Update on Valve Durability and Leaflet Thrombosis

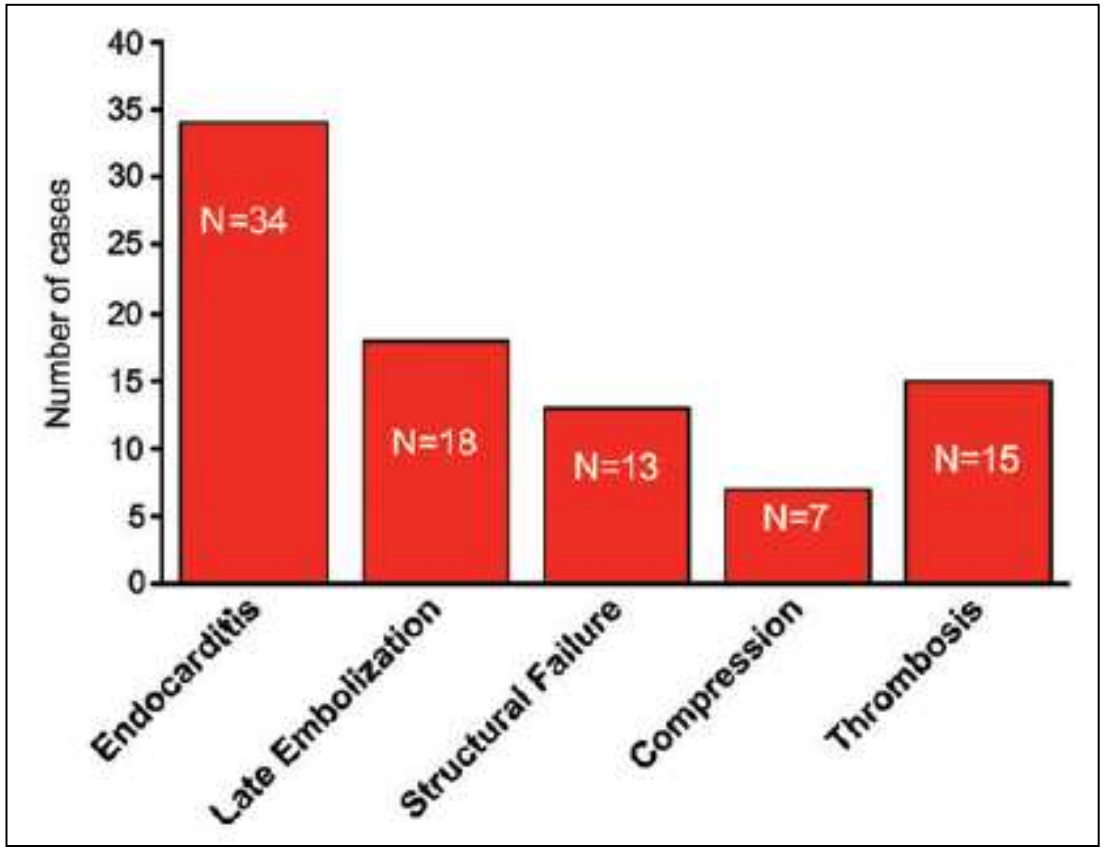
Raj R. Makkar, MD
Associate Director of Cedars Sinai Heart Institute
Director, Interventional Cardiology and Cardiac Catheterization Laboratories
Professor, David Geffen School of Medicine at UCLA

Disclosure Statement of Financial Interest

No conflicts of interest

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

Spectrum

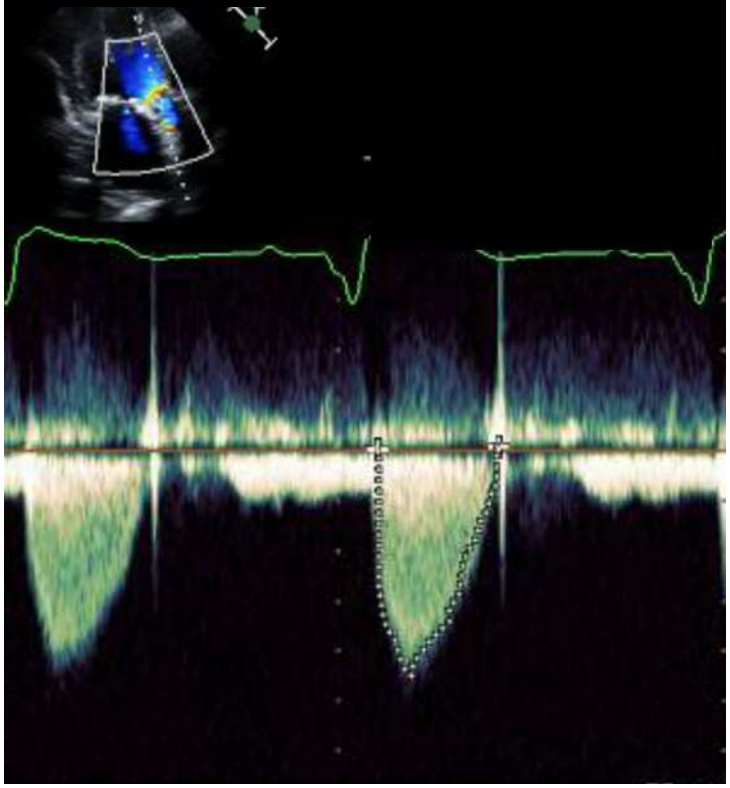
- Reduced Leaflet Motion on 4D-CT (often normal gradient)
- Hemodynamic deterioration (gradients>10mm Hg increase compared to baseline)
- Valve Thrombosis with symptoms or elevated gradients
- Valve degeneration (Variable definitions)

Case 1

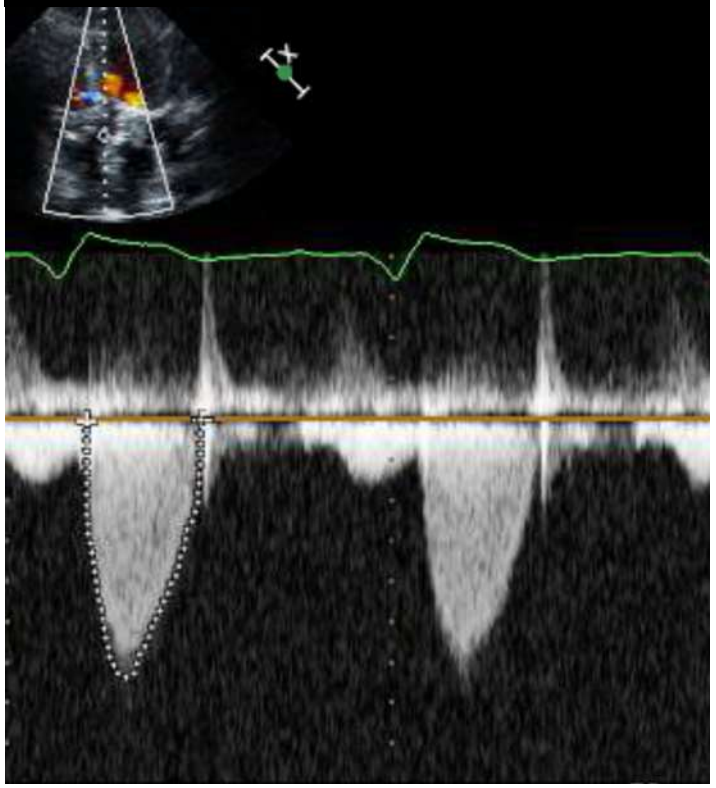
67 y/o male physician s/p TAVR with 29mm Sapien3 valve

Worsening shortness of breath 4 months post-TAVR
Transvalvular gradients elevated from 10 mmHg to 23 mmHg

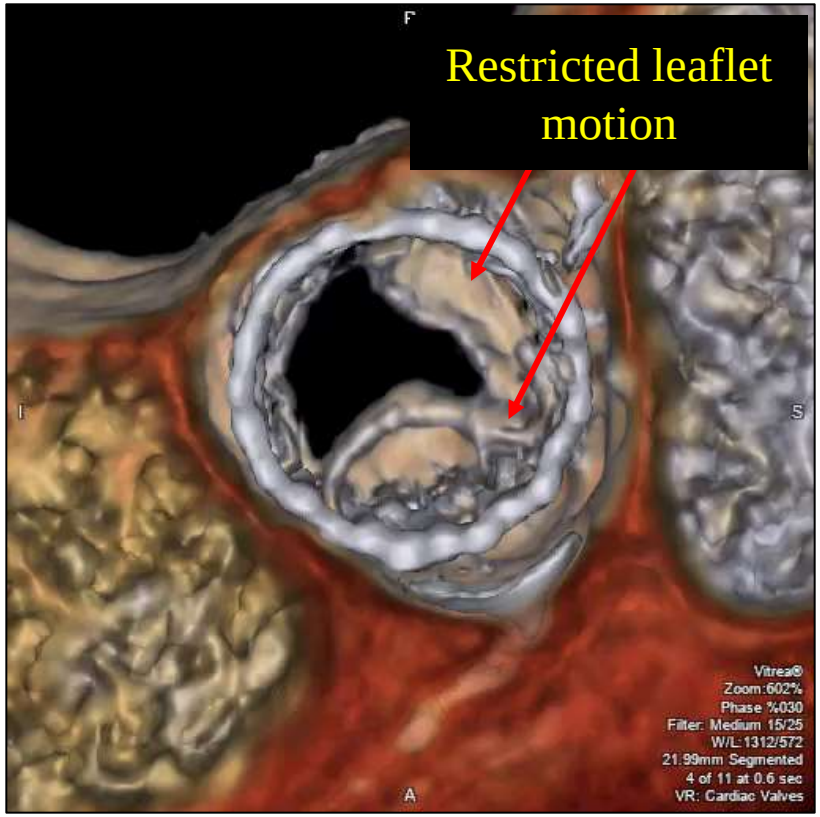
Day 1 TTE
Gradient 10mmHg

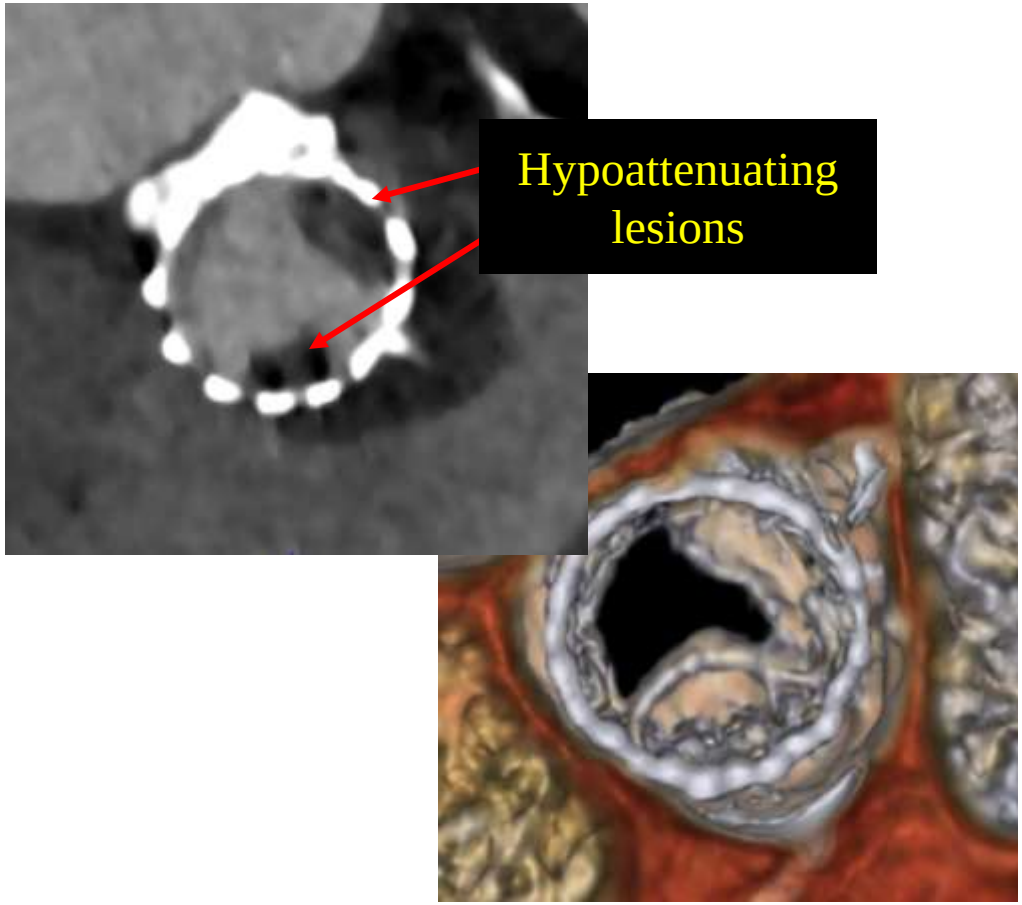


4 months post-TAVR
Gradient 23mmHg



Leaflet thickening and restricted leaflet motion noted on 4D VR-CT

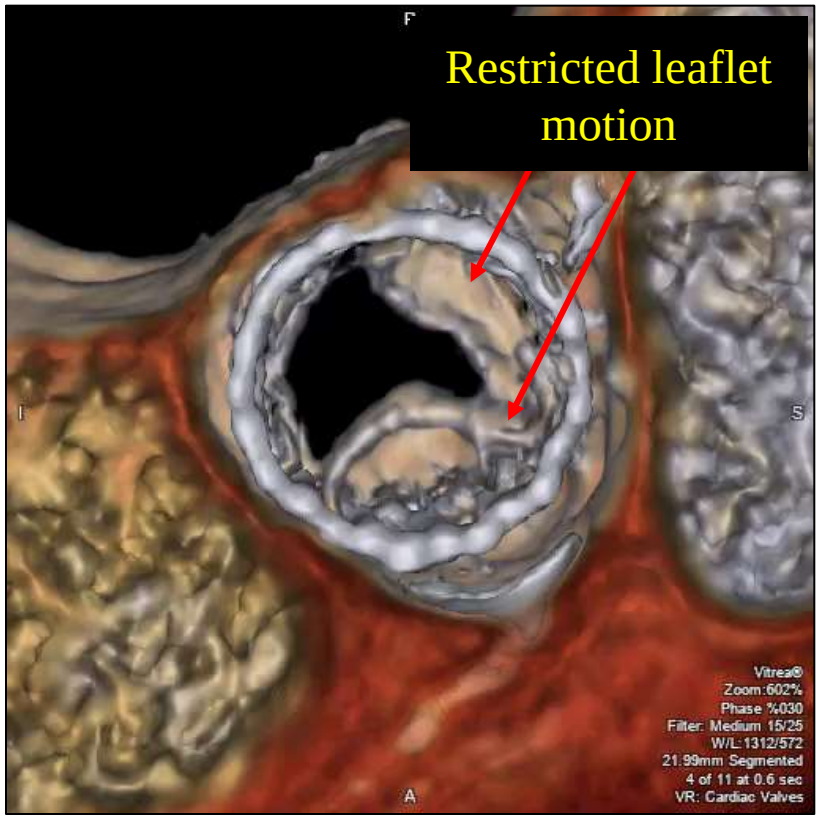


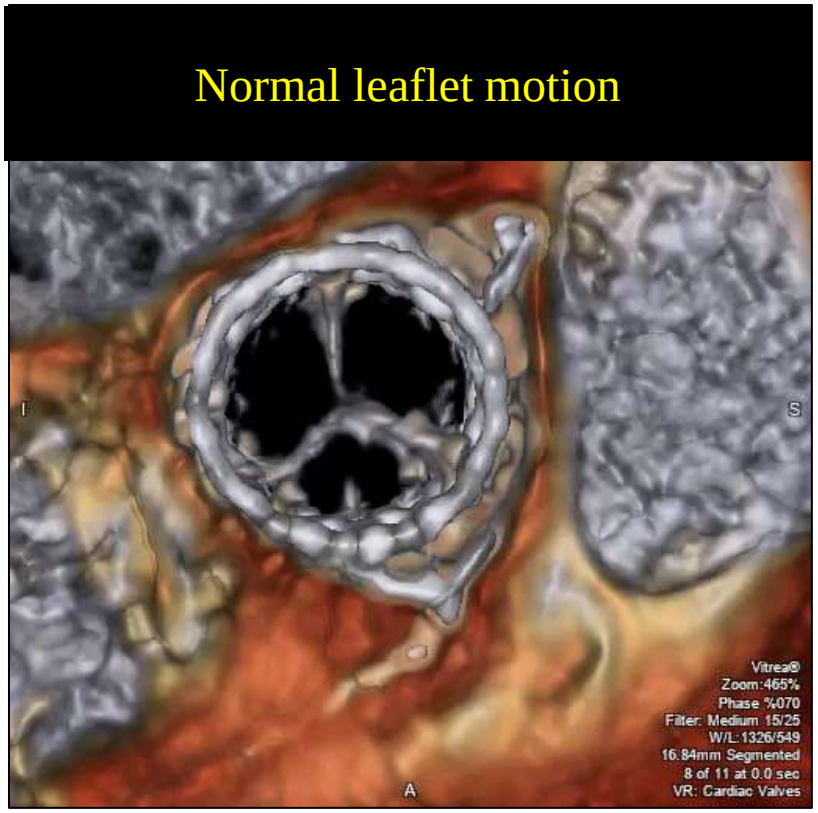


Leaflet motion restored following anticoagulation with warfarin (INR 2-3)

