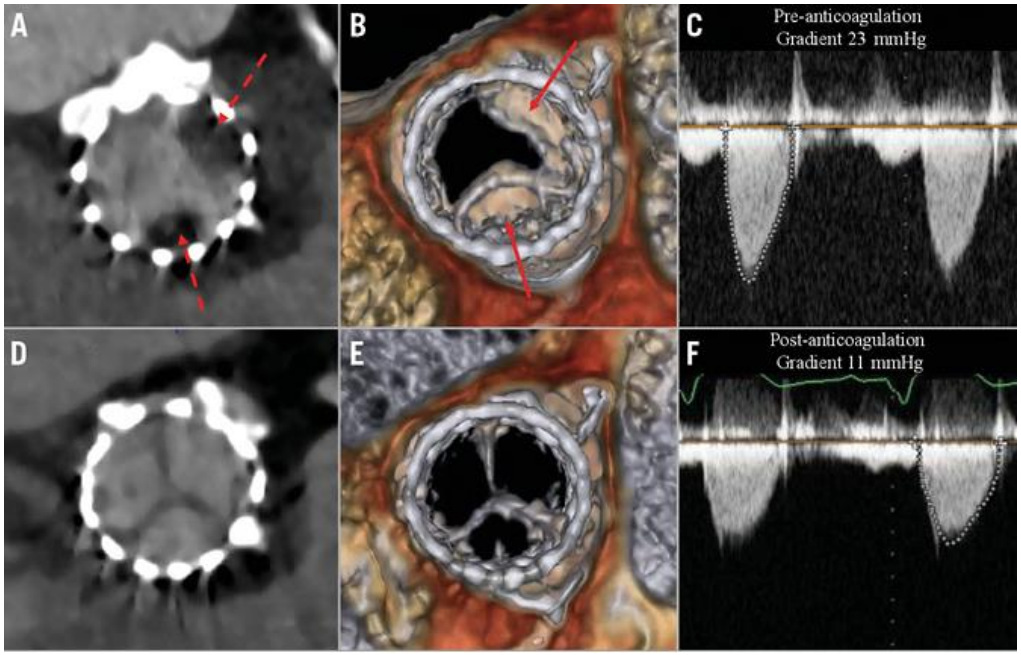
JIncidence, Timing, and Predictors of Valve Hemodynamic Deterioration After Transcatheter Aortic Valve Replacement Multicenter Registry Am Coll Cardiol 2016;67:644–55)

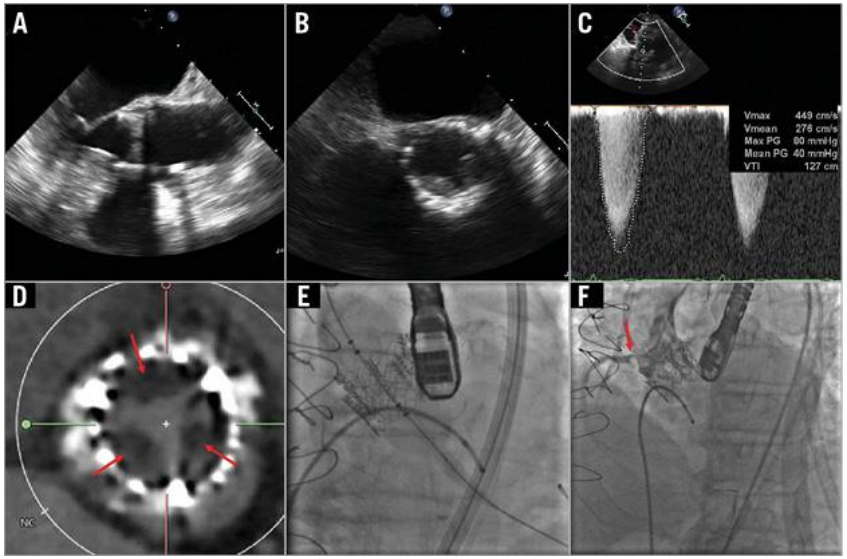
COHORTE TAVI Hospital Italiano 2 y 5 AÑOS DE SEGUIMIENTO.





Romeo, Agatiello y col. Seguimiento alejado TAVI. En prensa SAC





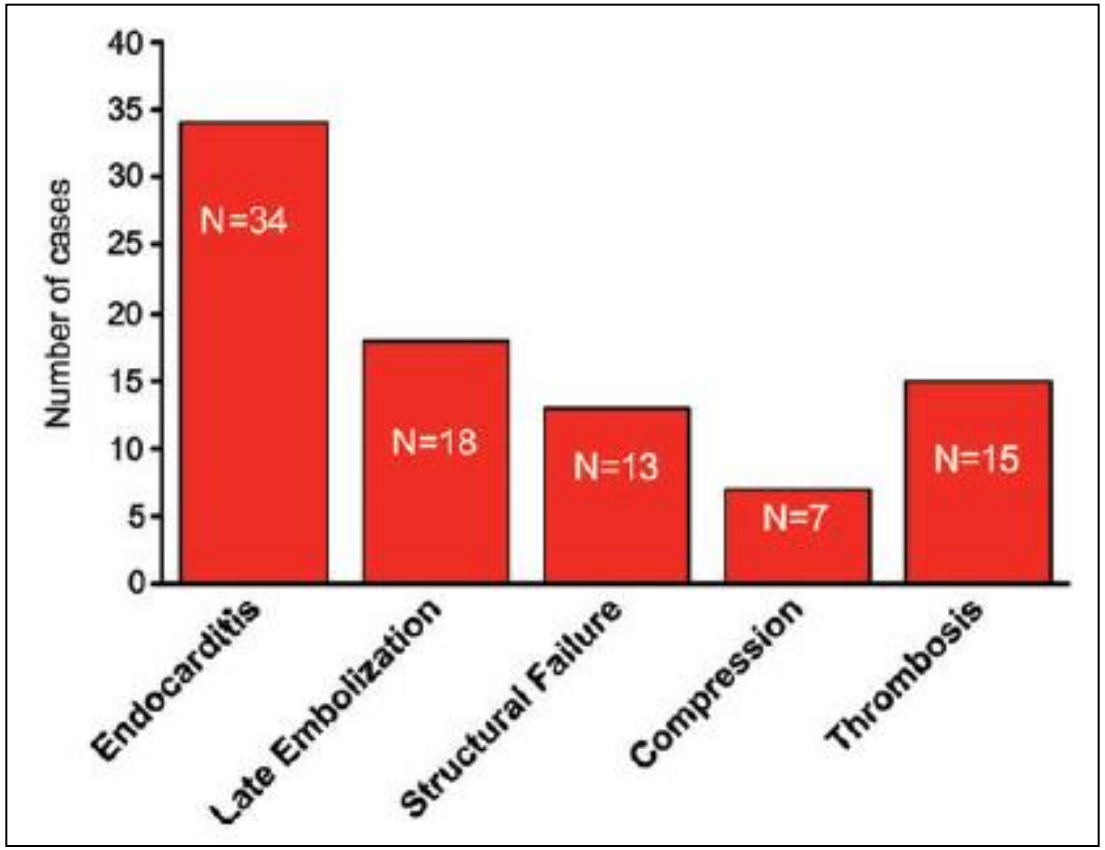
TAVI TROMBOSIS/ DURABILIDAD ?

- Raro, menos 1%
- Aumento de Síntomas
- Aumento gradiente transvalvular
- ACO
- V in V

Leaflet motion abnormality after TAVI: genuine threat or much ado about nothing? Eurointervention 2016;12:Y28-Y32

Transcatheter heart valve failure: a systematic review

Darren Mylotte[1,2], Ali Andalib[1], Pascal Thériault-Lauzier[1], Magdalena Dorfmeister[3], Mina Girgis[1], Waleed Alharbi[1], Michael Chetrit[1], Christos Galatas[1], Samuel Mamane[1], Igal Sebag[4], Jean Buithieu[1], Luc Bilodeau[1], Benoit de Varennes[5], Kevin Lachapelle[5], Ruediger Lange[3], Giuseppe Martucci[1], Renu Virmani[6], and Nicolo Piazza[1,3*]



15 cases of TAVR valve thrombosis reported from 12/02-03/14

14 symptomatic
1 subclinical

Mylotte D. et al. European Heart Journal 2015

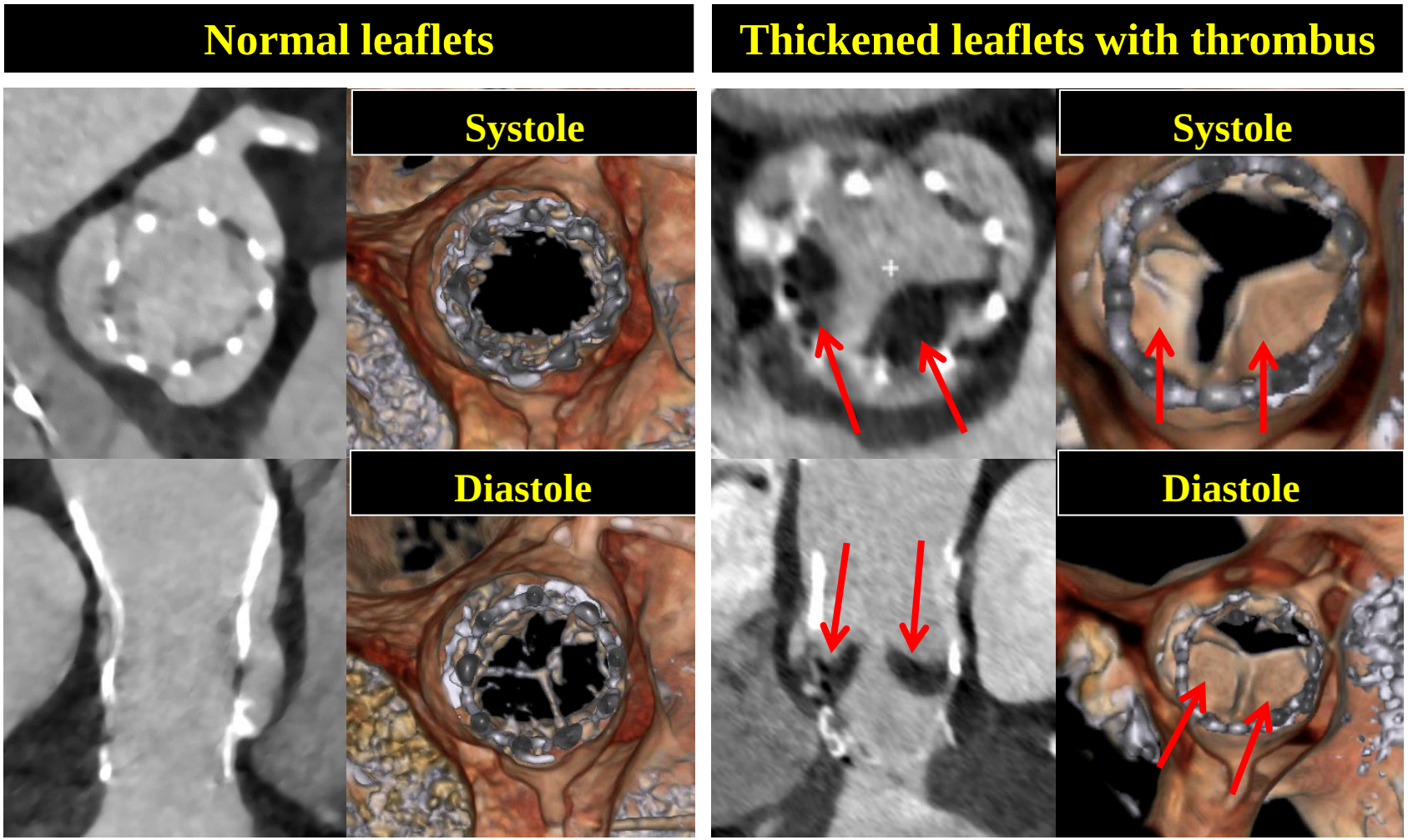