Repeat CT performed after 3 months

Resolution of symptoms with anticoagulation





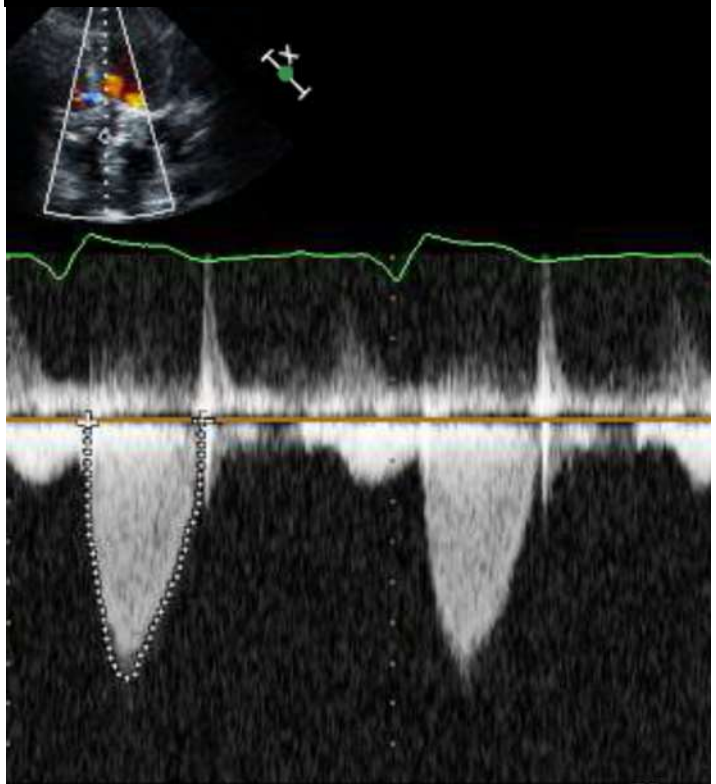
Normalized transvavular gradients with anticoagulation (warfarin, INR 2-3)

Repeat TTE performed after 3 months

Resolution of symptoms with anticoagulation

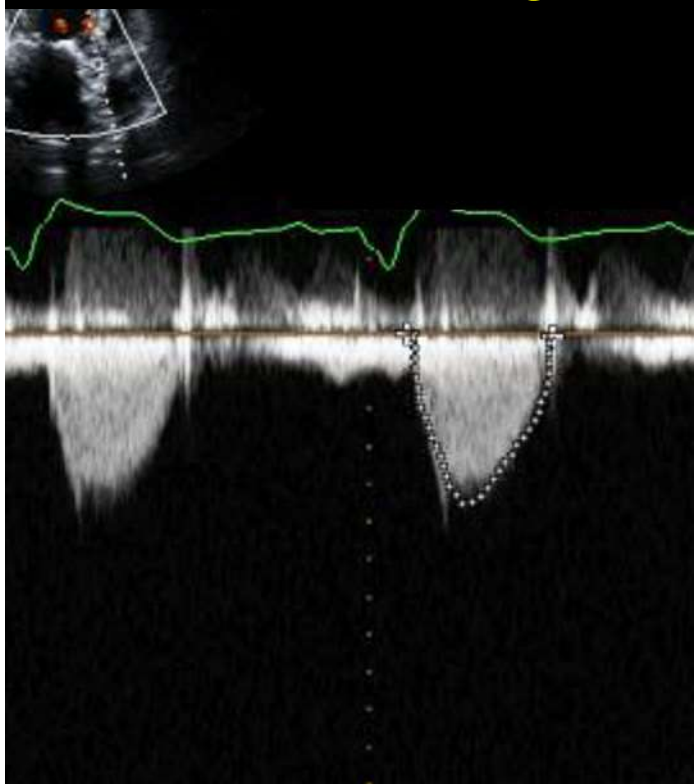
Pre-anticoagulation

Gradient 23mmHg



Post-anticoagulation

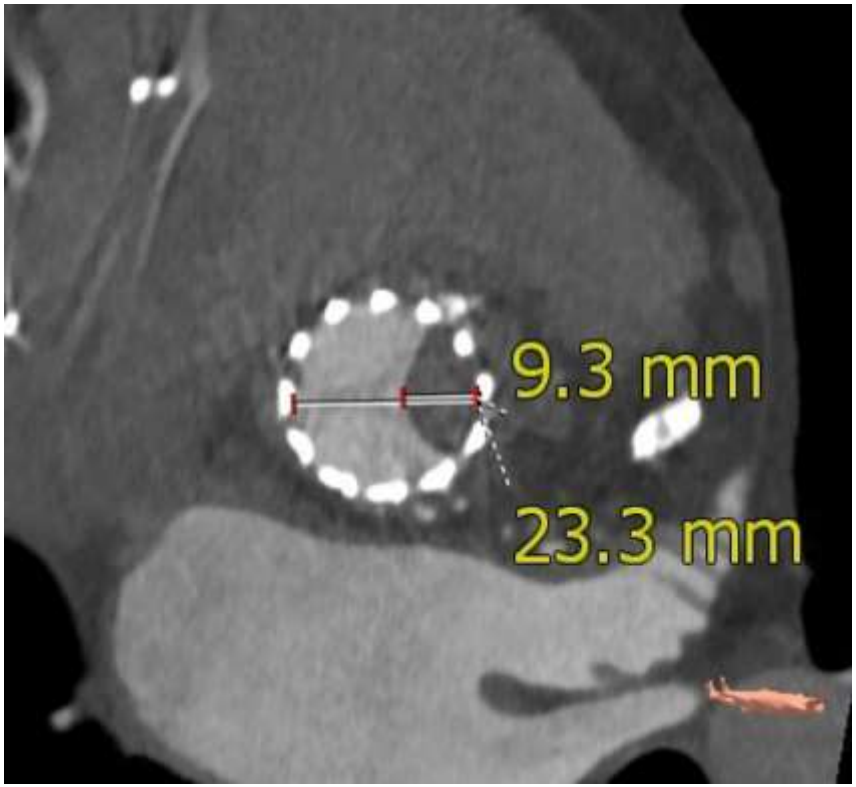
Gradient 11mmHg



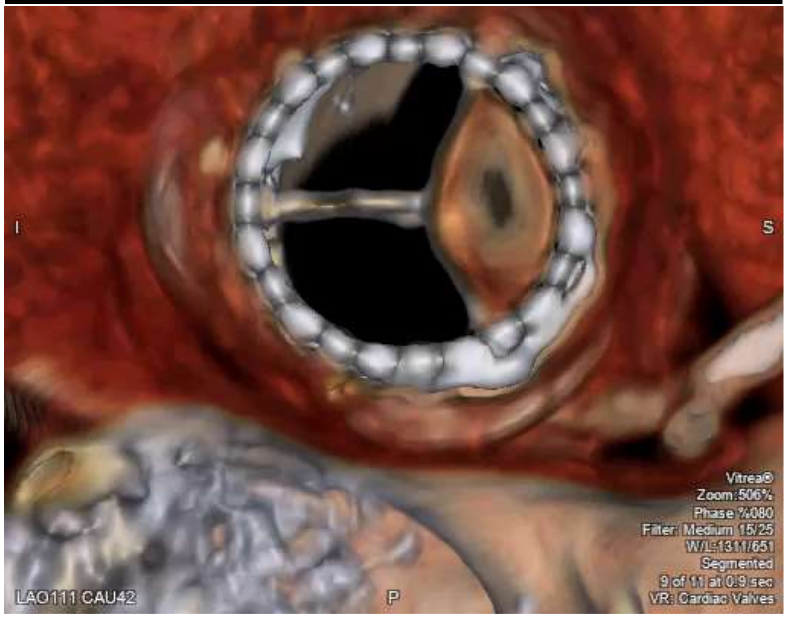
Case 2

80 y/o male s/p TAVR with 29mm Sapien 3 enrolled in RESOLVE registry

CT performed at 1 month post-TAVR



Severely reduced leaflet motion



80 y/o male s/p TAVR with 29mm Sapien 3 enrolled in RESOLVE registry

CT performed at 1 month post-TAVR

Thrombus also noted in the left main, new compared to the pre-TAVR CT

Pre TAVR

Post TAVR

Case 3

94 y/o male s/p 29mm Sapien 3 valve

Experiencing recurrent strokes and thromboemboli

Cardiac CT performed to rule out valve thrombus

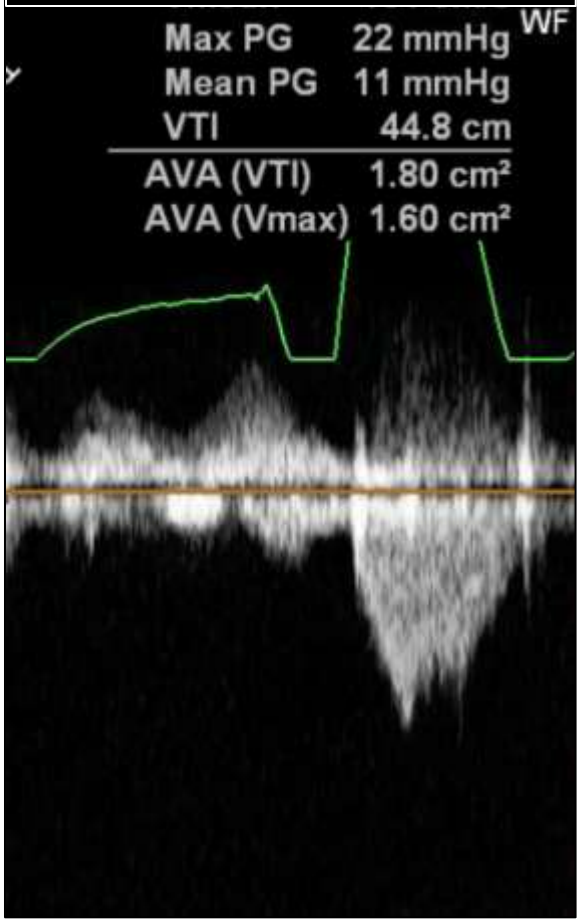
Hypoattenuating lesions

Severely restricted leaflet motion

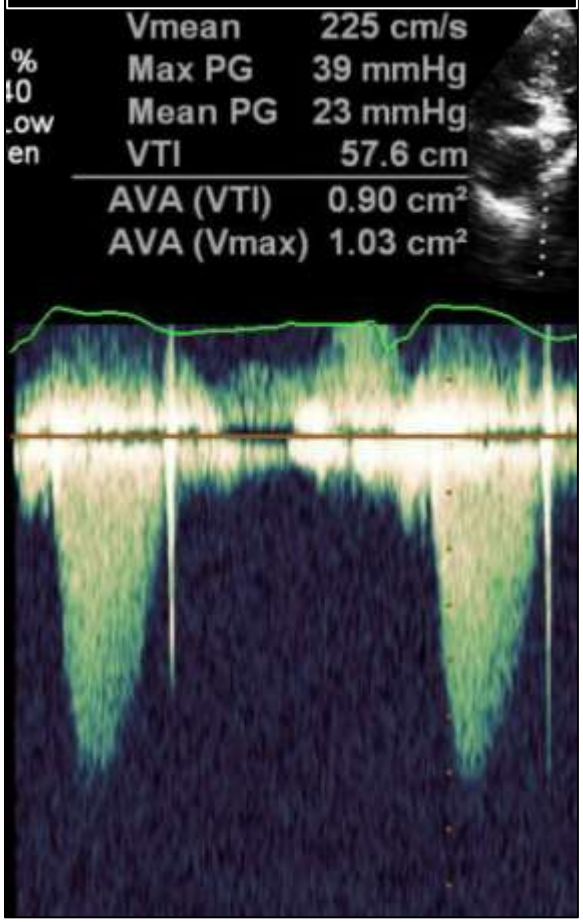
TTE revealed rise in gradients

Patient started on rivaroxaban 10mg daily, repeat CT pending

Day 1 post-TAVR
Mean gradient 11mmHg



30-day post-TAVR
Mean gradient 23mmHg

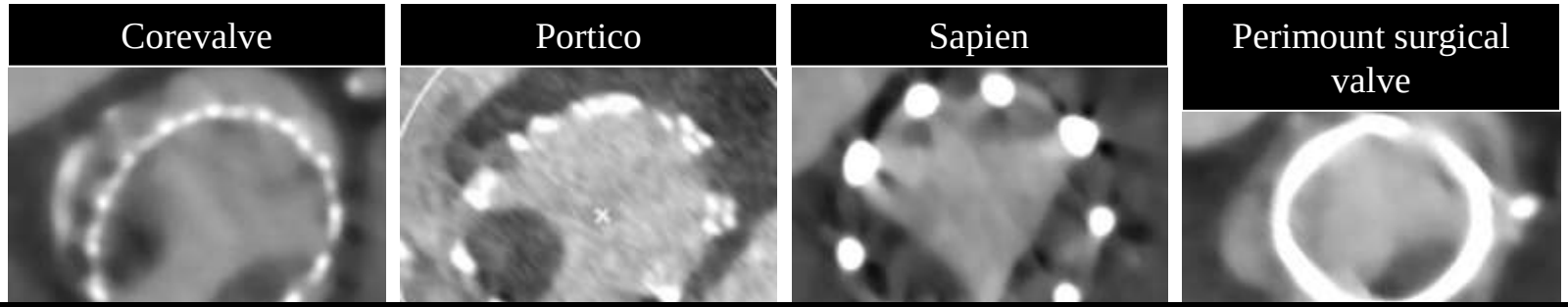


ORIGINAL ARTICLE

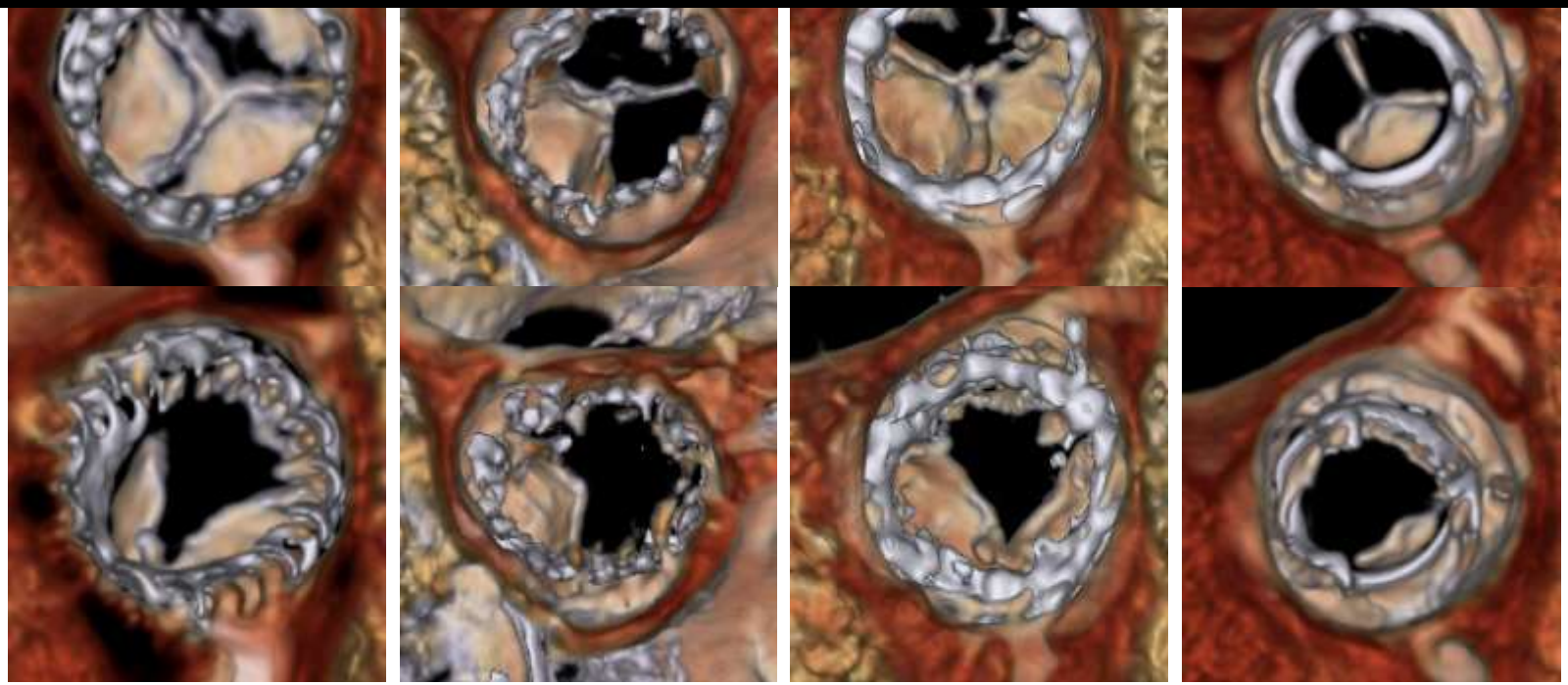
Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