ORIGINAL ARTICLE

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

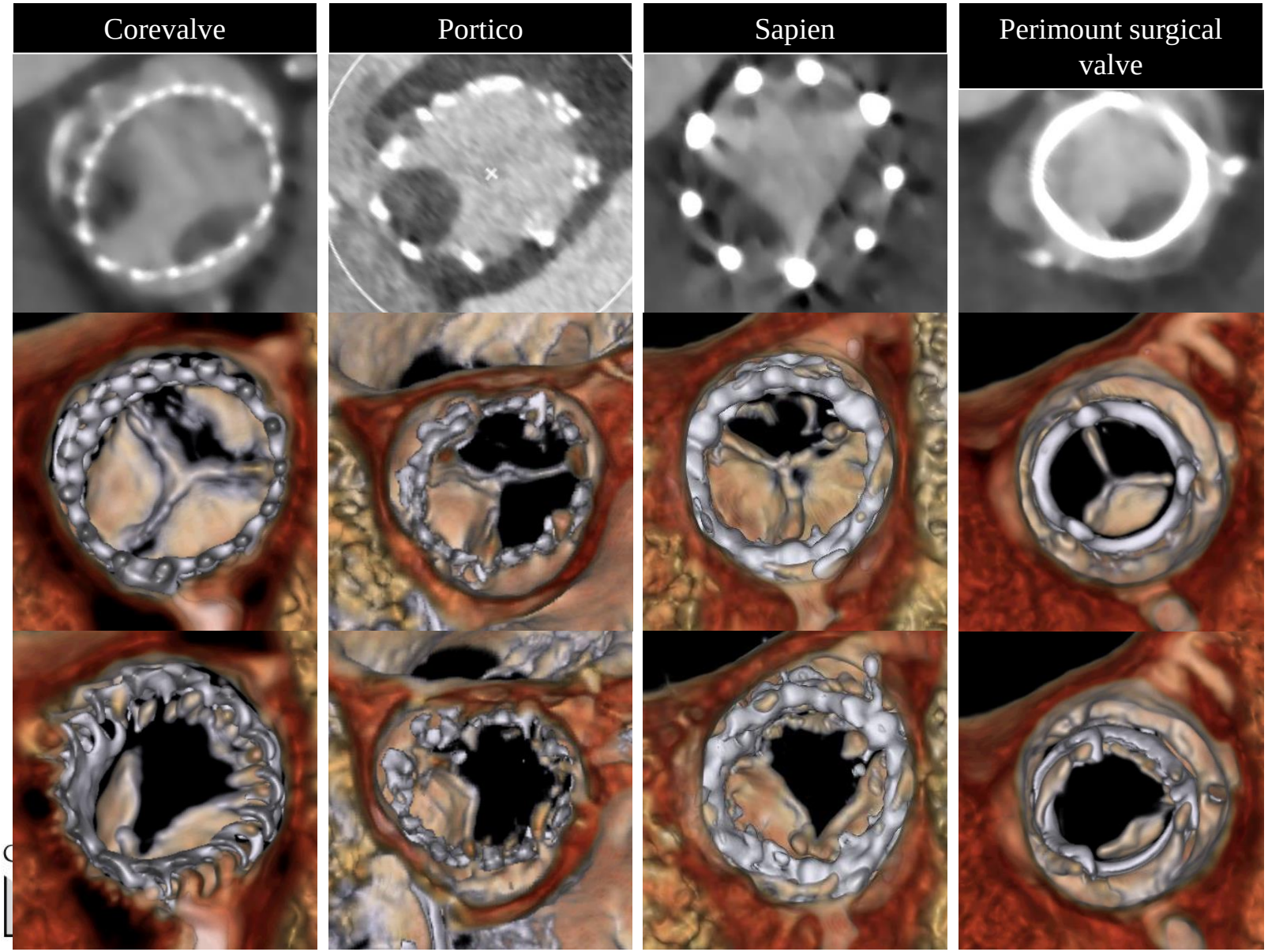
R.R. Makkar, G. Fontana, H. Jilaihawi, T. Chakravarty, K.F. Kofoed, O. de Backer, F.M. Asch, C.E. Ruiz, N.T. Olsen, A. Trento, J. Friedman, D. Berman, W. Cheng, M. Kashif, V. Jelnin, C.A. Kliger, H. Guo, A.D. Pichard, N.J. Weissman, S. Kapadia, E. Manasse, D.L. Bhatt, M.B. Leon, and L. Søndergaard

NEJM 2015

Volume rendered CT images of bioprosthetic valves

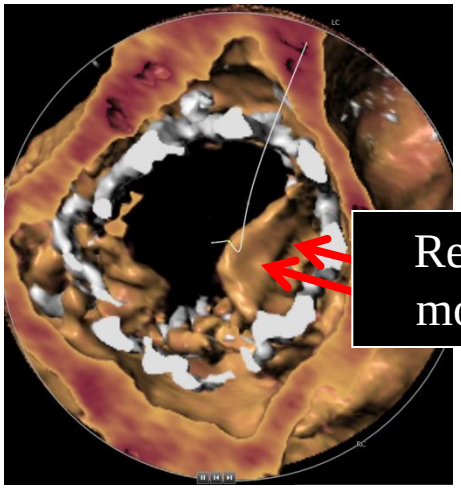


Reduced leaflet motion was observed in all valve types including surgical bioprostheses



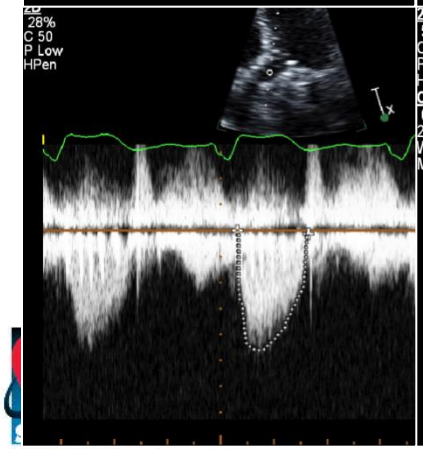
Results: Role of TTE

This finding was invariably missed on TTE, which demonstrated normal transvalvular gradients

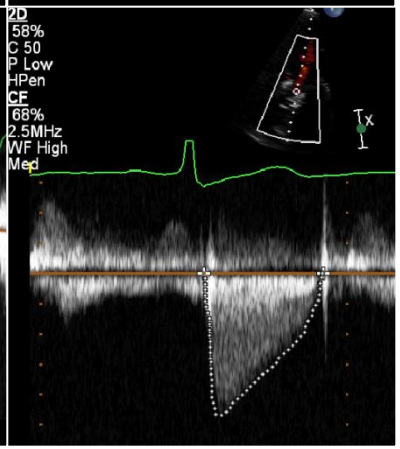


Reduced mobility

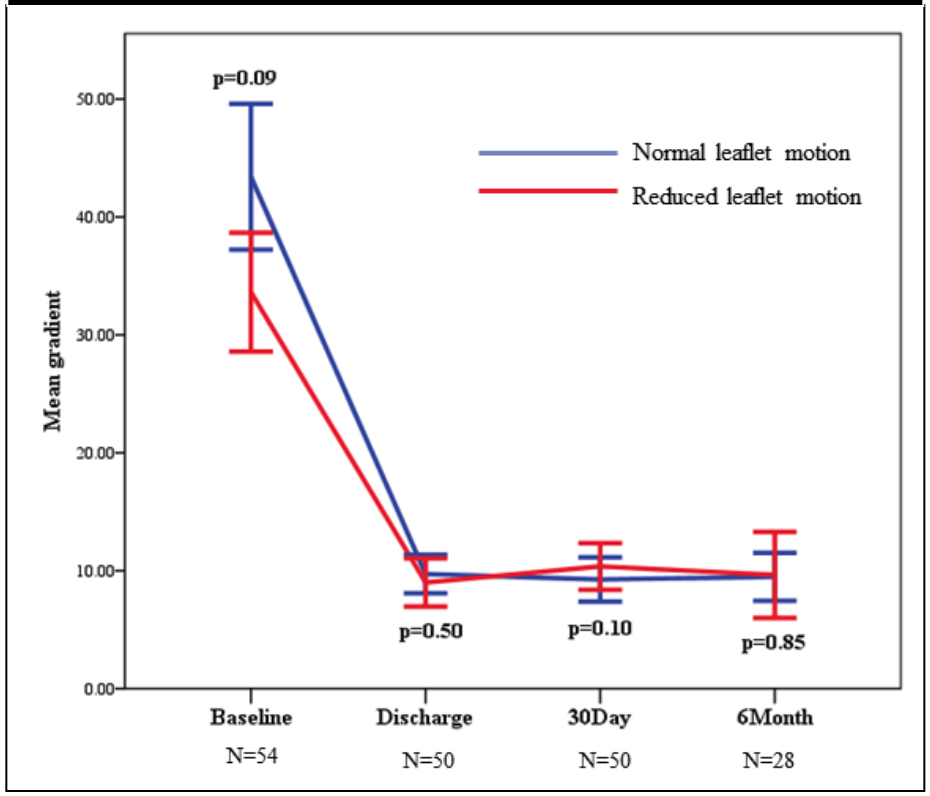
Day 1 mean gradient = 9 mmHg



Day 30 mean gradient = 9 mmHg

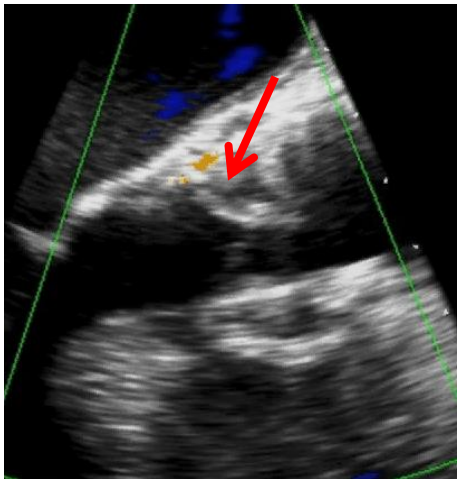


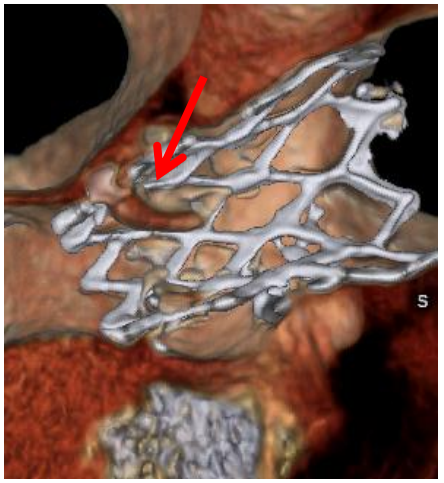
Portico IDE gradients in patients with and without reduced leaflet motion

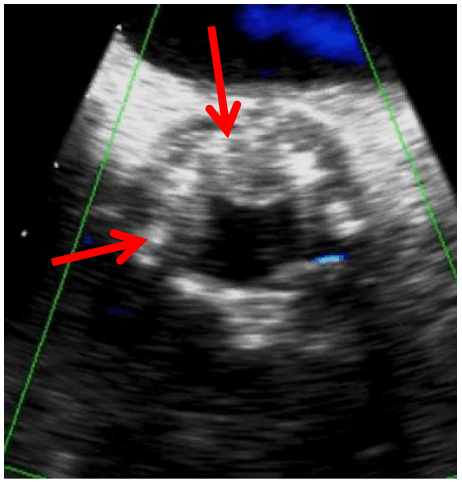


Results: Role of TEE

There was 100% concordance in the assessment of leaflet motion between TEE and 4D VR-CT in 10 out 22 patients with reduced leaflet motion undergoing TEE