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

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

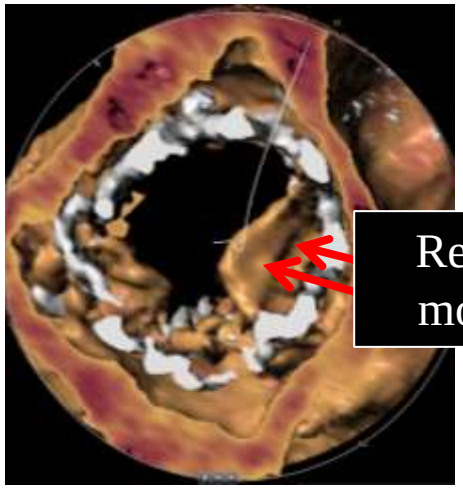


Prevelance was 13% in real life registries, 40% in a small IDE subset, overall 20% in 187 patients

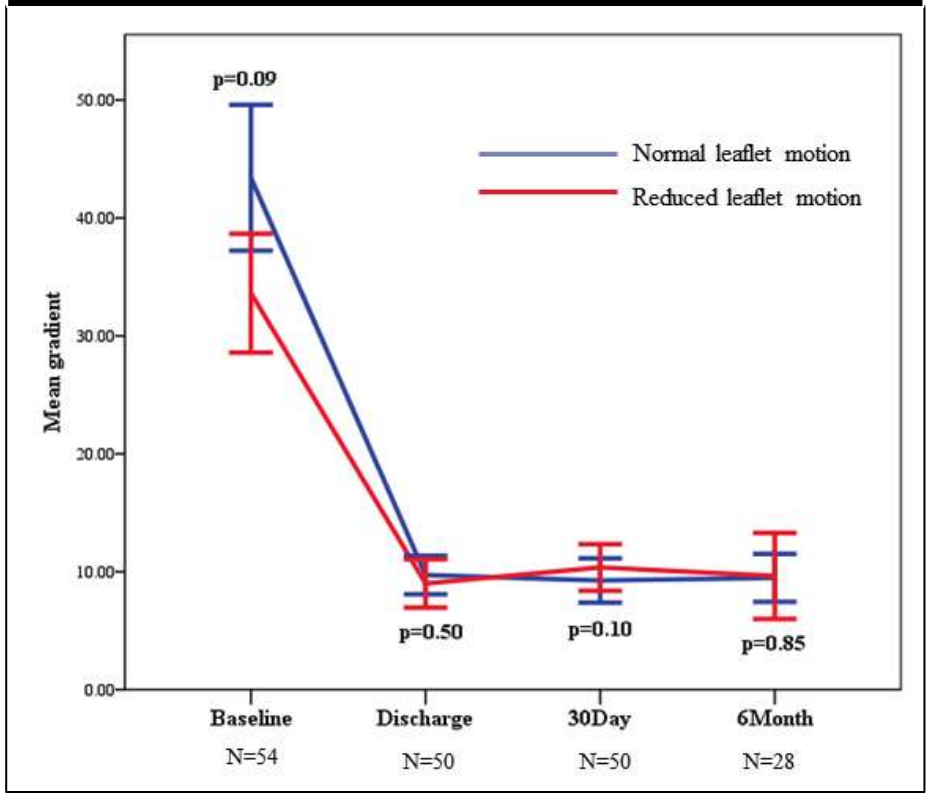


Results II: Role of TTE

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

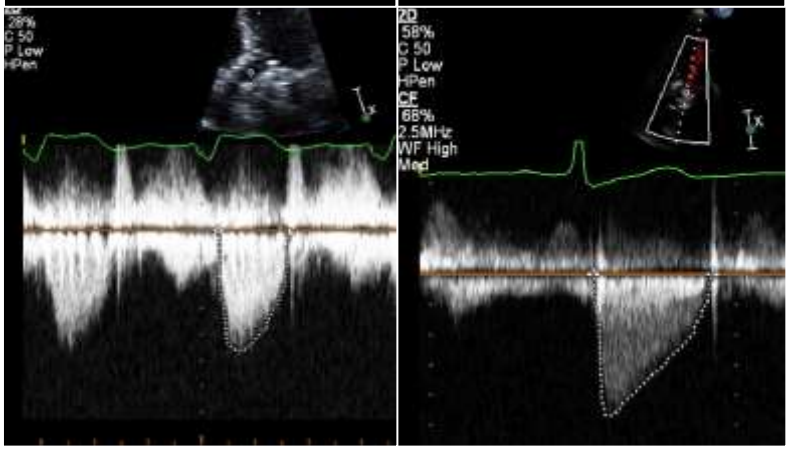


Portico IDE gradients in patients with and without reduced leaflet motion



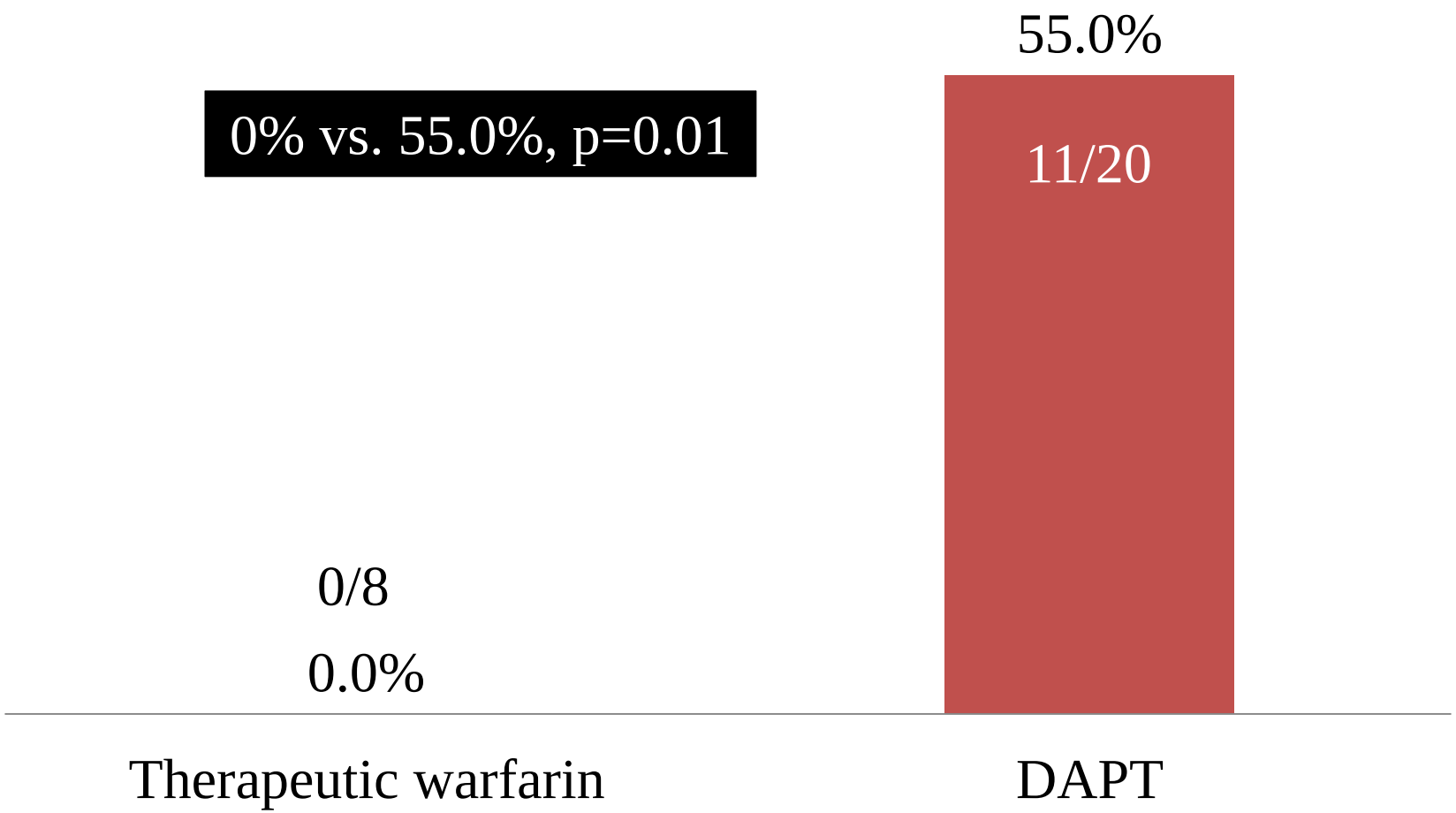
Day 1 mean gradient = 9 mmHg

Day 30 mean gradient = 9 mmHg



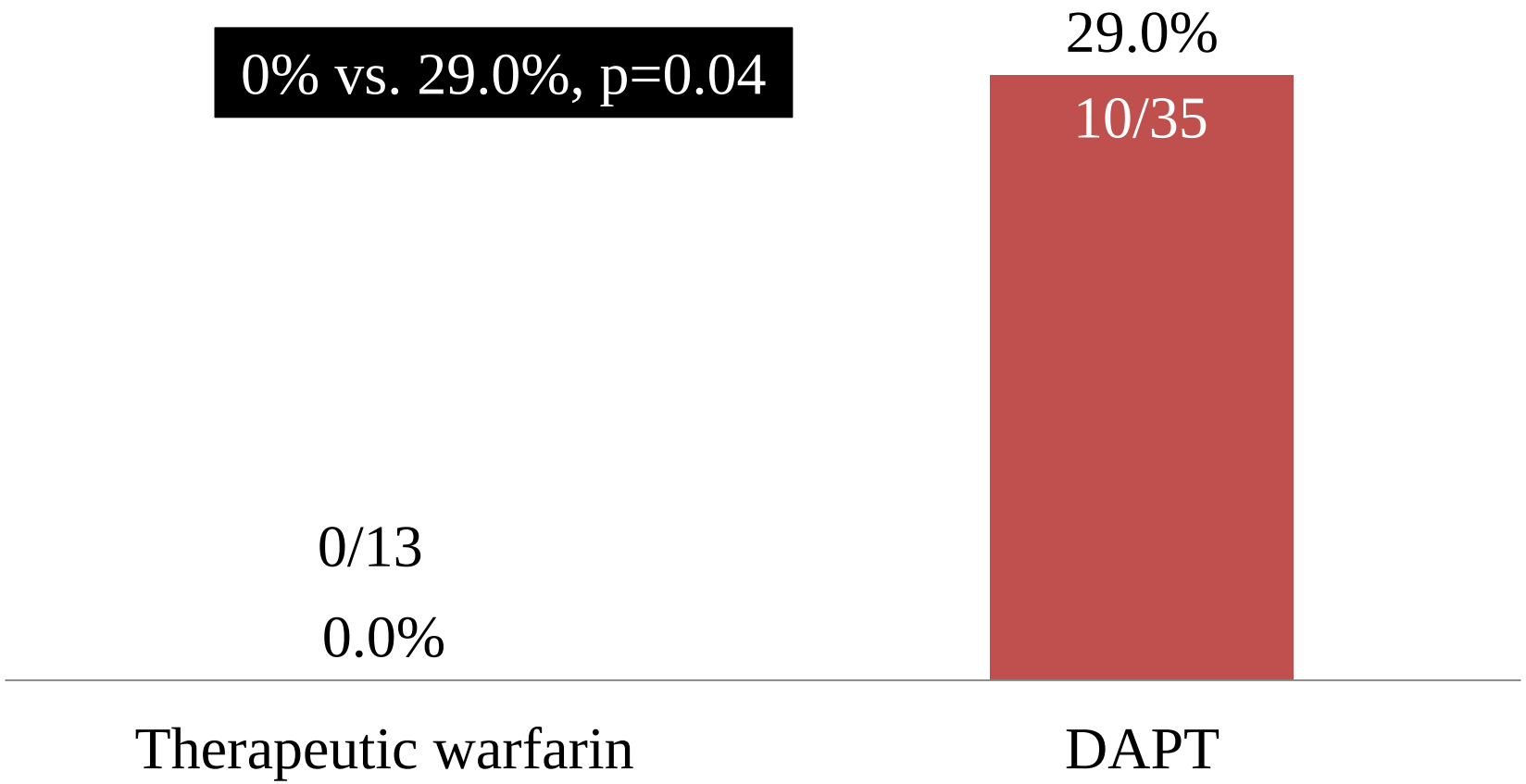
Results IV: Therapeutic warfarin vs. DAPT: Portico-IDE

Decreased incidence of subclinical leaflet thrombosis



Results IV: Therapeutic warfarin vs. DAPT: Registries

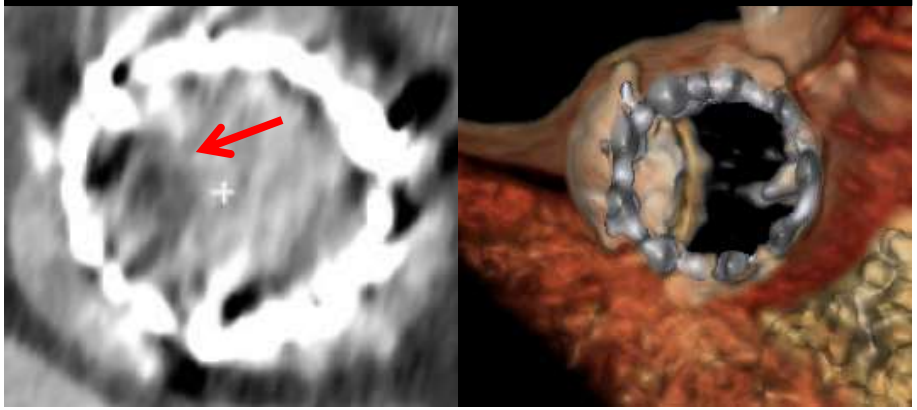
Decreased incidence of subclinical leaflet thrombosis



Results V: Natural history of this phenomenon

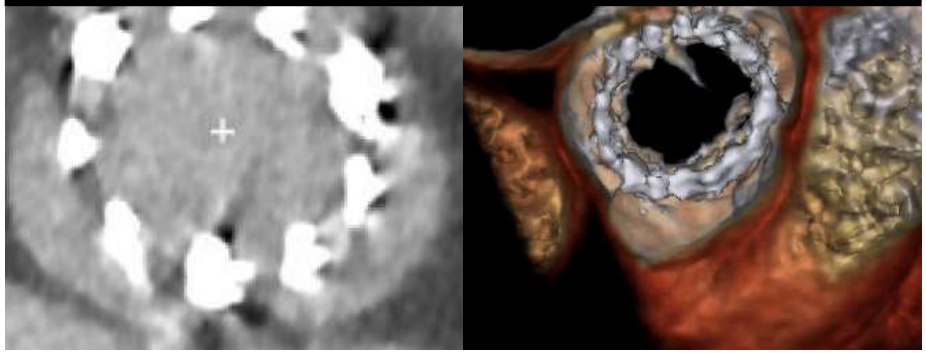
Anticoagulation was associated with resolution of thrombus and restoration of leaflet motion in 11 out of 11 patients

Reduced leaflet motion on 30-day CT



Patient was started on Warfarin

Resolution of thrombus and restoration of leaflet motion on 7 month follow-up CT



Results V: Natural history of this phenomenon

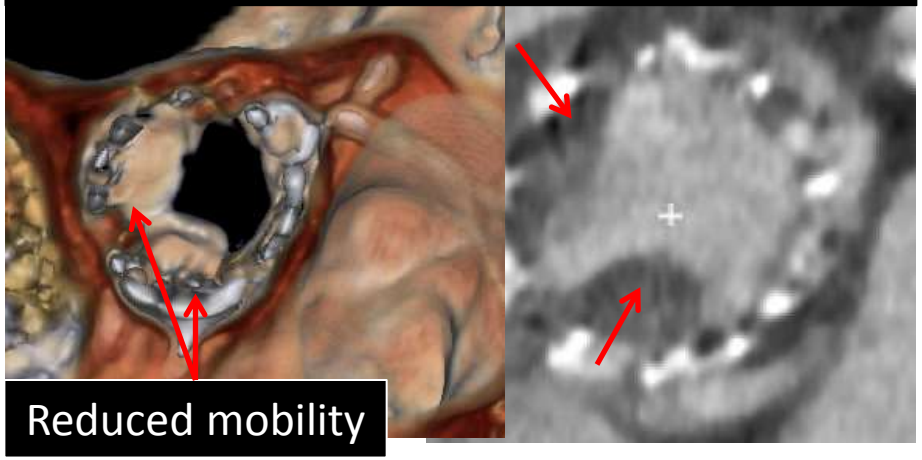
Persistence of thrombus and reduced leaflet motion in 9 out of 10 patients without therapeutic anticoagulation

Persistent reduced leaflet motion on subtherapeutic warfarin (INR 1.1)

30-day post-TAVR CT
Reduced leaflet motion

Reduced mobility

Follow-up CT 7 months later
Reduced leaflet motion



Reduced mobility

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**

Lancet online March 19, 2017

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%), 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).