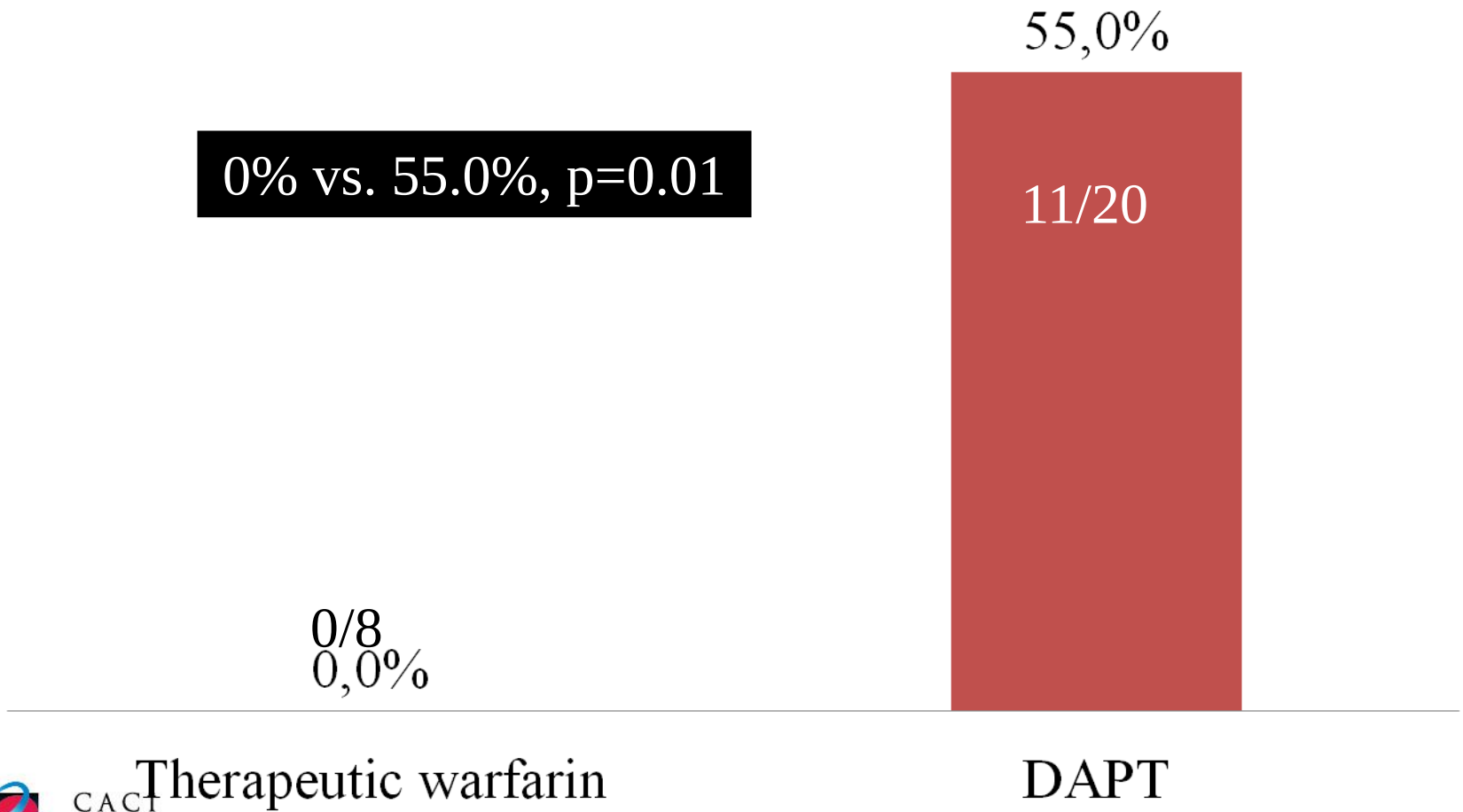




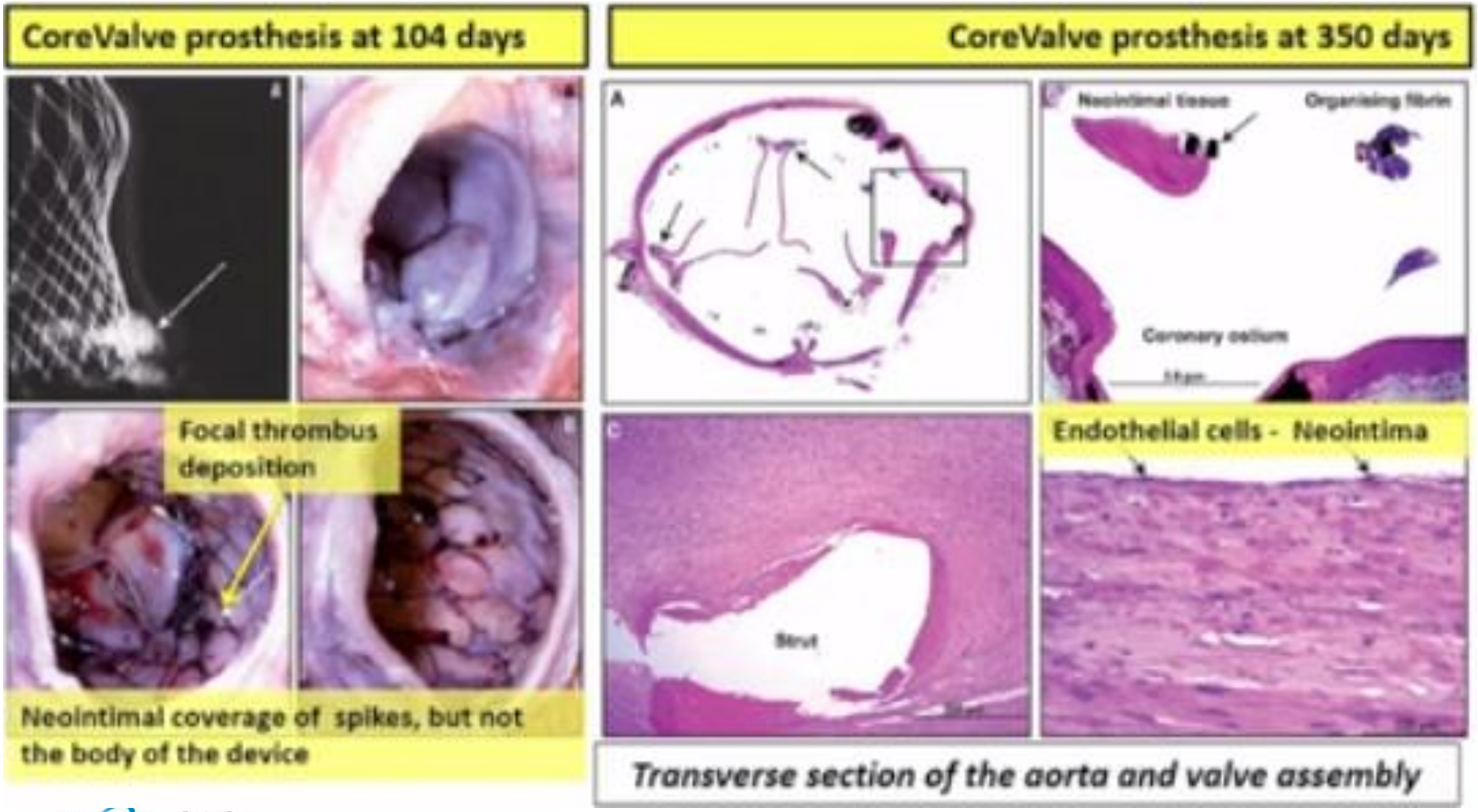


Therapeutic warfarin vs. DAPT: Portico-IDE

Decreased incidence of subclinical leaflet thrombosis



Endotelizacion post TAVI



Noble S et al. Eurointervention 2009;5:78-85

Prevalencia de Trombosis by CT/ECo

Autor	n	Prevalencia trombosis por TC	Prevalencia trombosis por ETE	Gradiente medio(mmHG) EOA(cm2)
Pache et al (2016)	156	10.6% (5dias)	NA	8±3.5/ NA
Leetma et al (2016)	140	4% (1-3meses)	NA	19.2/ 1.44
Del Trigo et al (2016)	1521	NA	4.5%(4años)	26.11±11/ NA
Hansson et al(2016)	405	7% ()	NA	10±7/ 1.5±0.5
Makkar et al(2016)	55	40% (32dias media)	NA	9.2±4.9/ NA
Makkar et al(2016)	132	13% (86dias)	NA	8.4±2.9/ NA
Yaganisawa et al(2017)	70	14.3%(1año)	NA	8.3±0.8/ NA
Vallema et al(2017)	434	12% (35dias)	3%(3años)	9.3±04.7/ 1.99±0.56
Jose et al(2017)	642	9%	2.8%(181dias)	34±14/ 1.06±0.46

Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study

*Tarun Chakravarty, Lars Søndergaard, John Friedman, Ole De Backer, Daniel Berman, Klaus F Kofoed, Hasan Jilaihawi, Takahiro Shiota, Yigal Abramowitz, Troels H Jørgensen, Tanya Rami, Sharjeel Israr, Gregory Fontana, Martina de Knegt, Andreas Fuchs, Patrick Lyden, Alfredo Trento, Deepak L Bhatt, Martin B Leon, Raj R Makkar, on behalf of the RESOLVE and SAVORY Investigators**

Research in context

Evidence before this study

We searched MEDLINE on Feb 1, 2017, for articles published in English, with the search terms "bioprosthetic valve thrombosis", "transcatheter aortic valve thrombosis", "subclinical leaflet thrombosis", "hypoattenuating leaflet thickening", and "TAVR thrombosis". Although symptomatic thrombosis represents the extreme end of the spectrum of bioprosthetic aortic valve thrombosis and is probably under-reported (prevalence of 1–2%), subclinical leaflet thrombosis with no associated symptoms is more frequent (prevalence of 10–15%) than is symptomatic bioprosthetic aortic valve thrombosis. Reduced leaflet motion detected with high-resolution CT in bioprosthetic aortic valves has been attributed to subclinical leaflet thrombosis in previously reported series. The published series have several limitations, including absence of complete clinical follow-up, no core laboratory assessment of transthoracic echocardiograms, no information about differences in the prevalence and severity of subclinical leaflet thrombosis between transcatheter and surgical valves, no adjudication of neurological events, and no information about the efficacy of novel oral anticoagulants (NOACs).

Added value of this study

We report, to our knowledge, the largest study to date of 931 patients who had CT scans done after surgical or transcatheter aortic valve replacement (TAVR) to assess reduced leaflet thrombosis between surgical and transcatheter aortic valves. Findings from this study are also the first, to our knowledge, to show the potential efficacy of NOACs in the prevention and treatment of subclinical leaflet thrombosis in bioprosthetic aortic valves. The frequency and severity of subclinical leaflet thrombosis was lower in surgical than in transcatheter aortic valves. Patients with reduced leaflet motion had a small, but significant, increase in valve gradients. Anticoagulation was better than dual antiplatelet therapy (DAPT; standard of care for patients after TAVR) or monoantiplatelet therapy in the prevention and treatment of subclinical leaflet thrombosis; both NOACs and warfarin were effective. We also observed increased rates of neurological events, including transient ischaemic attacks and strokes or transient ischaemic attacks associated with reduced leaflet motion, although the rates of strokes were not significantly different.

Implications of all the available evidence

Our findings question the guidelines recommending DAPT after TAVR and raise the issue of whether or not warfarin or NOACs are more appropriate in certain patients than is DAPT. The risk-benefit profile of anticoagulation will be established in future clinical trials. Despite excellent outcomes after TAVR with the new-generation valves, room might exist for further improvement in outcomes through an understanding of the predictors of reduced leaflet motion and consideration of a

Lancet online March 19, 2017

Study design

657 patients underwent CTs in the RESOLVE registry
Cedars-Sinai Medical Center, Los Angeles

274 patients underwent CTs in the SAVORY registry
Rigshospitalet, Copenhagen

931 patients undergoing CTs

890 patients with interpretable CTs were included in the analysis
RESOLVE registry: 626 patients
SAVORY registry: 264 patients

Prevalence of reduced leaflet motion

Transcatheter vs. surgical bioprosthetic aortic valves: p=0.001

Reduced leaflet motion was present in 106 (11.9%) patients

Transcatheter valves
13.4% (101 out of 752)

Surgical valves
3.6% (5 out of 138)

Baseline characteristics

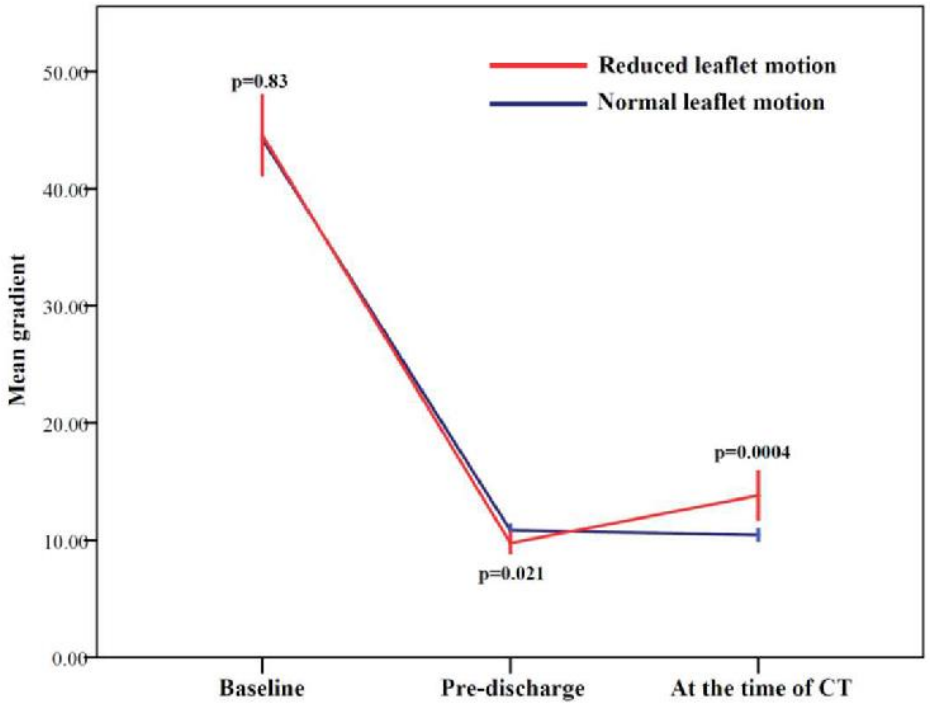
Patients with surgical and transcatheter aortic valves

Characteristic	SAVR (N=138)	TAVR (N=752)	p-value
Age-year	71·9±8·6	80·7±8·4	<0·0001
Male sex-no. (%)	88 (63·8%)	413 (54·9%)	0·05
Medical condition - no. (%)			
Chronic kidney disease	6 (4·8%)	82 (11·7%)	0·02
Hemodialysis	0 (0%)	9 (1·3%)	0·23
Hypercoagulable disorder	0 (0%)	9 (1·4%)	0·61
Hypertension	101 (73·2%)	666 (88·7%)	<0·0001
Prior stroke	9 (6·6%)	63 (8·4%)	0·47
Prior transient ischemic attack	3 (2·2%)	39 (5·2%)	0·19
Hyperlipidemia	93 (67·9%)	584 (77·8%)	0·01
Diabetes	28 (20·3%)	187 (24·9%)	0·25
PCI within 3 months prior to AVR	7 (5·2%)	90 (12·0%)	0·02
Congestive heart failure	68 (49·3%)	604 (80·6%)	<0·0001
Syncope	2 (1·5%)	48 (6·4%)	0·02
Atrial fibrillation	31 (22·6%)	219 (29·2%)	0·11
Baseline echocardiogram			
Ejection fraction - %	57·2±11·5	57·7±12·9	0·30
Mean aortic valve gradient - mmHg	43·6±14·4	44·4±14·1	0·91
Peak aortic valve gradient - mmHg	72·5±22·3	74·4±22·7	0·82
VTI ratio	0·26±0·12	0·23±0·08	0·04
Anticoagulation at the time of discharge	31 (22·5%)	187 (24·9%)	0·54
Anticoagulation at the time of CT	38 (27·5%)	186 (24·7%)	0·49
Timing from AVR to CT	162·5 days (80 – 417 days)	58 days (32 – 235 days)	<0·0001
0-6 months	74 (53·6%)	520 (69·2%)	
6-12 months	26 (18·8%)	84 (11·2%)	
>12 months	38 (27·5%)	148 (19·7%)	

AVR=Aortic valve replacement; CT=computed tomogram

Data are mean ± standard deviation or median (interquartile range) for continuous variables; N (%) for categorical variables