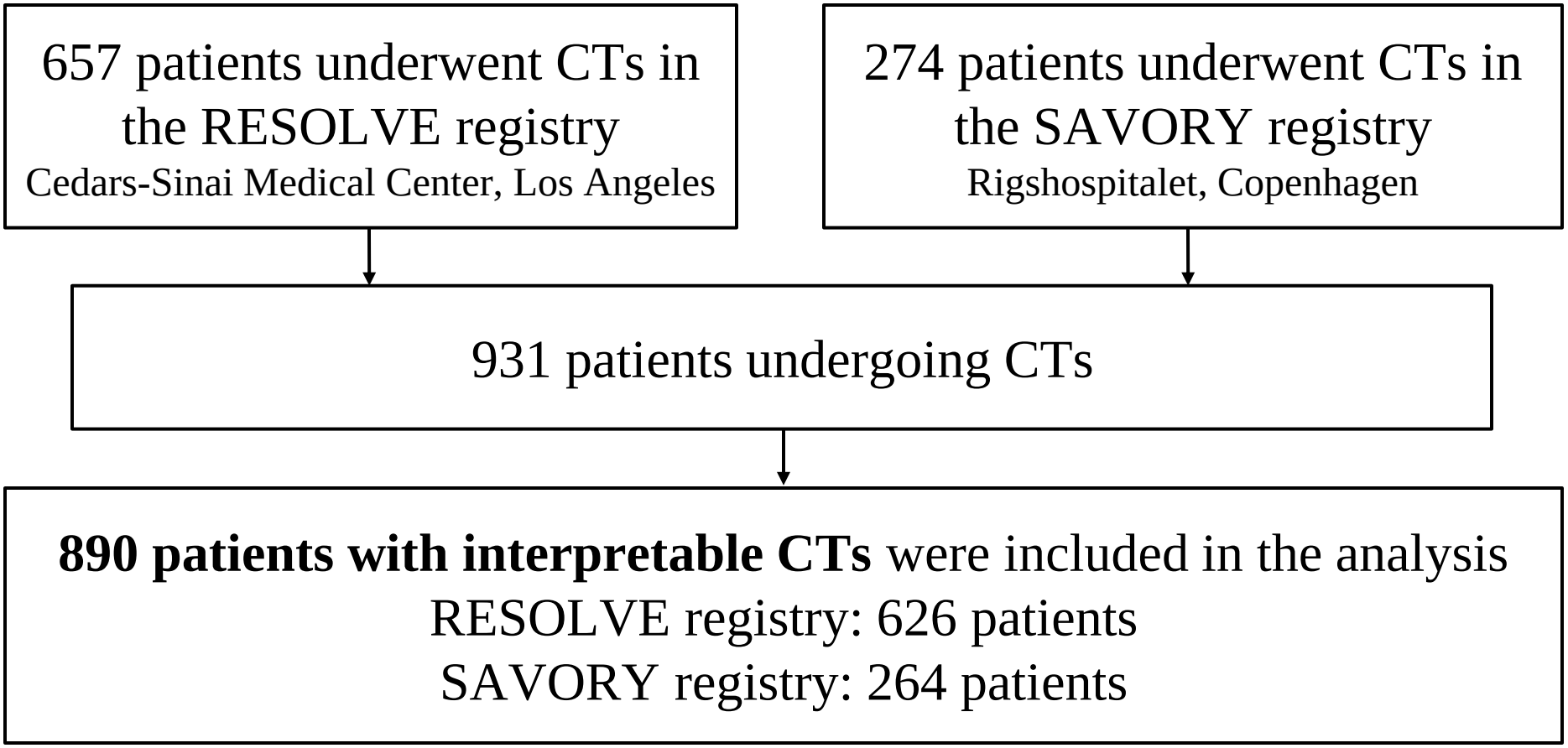
Added value of this study

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 motion and its effect on clinical outcomes. This study is the first, to our knowledge, to report differences in subclinical 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; 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 short course of anticoagulation if findings from ongoing randomised trials substantiate these existing findings.

Study design



Prevalence of reduced leaflet motion

Transcatheter vs. surgical bioprosthetic aortic valves: p=0.001

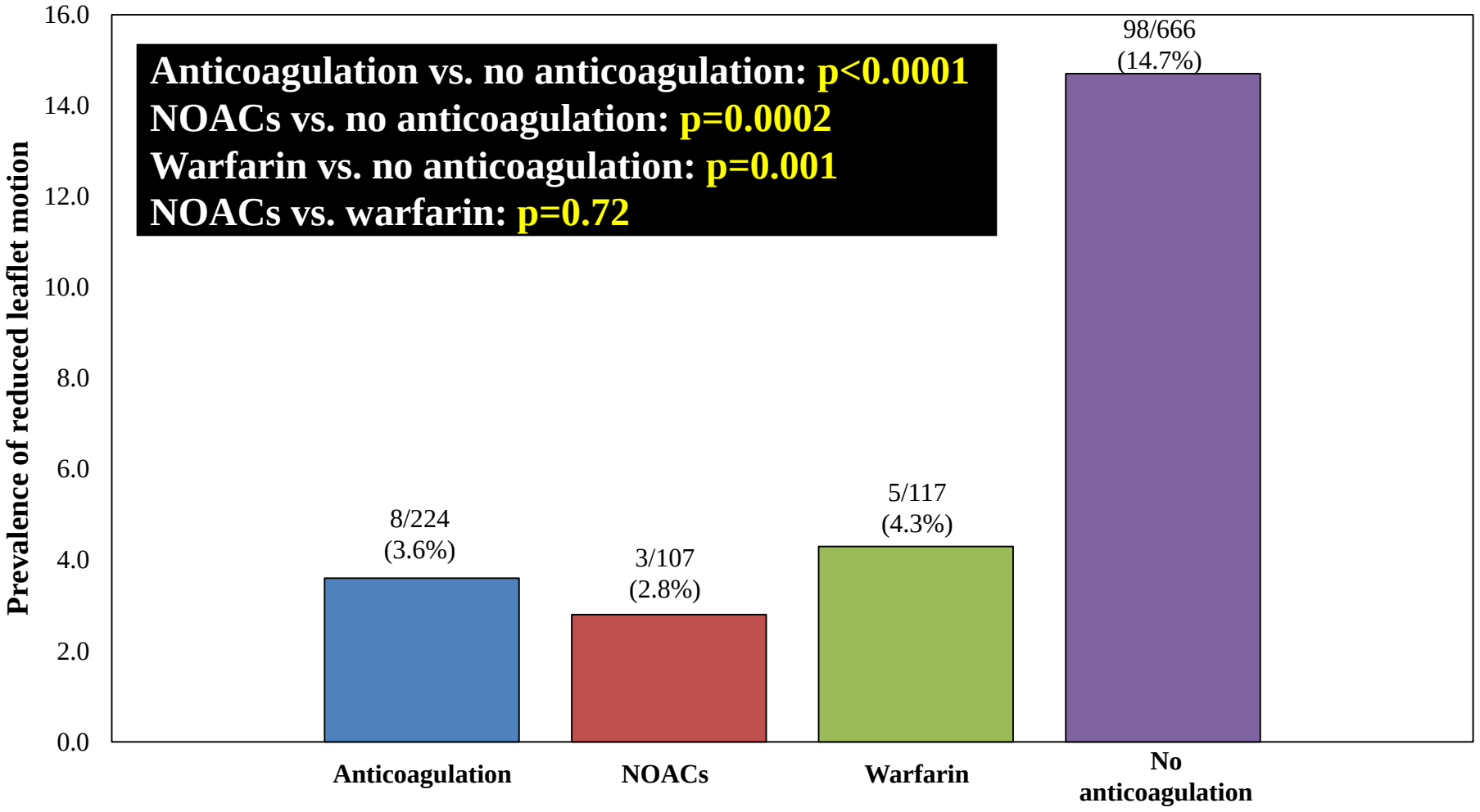
Reduced leaflet motion was present in 106 (11.9%) patients

Transcatheter valves
13.4% (101 out of 752)

Surgical valves
3.6% (5 out of 138)

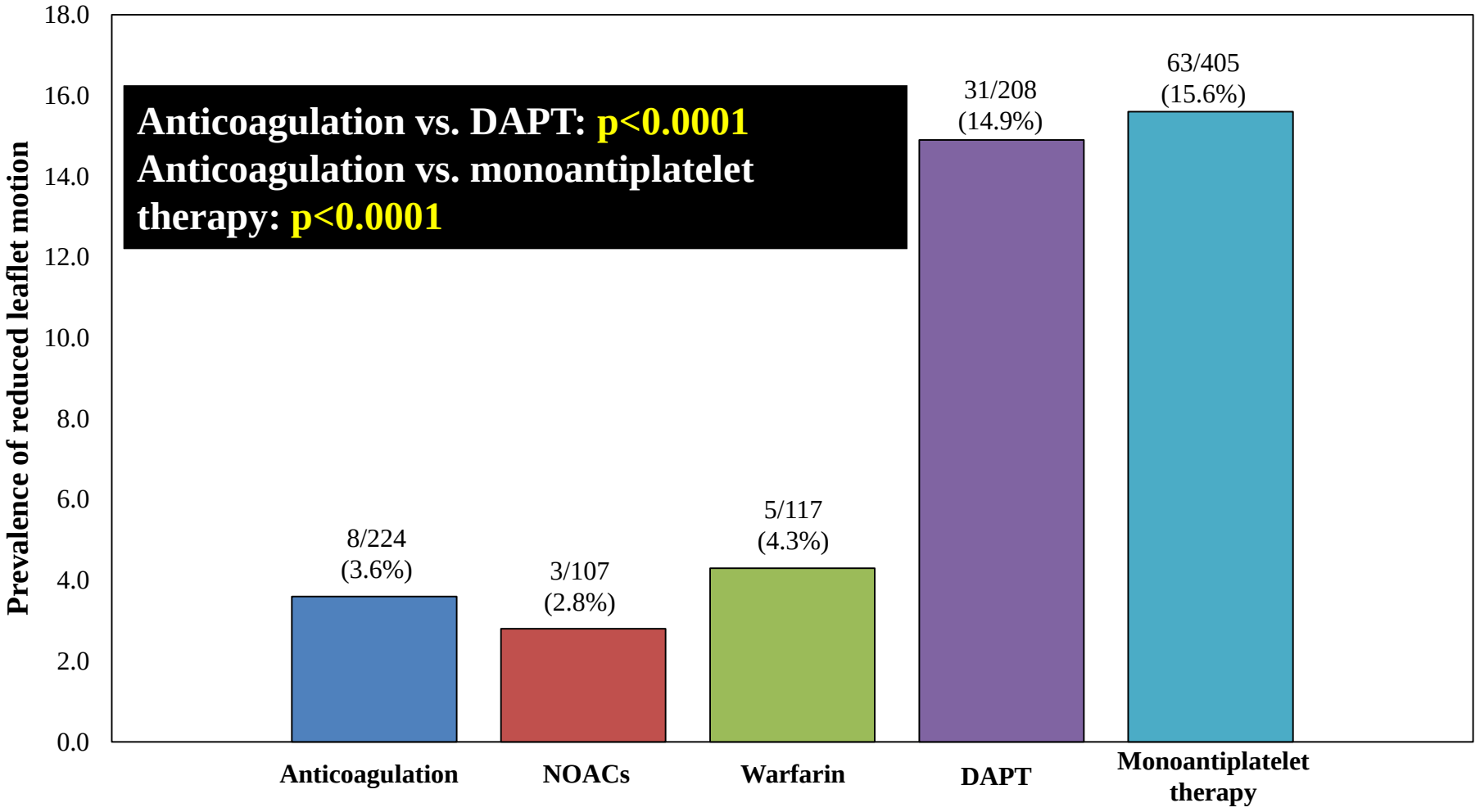
Anticoagulation and reduced leaflet motion

Anticoagulation vs. no anticoagulation



Anticoagulation and reduced leaflet motion

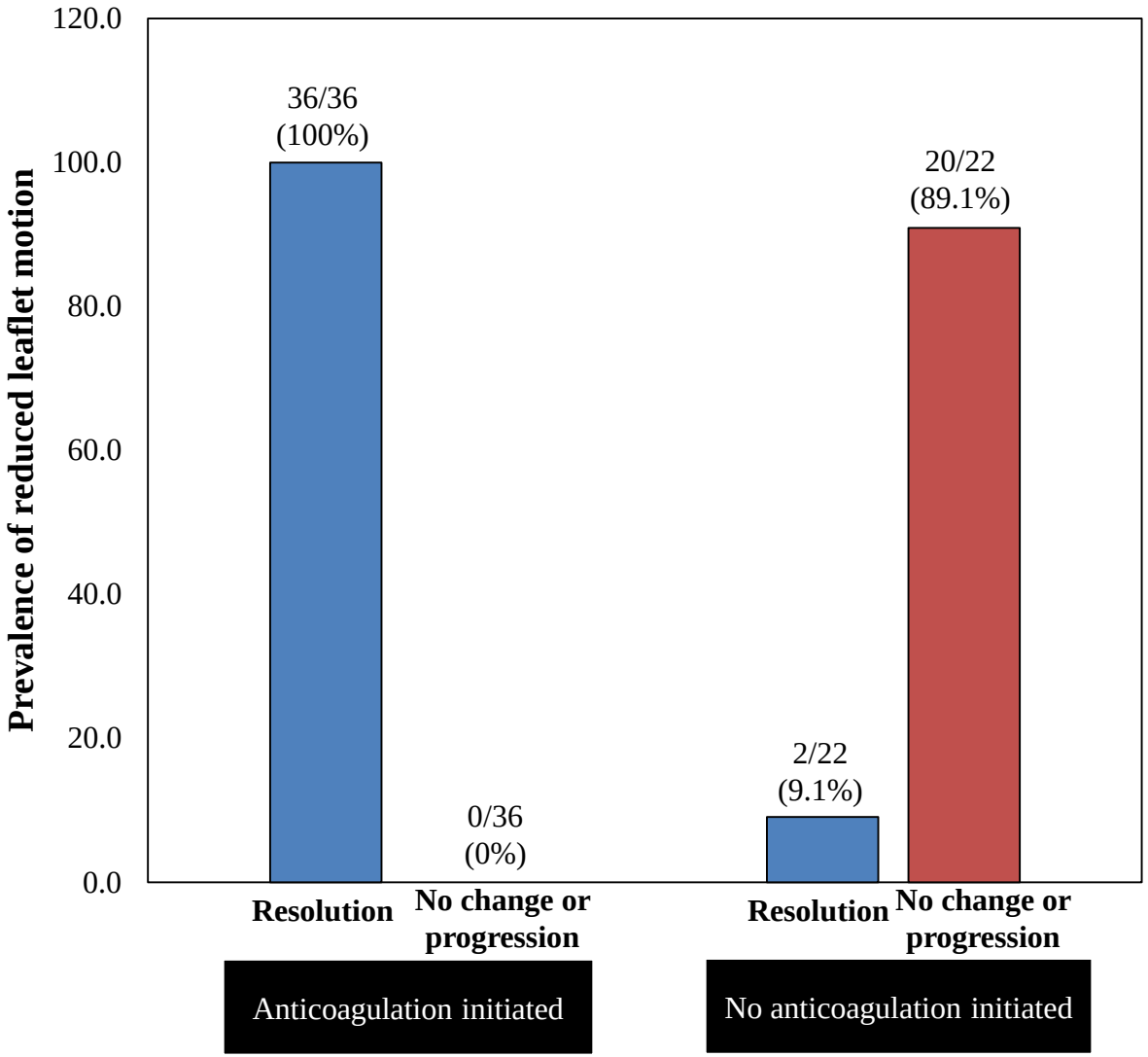
Anticoagulation vs. antiplatelet therapy



Multivariate predictors of reduced leaflet motion

	Odds ratio (95% CI)	p-value
Age	1·04 (1·01-1·07)	0·01
Ejection fraction	0·98 (0·97-1·00)	0·02
Surgical vs transcatheter valve	0·33 (0·11-0·96)	0·04
Anticoagulation	0·24 (0·10-0·58)	0·002
Time to CT	1.00 (0.98-1.02)	0.67
Atrial fibrillation	0.62 (0.31-1.23)	0.17
BMI	0.97 (0.93-1.02)	0.17

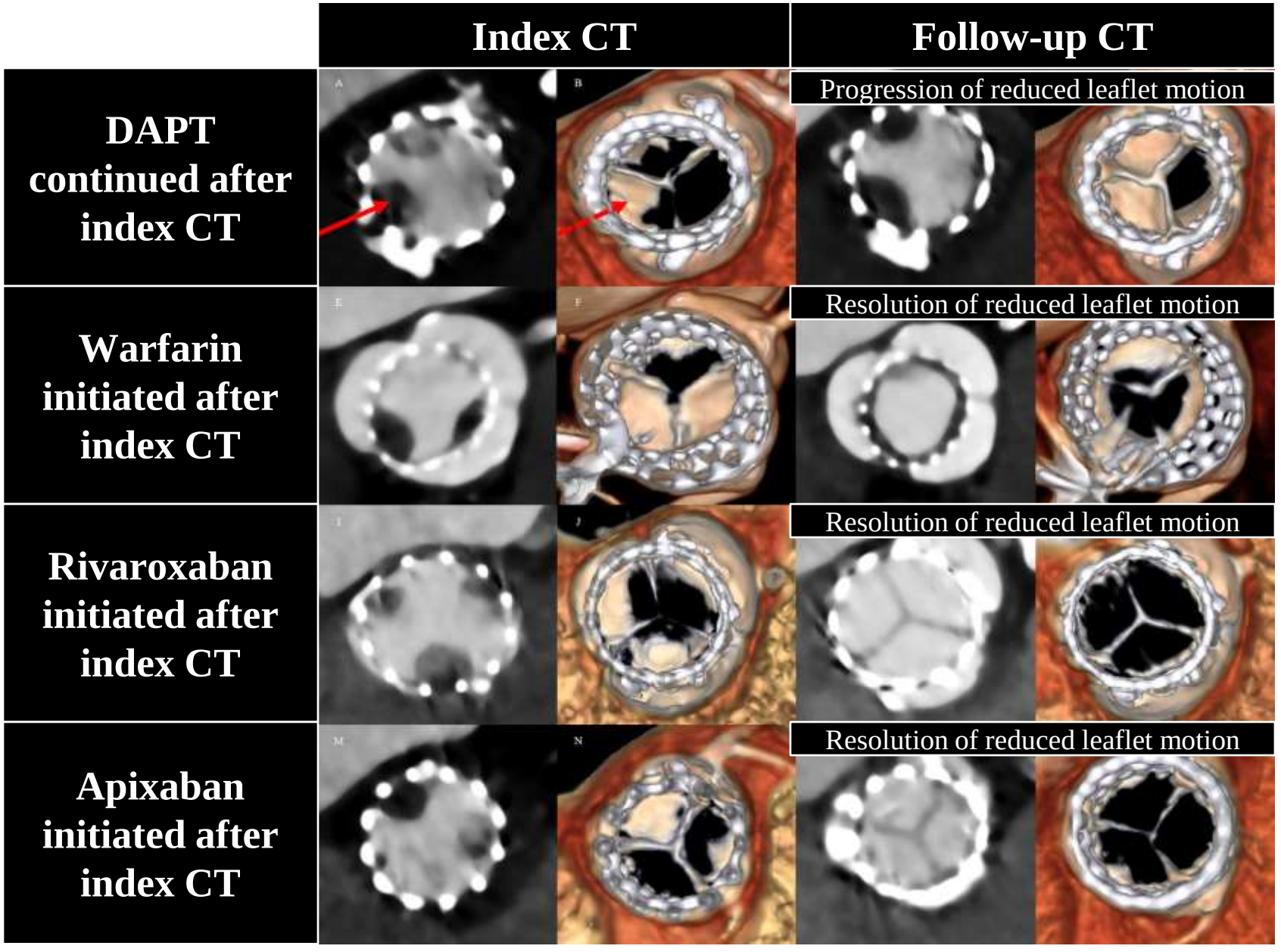
Impact of initiation of anticoagulation on reduced leaflet motion



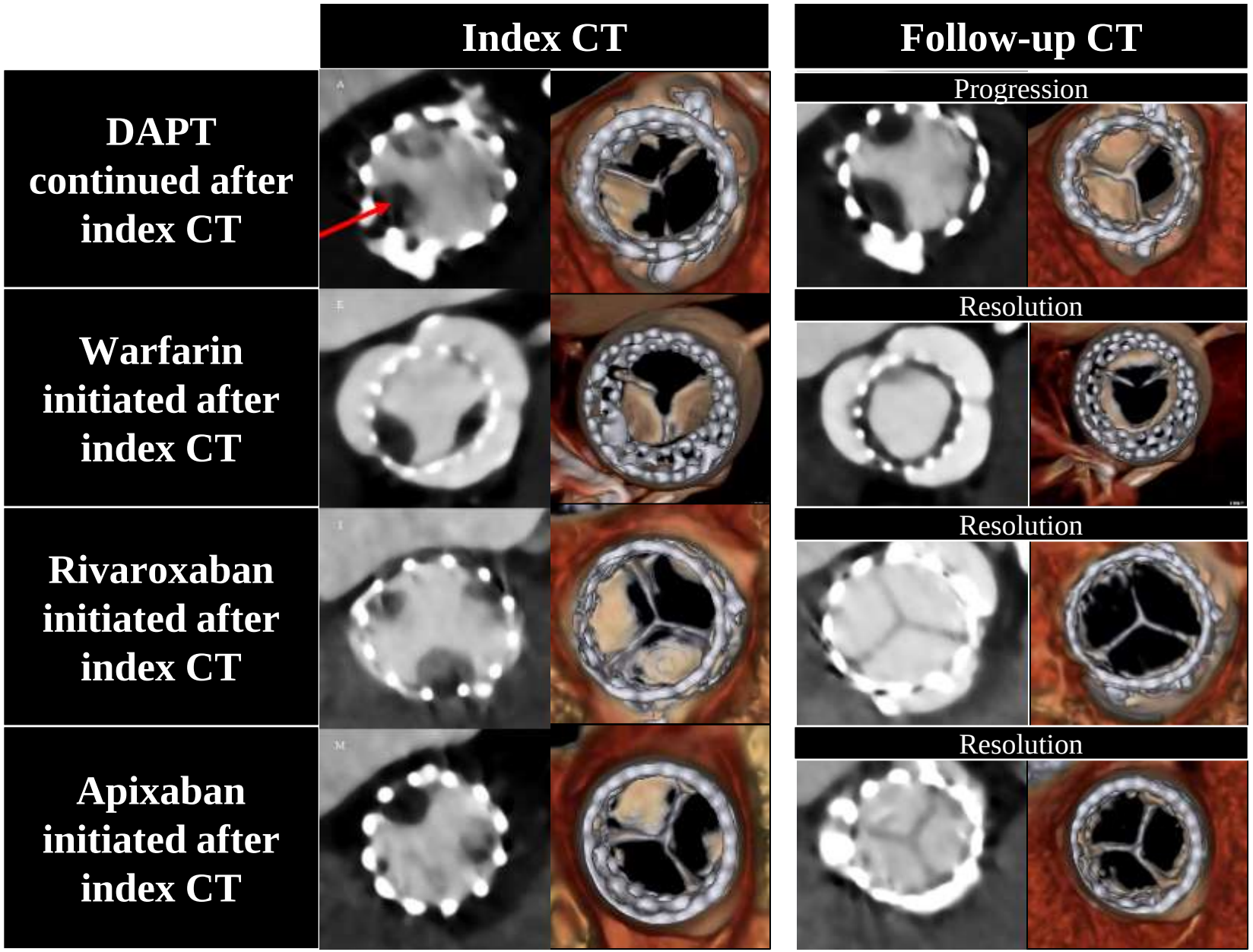
- **Resolution in 36 out of 36 patients** treated with anticoagulation (NOACs, n=12; warfarin, n=24)
- **Persistence/progression in 20 out of 22 patients** not treated with anticoagulation

P<0.0001

Anticoagulation vs. DAPT

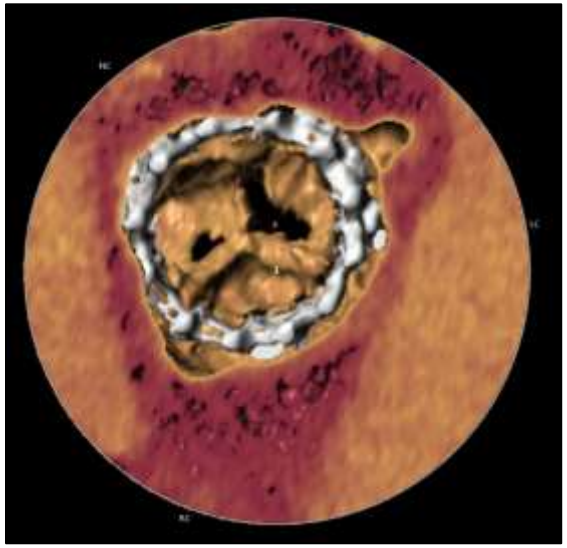


Anticoagulation vs. DAPT

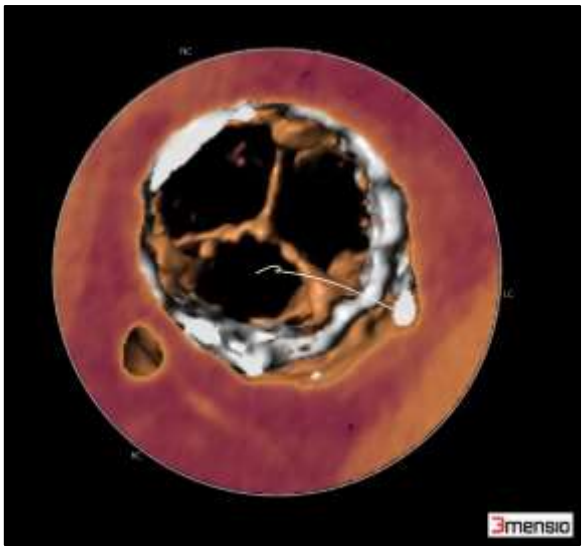


Recurrence of reduced leaflet motion following discontinuation of anticoagulation

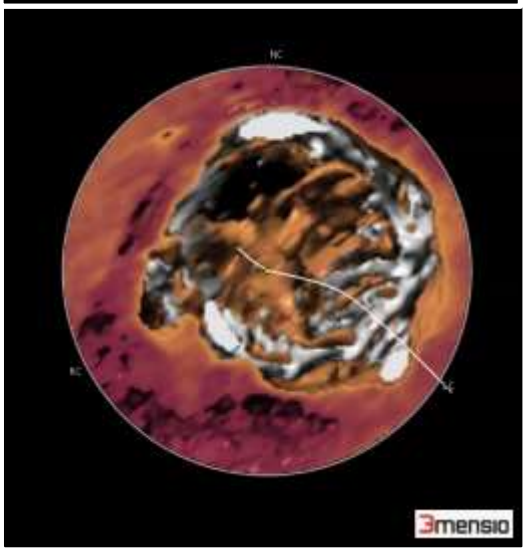
Baseline
Reduced leaflet motion



s/p Xarelto 10mg
Normal leaflet motion

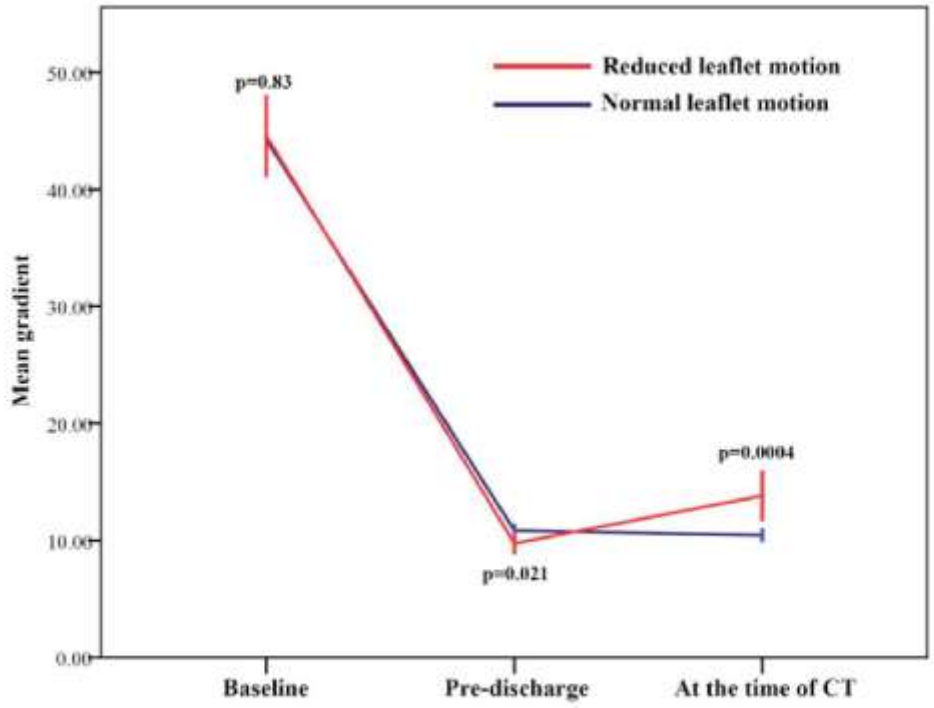


Six months following discontinuation of xarelto
Reduced leaflet motion



Reduced leaflet motion recurred in 4 out of 8 patients in whom anticoagulation was discontinued