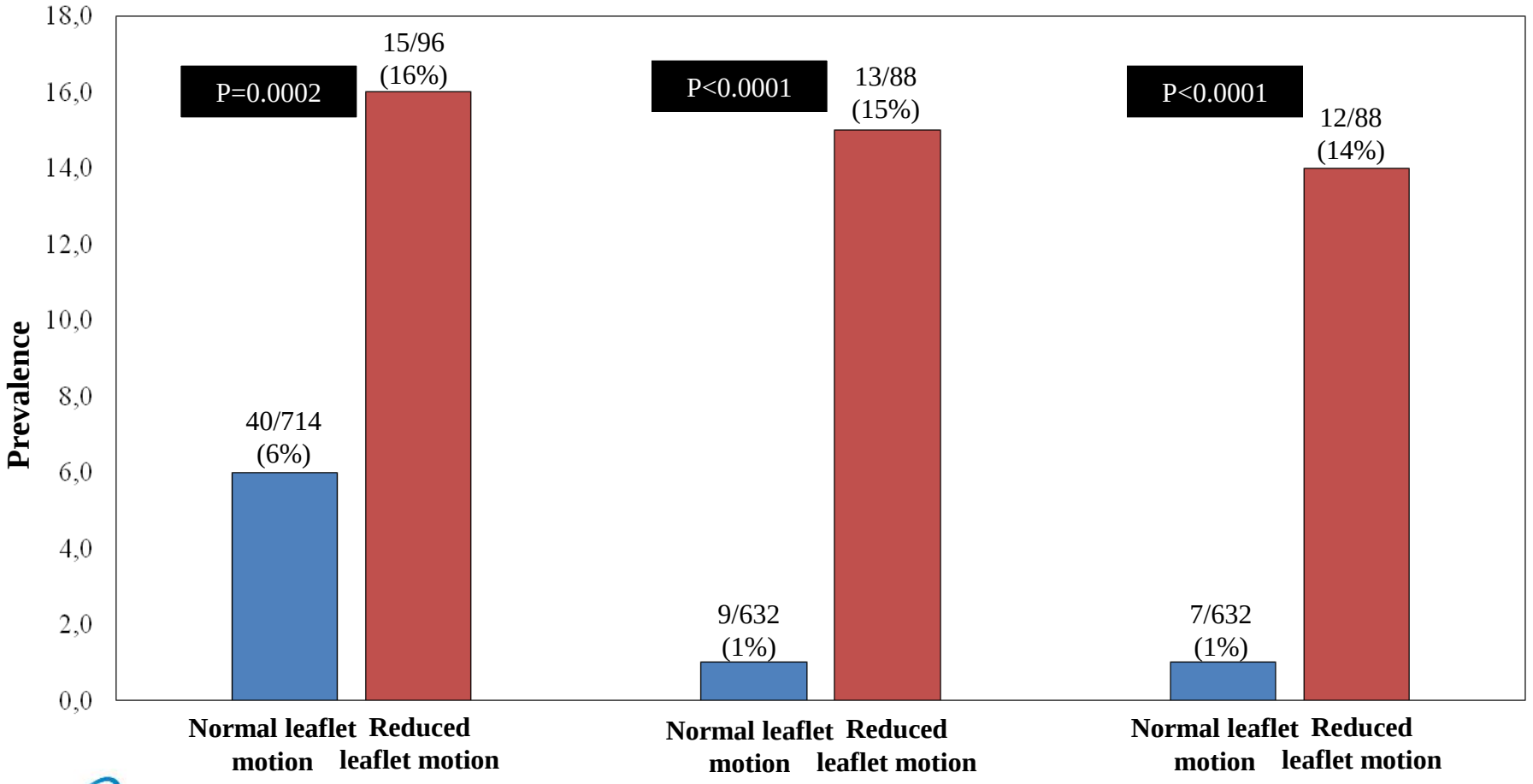
Impact of reduced leaflet motion on valve hemodynamics



Increased mean gradients at the time of CT in patients with reduced leaflet motion

13·8±10·0 mmHg vs. 10·4±6·3 mmHg, p=0.0004

Increased gradients in patients with reduced leaflet motion



Mean aortic gradient > 20mmHg

Increase in gradients > 10mmHg

Mean aortic gradient > 20mmHg AND Increase in gradients > 10mmHg

Impact of reduced leaflet motion on clinical outcomes

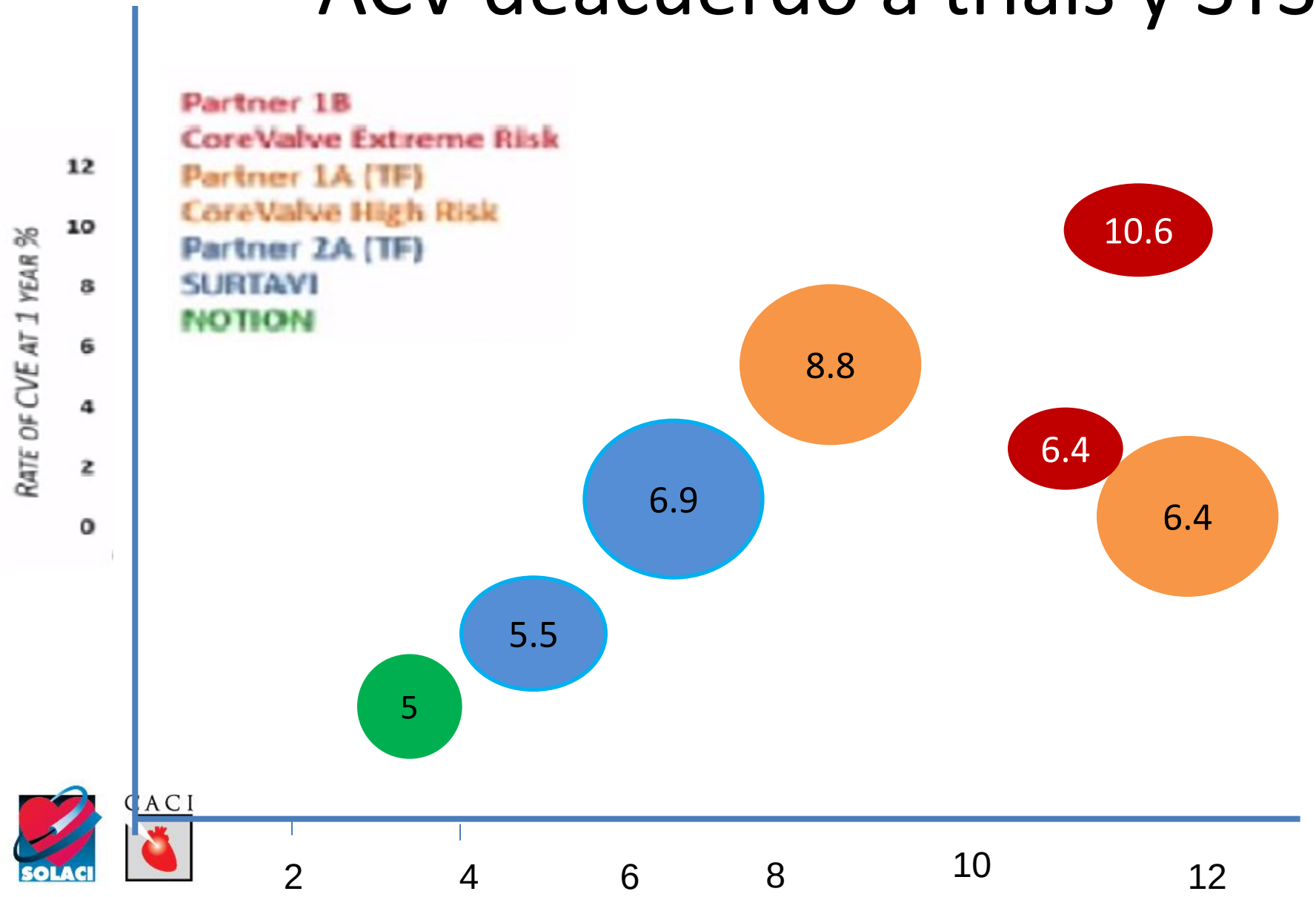
All clinical events post-TAVR/SAVR included