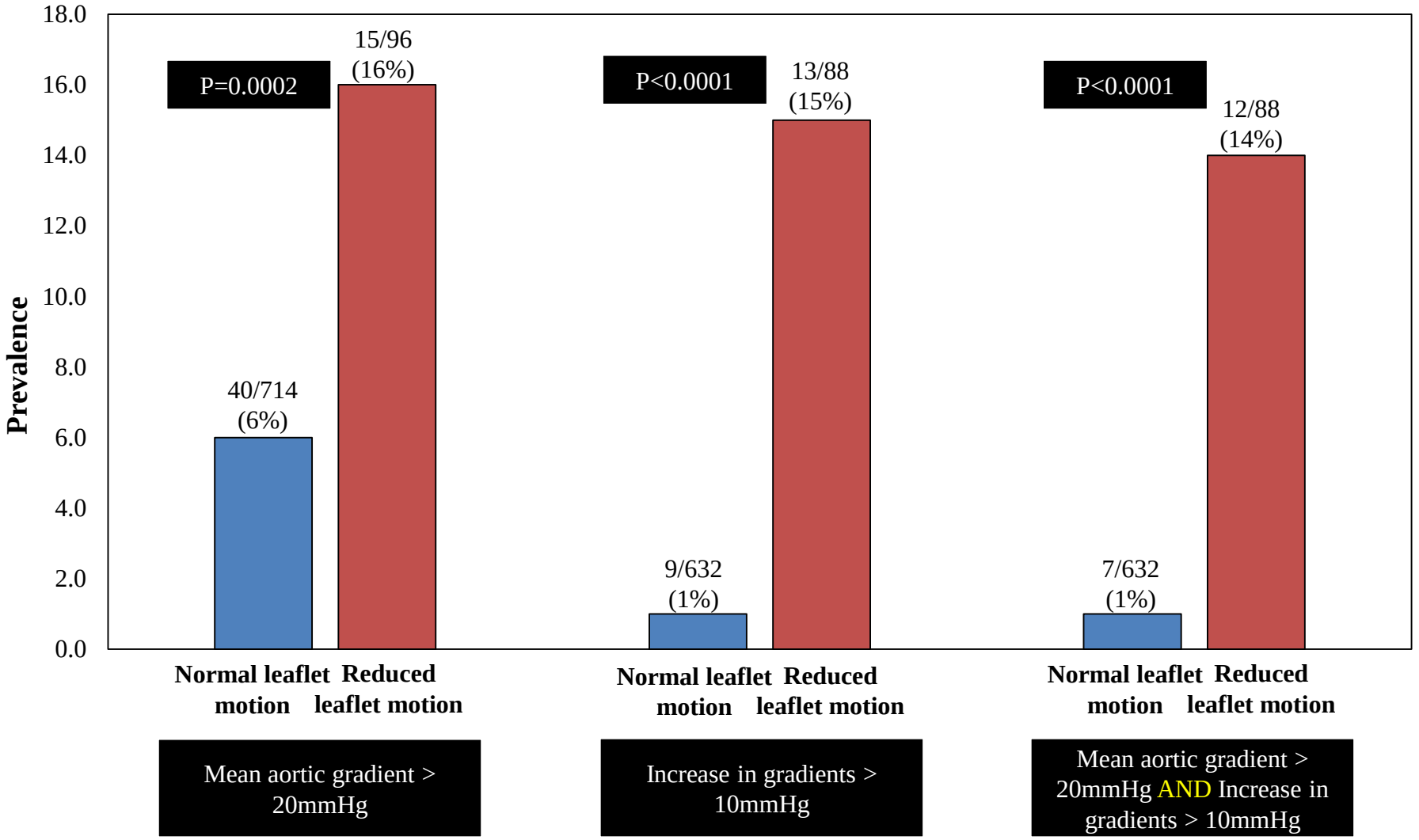
Impact of reduced leaflet motion on valve hemodynamics



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



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

Impact of reduced leaflet motion on clinical outcomes

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* All strokes include hemorrhagic and ischemic strokes

Early hypo-attenuated leaflet thickening in balloon-expandable transcatheter aortic heart valves

Gregor Pache[1*], Simon Schoechlin[2], Philipp Blanke[3], Stephan Dorfs[2], Nikolaus Jander[2], Chesnal D. Arepalli[3], Michael Gick[2], Heinz-Joachim Buettner[2], Jonathon Leipsic[3], Mathias Langer[1], Franz-Josef Neumann[2], and Philipp Ruile[2]

Prevalence of hypoattenuating lesions
10% (16/156 patients)

EHJ 2015

Transcatheter Aortic Valve Thrombosis

Incidence, Predisposing Factors, and Clinical Implications

Nicolaj C. Hansson, MD,[a] Erik L. Grove, MD, PhD,[a,b] Henning R. Andersen, MD, DMSc,[a] Jonathon Leipsic, MD,[c] Ole N. Mathiassen, MD, PhD,[a] Jesper M. Jensen, MD, PhD,[a] Kaare T. Jensen, MD, PhD,[a] Philipp Blanke, MD,[c] Tina Leetmaa, MD,[a] Mariann Tang, MD,[d] Lars R. Krusell, MD,[a] Kaj E. Klaaborg, MD,[d] Evald H. Christiansen, MD, PhD,[a] Kim Terp, MD,[d] Christian J. Terkelsen, MD, DMSc,[a] Steen H. Poulsen, MD, DMSc,[a] John Webb, MD,[c] Hans Erik Bøtker, MD, DMSc,[a,b] Bjarne L. Nørgaard, MD, PhD[a]

JACC

- 405 patients with Sapien-XT or Sapien 3 valve undergoing MDCT
- Prospective gated CT scan using 2nd generation CT scanner
- Echocardiograms performed 1-3 months and 12 months post-TAVR

- **THV thrombosis noted in 28/405 (7%) patients**
- **Subclinical leaflet thrombosis 23/405 (5.7%)**
- **Clinical leaflet thrombosis 5/28 (1.2%)**

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- Echocardiograms performed 1-3 months and 12 months post-TAVR
- **THV thrombosis noted in 28/405 (7%) of patients**

Risk of THV thrombosis was lower in patients on warfarin, compared to those not on warfarin

1.8% vs. 10.7%

RR 6.09, 95% CI 1.86-19.84

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Treatment with warfarin resulted in resolution of THV thrombosis and normalized THV function in 85% of patients

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		THV Thrombosis		
	Total (n = 246)	Without (n = 229)	With (n = 17)	p Value
Stroke	10 (4)	8 (3)	2 (12)	0.15
Echocardiography				
LVEF ≤35%	30 (12)	27 (12)	3 (18)	0.44
Mean trans-THV gradient, mm Hg	8 ± 4	8 ± 4	9 ± 4	0.32
EOA_{THV}, cm^2	1.7 ± 0.5	1.6 ± 0.5	1.6 ± 0.6	0.43
Moderate/severe MR	17 (7)	15 (7)	2 (12)	0.33
PAR				0.29
None	162 (66)	154 (67)	8 (47)	
Mild	71 (29)	64 (28)	7 (41)	
Moderate	12 (5)	10 (4)	2 (12)	
Severe	1 (0.4)	1 (0.4)	0	

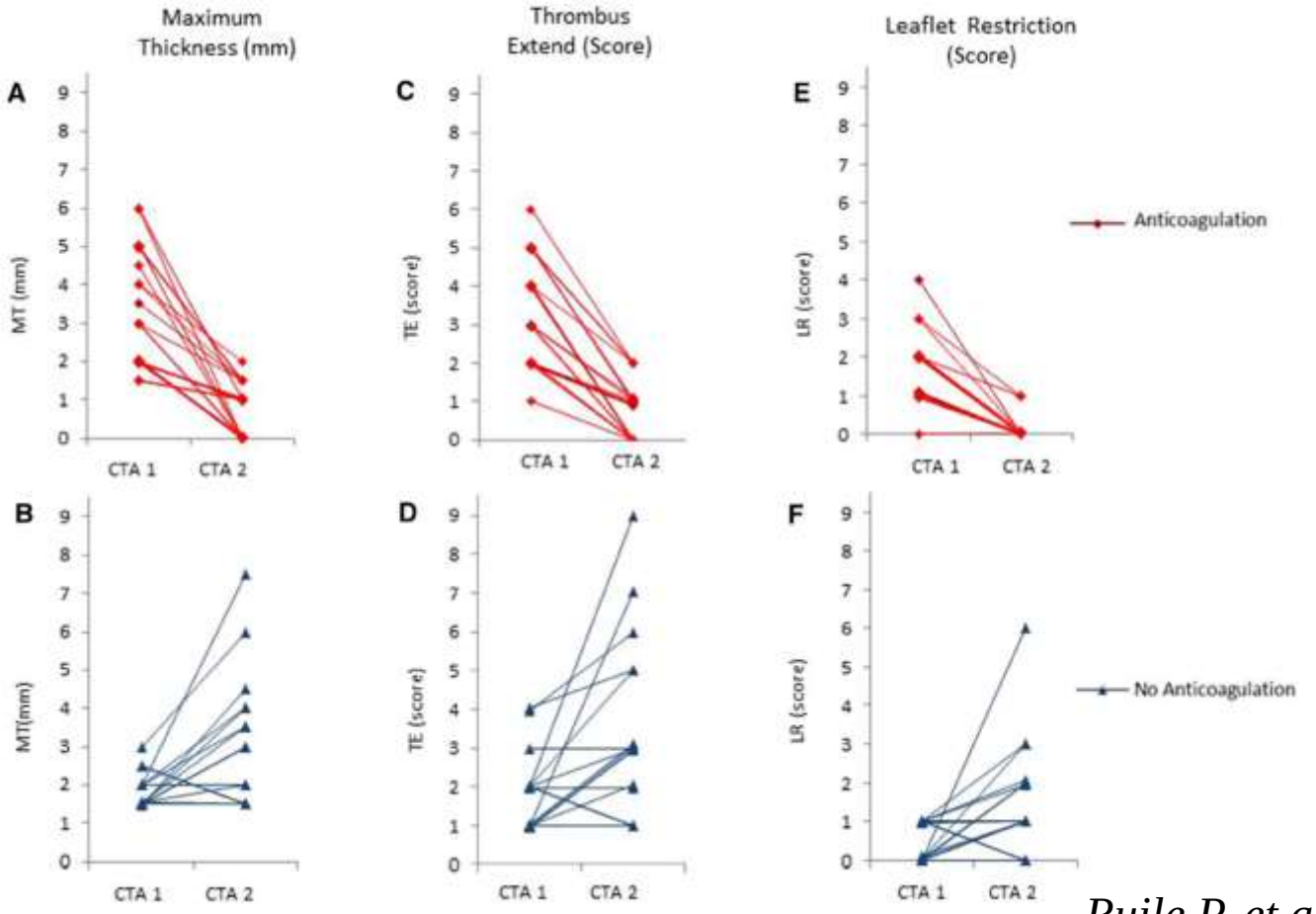
No significant difference in stroke rates

8/229 (3%) vs. 2/17 (12%), p=0.15

Course of early subclinical leaflet thrombosis after transcatheter aortic valve implantation with or without oral anticoagulation

51 patients with leaflet thickening (29 patients treated with anticoagulation and 22 patients treated with DAPT)

Repeat CT obtained in 22 patients on AC and 16 patients on DAPT



Leaflet thickening regressed in all 22 patients undergoing repeat CT

Leaflet thickening progressed in 11 of 16 patients

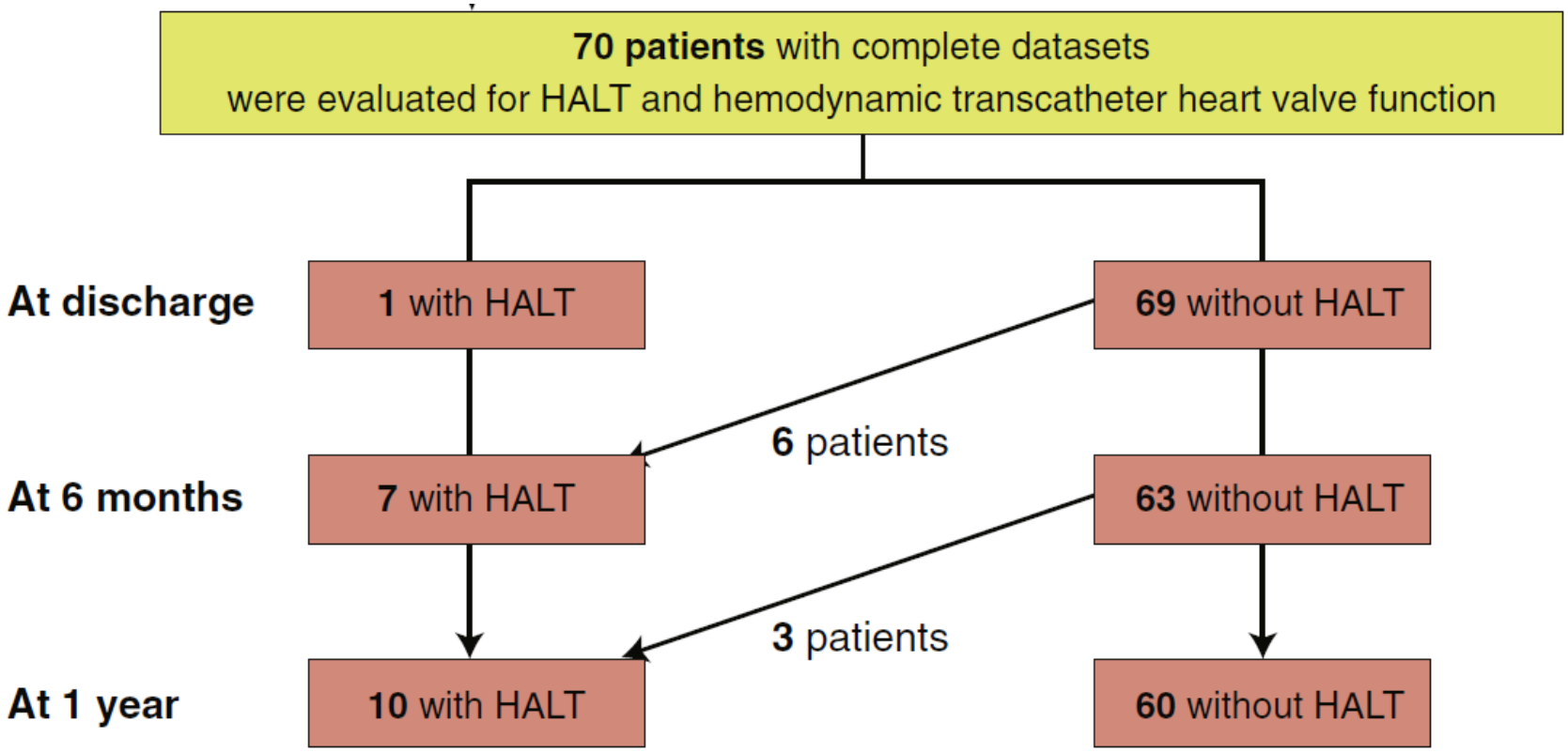
Ruile P. et al. Clin Res Cardiol 2017

Incidence, Predictors, and Mid-Term Outcomes of Possible Leaflet Thrombosis After TAVR

- 70 patients with Sapien-XT valve
- CTs performed at discharge, 6 months and 1 year post-TAVR

Prevalence of hypoattenuation associated leaflet thickening

1.4% at discharge, 10% at 6 months, 14.3% at 1 year



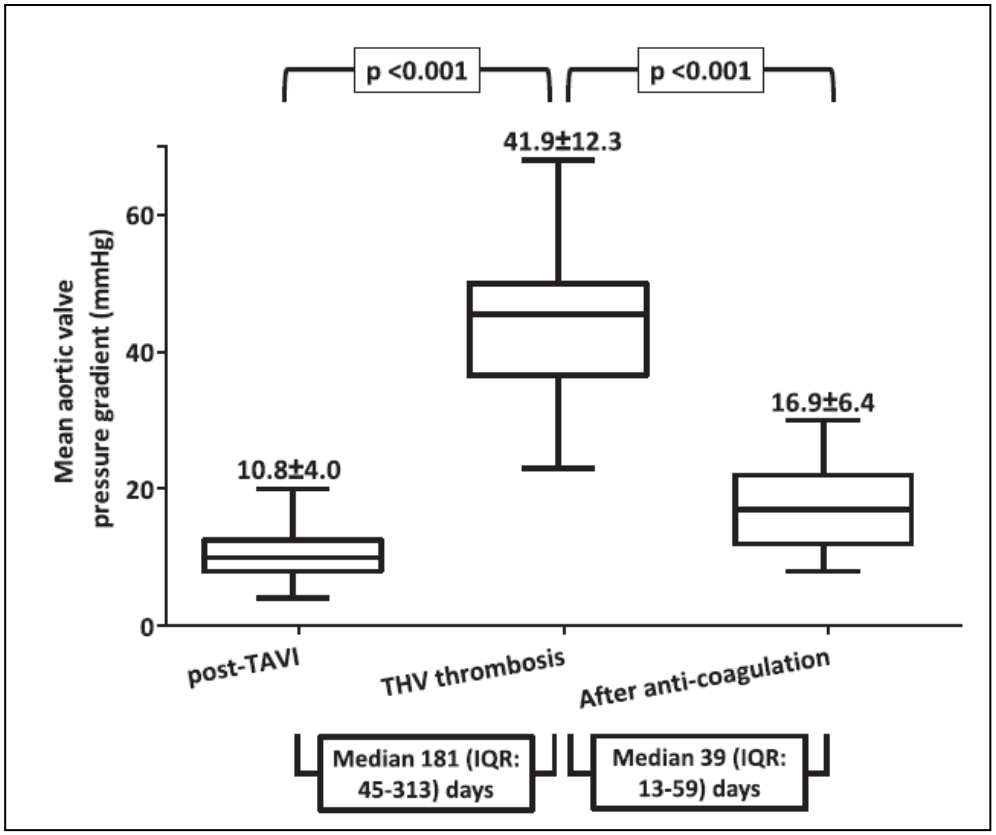
Yanagisawa. R. et al. JACC: Cardiovascular Imaging 2017

Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

Circulation: Cardiovascular Interventions

Multicenter, multinational registry of patients with TAVR thrombosis

26 out of 4266 patients undergoing TAVR (0.61%)



- **Median time to THV thrombosis: 181 days**
- **Median time to resolution of thrombus with anticoagulation: 39 days**

Latib A. et al. Circulation: Cardiovascular Interventions 2015

Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

Circulation: Cardiovascular Interventions

Multicenter, multinational registry of patients with TAVR thrombosis

26 out of 4266 patients undergoing TAVR (0.61%)

	n=26
Median time to THV thrombosis, d	181 (IQR, 45–313; range, 3–735)
Incidence of THV thrombosis	26/4266 (0.61)
Edwards Sapien or Sapien XT	20/2813 (0.71)
Medtronic CoreValve	6/1453 (0.41)
Clinical presentation	
Dyspnea	17 (65.4)
No worsened symptoms	8 (30.8)
NSTEMI, acute heart failure	1 (3.8)
Echo findings at THV thrombosis	
LVEF, %	58.0±10.6
Mean aortic valve gradient, mm Hg	40.5±14.0
Mean aortic valve gradient <20 mm Hg*	2 (7.7)
Maximal aortic valve gradient, mm Hg	65.1±19.0
Worsened AR (to more than moderate) as compared with post procedure	2 (7.7)
Thrombus morphology	
Thickened leaflets or thrombotic apposition of leaflets	20 (76.9)
Thrombotic mass on leaflets	6 (23.1)

All cases had clinical evidence of valve thrombus

- 17/26 (65.4%) had worsening dysnea on exertion
- 1/26 (3.8%) presented with NSTEMI
- 24/26 (92%) patients had elevated gradients

Latib A. et al. Circulation: Cardiovascular Interventions 2015

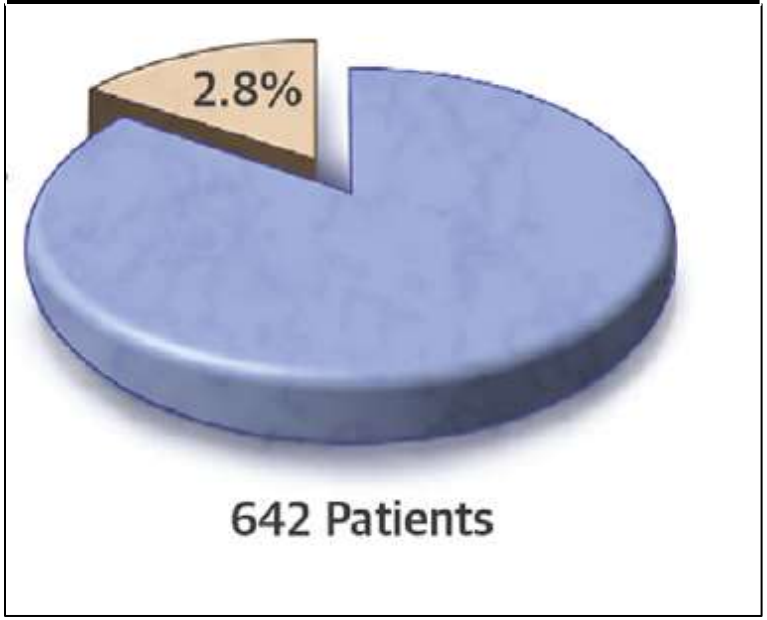
Clinical Bioprosthetic Heart Valve Thrombosis After Transcatheter Aortic Valve Replacement

Incidence, Characteristics, and Treatment Outcomes

Single center registry of 642 patients undergoing TAVR

- 305 CoreValve, 281 Sapien and 56 Lotus
- Oral anticoagulation in 261 patients, DAPT in 377 patients
- No case of valve thrombosis in patients on anticoagulation

Incidence of valve thrombosis



Predictors of valve thrombosis

- Balloon-expandable valves

- Valve-in-valve TAVR

- Use of antiplatelet therapy alone

Jose et al. JACC: Cardiovascular Interventions 2017

Subclinical leaflet thrombosis

- This is a real finding
- This finding occurs frequently
- This finding is noted in multiple valve types
- This finding is less frequent in patients on anticoagulation
- This finding resolves with the initiation of anticoagulation
- The impact of this finding on clinical outcomes requires further studies

Should we treat Leaflet Thrombosis?

- Should we treat *symptomatic* leaflet thrombosis? Definitely YES

- Should we treat *asymptomatic* leaflet thrombosis?

Yes-we treat thrombus in other location why not here, may be too late to find out if it affects valve durability, there is a signal for TIAs

No-there is no definite impact on outcomes yet, risk of bleeding may not be trivial. We need to elucidate this phenomenon better.

Should we routinely do CTs on all patients post TAVR?

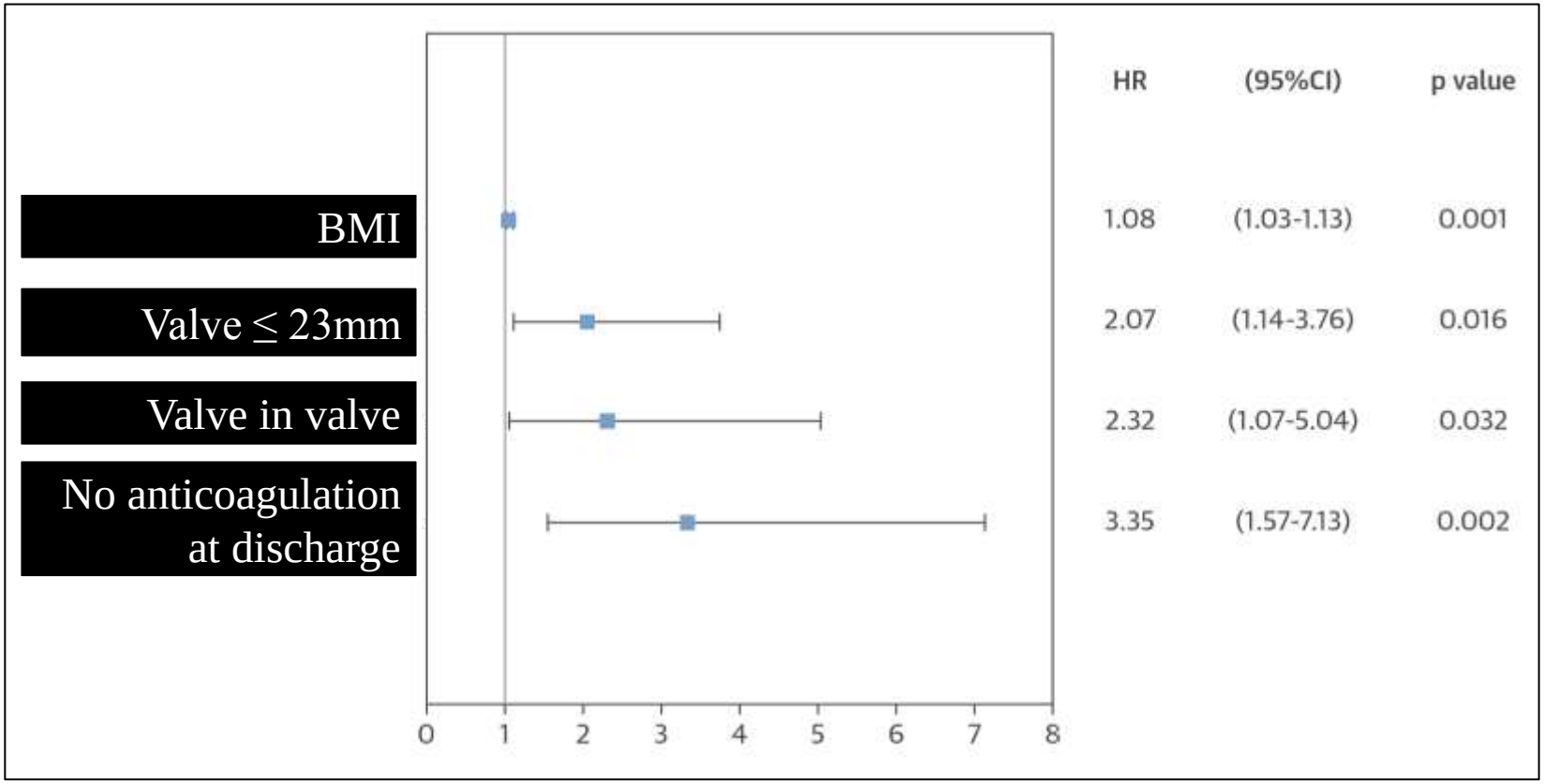
- Best done systematically in research protocols with the involvement of imaging experts
- Radiation and contrast use may be an issue
- What would we do with the information in patients who are not candidates for anticoagulation?
- There should be low threshold to image in patients with suspected valve dysfunction, thrombo-embolic events

RESOLVE Study (NCT02318342)

- Ongoing, multicenter registry being expanded to 1000 patients post-TAVR/Surgical AVR
- Corelab analysis of contrast CT scans
- Corelab analysis of echocardiograms
- Contact:
  - makkarr@cshs.org
  - Hasan.Jilaihawi@cshs.org
  - Tarun.Chakravarty@cshs.org

Predictors of valve hemodynamic degeneration after TAVR

1521 patients undergoing TAVR
Valve hemodynamic degeneration = 10mmHg rise in transvalvular gradients



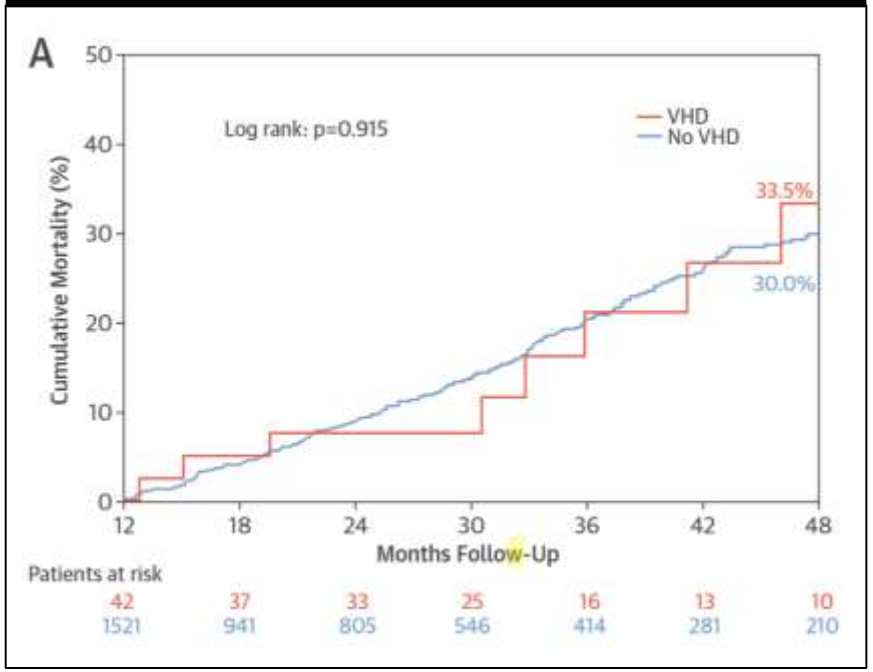
Del Trigo M. et al. JACC 2016

Valve hemodynamic degeneration and clinical outcomes

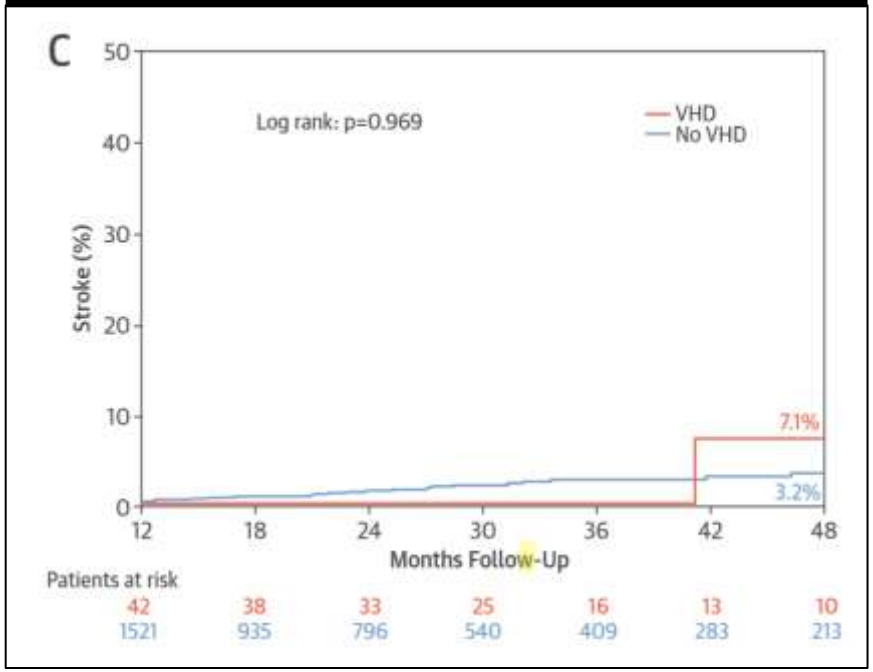
1521 patients undergoing TAVR
Valve hemodynamic degeneration = 10mmHg rise in transvalvular gradients

No significant increase in mortality or stroke

Mortality



Stroke



Del Trigo M. et al. JACC 2016

Surgical literature and valve durability

Significant heterogeneity in the definition for surgical bioprosthetic valve degeneration

Author / Year	Valve	Years	n. at risk	Earliest failure	FF from failure	Definition
Johnston, 2015	CEP	20	54	< 5 yrs	98% at 10 yrs / 85% at 20 yrs	explant
Bourguignon, 2015	CEP	20	18	< 5 yrs	78%	echocardiographic assessment
Alvarez, 2009	MF	10	1	3 yrs	95% at 5 yrs	Freedom from reoperation for SVD
Senage, 2014	MF	5	194	14 months	95%	progression of aortic transprosthetic gradient ≥30 mm Hg associated with a decreased effective orifice area ≤1 cm2 or intraprosthetic aortic regurgitation >2/4.
Piccardo, 2016	MF	15	2	< 4 yrs	56%	SVD determined by reop or echocardiographic investigtion.

Pieter Kappetein. TCT 2016

Updated Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation

The Valve Academic Research Consortium-2 Consensus Document†

A. Pieter Kappetein,* Stuart J. Head, Philippe Généreux, Nicolo Piazza, Nicolas M. van Mieghem, Eugene H. Blackstone, Thomas G. Brott, David J. Cohen, Donald E. Cutlip, Gerrit-Anne van Es, Rebecca T. Hahn, Ajay J. Kirtane, Mitchell W. Krucoff, Susheel Kodali, Michael J. Mack, Roxana Mehran, Josep Rodés-Cabau, Pascal Vranckx, John G. Webb, Stephan Windecker, Patrick W. Serruys, Martin B. Leon

Rotterdam, the Netherlands

Objectives The aim of the current Valve Academic Research Consortium (VARC)-2 initiative was to revisit the selection and definitions of transcatheter aortic valve implantation (TAVI) clinical endpoints to make them more suitable to the present and future needs of clinical trials. In addition, this document is intended to expand the understanding of patient risk stratification and case selection.