No significant difference in strokes; but increased risk of TIAs and strokes/TIAs

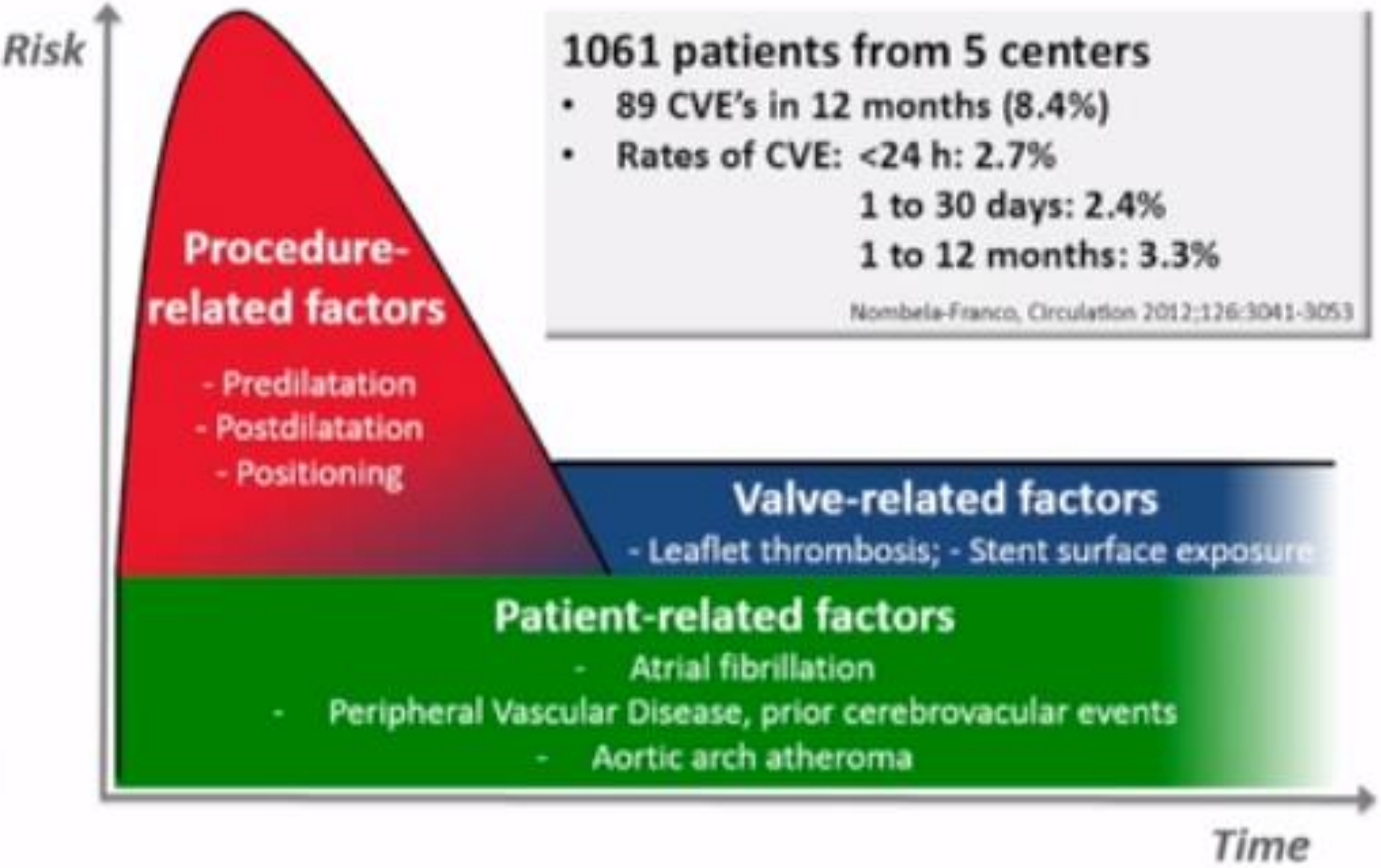
	Normal leaflet motion (N=784)		Reduced leaflet motion (N=106)			
	n/N (%)	Rate per 100 person-years	n/N (%)	Rate per 100 person-years	Hazard ratio (95% CI)	p-value
All events						
Death	34/784 (4·3%)	2·91	4/106 (3·8%)	2·66	0·96 (0·34-2·72)	0·94
Myocardial infarction	4/784 (0·5%)	0·34	1/106 (0·9%)	0·67	1·91 (0·21-17·08)	0·56
Strokes/TIAs	27/784 (3·4%)	2·36	11/106 (10·4%)	7·85	3·27 (1·62-6·59)	0·001
All strokes*	22/784 (2·8%)	1·92	6/106 (5·7%)	4·12	2·13 (0·86-5·25)	0·10
Ischemic strokes	21/784 (2·7%)	1·83	6/106 (5·7%)	4·12	2·23 (0·90-5·53)	0·08
TIAs	7/784 (0·9%)	0·60	6/106 (5·7%)	4·18	7·02 (2·35-20·91)	0·0005

TIA=Transient ischemic attack
* All strokes include hemorrhagic and ischemic strokes

ACV deacuerdo a trials y STS



Timing of Cerebrovascular Events & Determinants of Antithrombotic Strategy



Conclusión

- Durabilidad es una cuestión impostergable para estimar TAVI en paciente de riesgo intermedio-bajo

- La performance de las prótesis utilizadas esta demostrada a 5años, aunque la población tratada en los viejos trials son prácticamente pacientes «futiles» de hoy.

- La definición de VHD, debe ser consensuada , así como las visitas post TAVI (podría estar subestimada)

- Trombosis es una entidad, rara aunque se debe tener la sospecha ante cambio de gradientes y reinicio de síntomas