VARC2 Definition

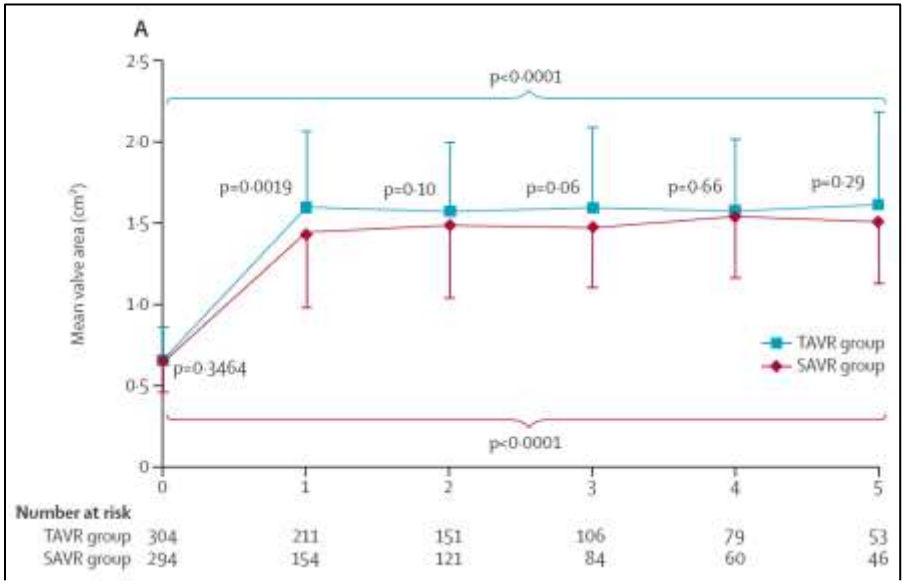
- *Valve-related dysfunction (mean aortic valve gradient >20 mm Hg, EOA < 0.9–1.1 cm^2 and/or DVI < 0.35 m/s, and/or moderate or severe prosthetic valve regurgitation)*
- *Requiring repeat procedure (TAVI or SAVR)*

Echocardiographic follow-up in PARTNER 1A

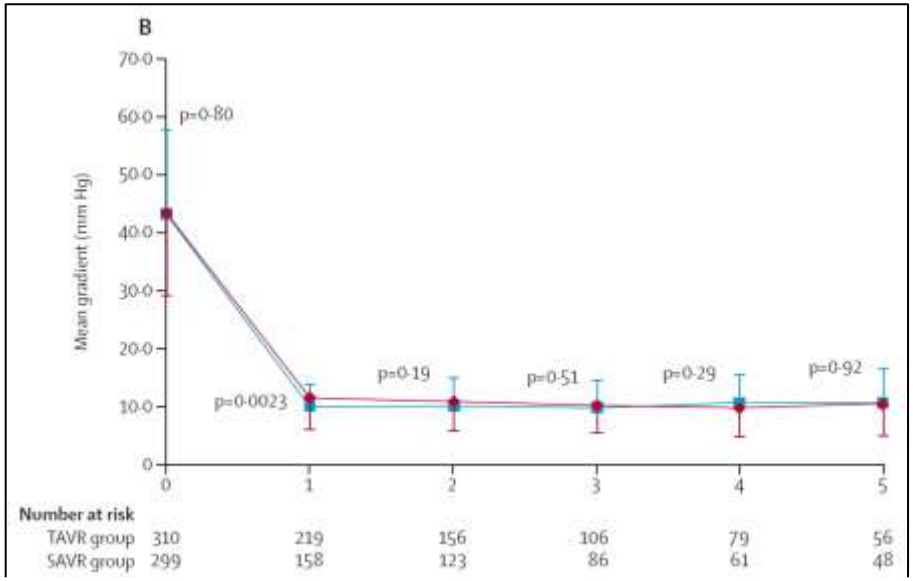
TAVR vs. SAVR in high-risk patients

- Similar valve hemodynamics btw TAVR & SAVR at 5 yrs
- No cases of structural valve degeneration requiring surgery

Aortic valve area



Aortic valve gradients

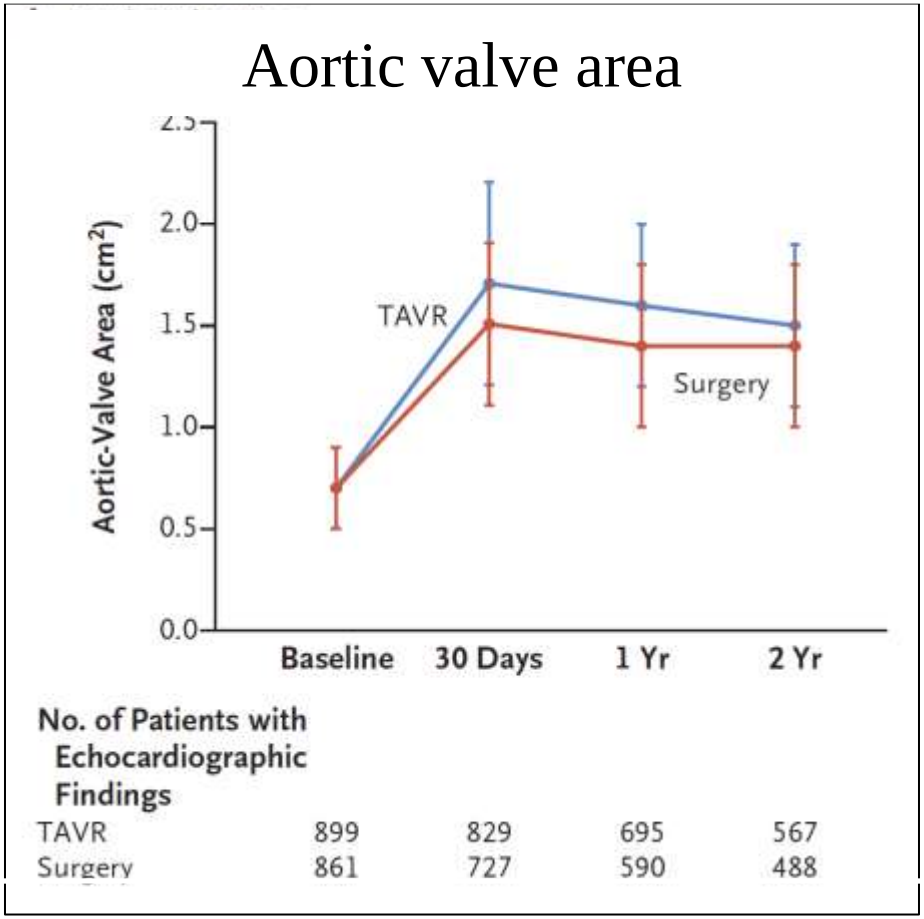


Mack M. et al. Lancet 2015

Echocardiographic follow-up in PARTNER 2

TAVR vs. SAVR in intermediate-risk patients

AVA superior with transcatheter versus surgical valves

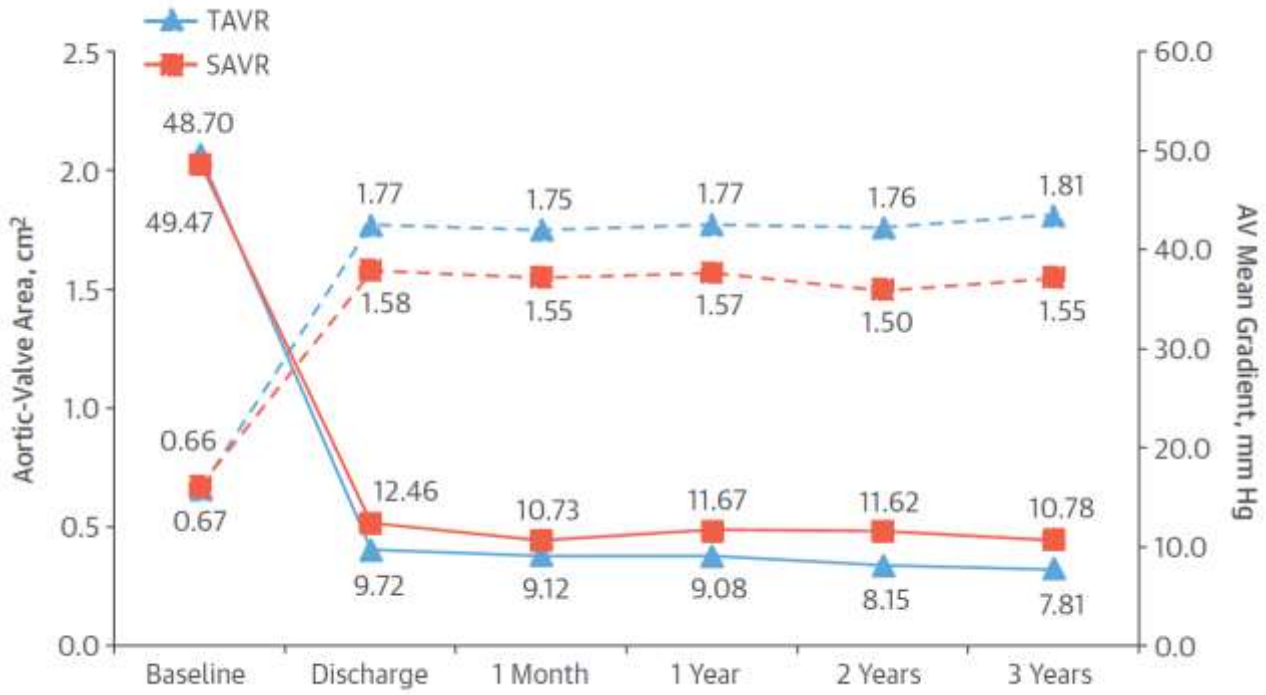


Leon M. et al. NEJM 2016

Echocardiographic follow-up in CoreValve IDE study

TAVR vs. SAVR in high-risk patients

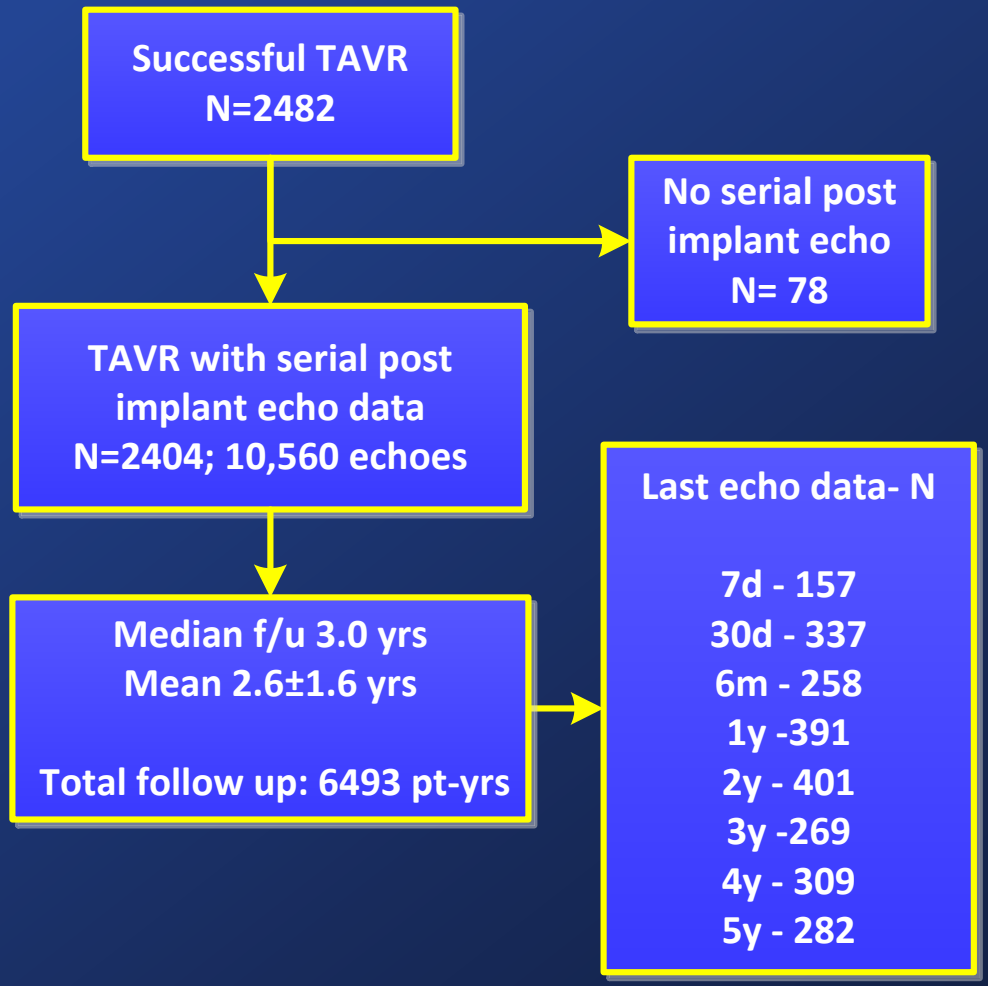
Higher AVA and lower mean gradients with CoreValve versus surgical valves



Deeb M. et al. JACC 2016

PARTNER 1 trial echo hemodynamic trends at 5 years

Cohort Derivation and Characteristics



Population characteristics

- Mean age 84.5 yrs
- 48% female
- 95% NYHA class 3-4
- 92% obstructive CAD
- Severe AS with AVA 0.65 cm^2

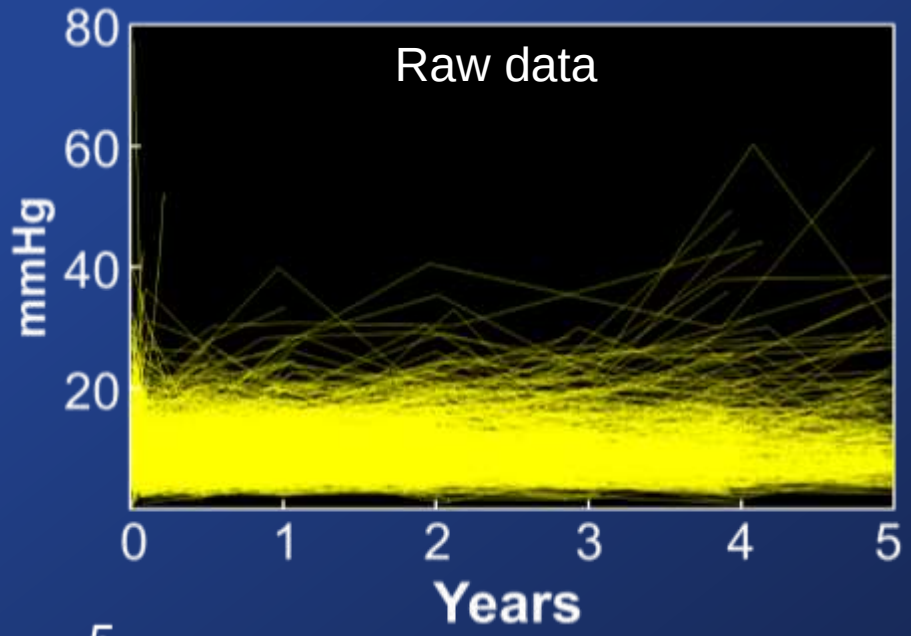
- THV size: 52% 23; 48% 26
- Access: 43% TA ; 57% TF

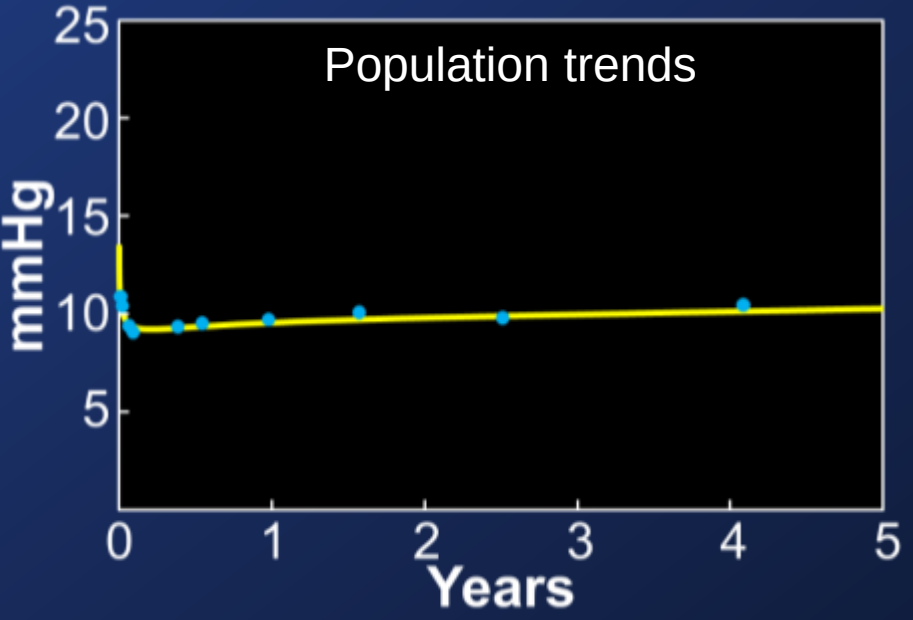
Survival w/o reintervention

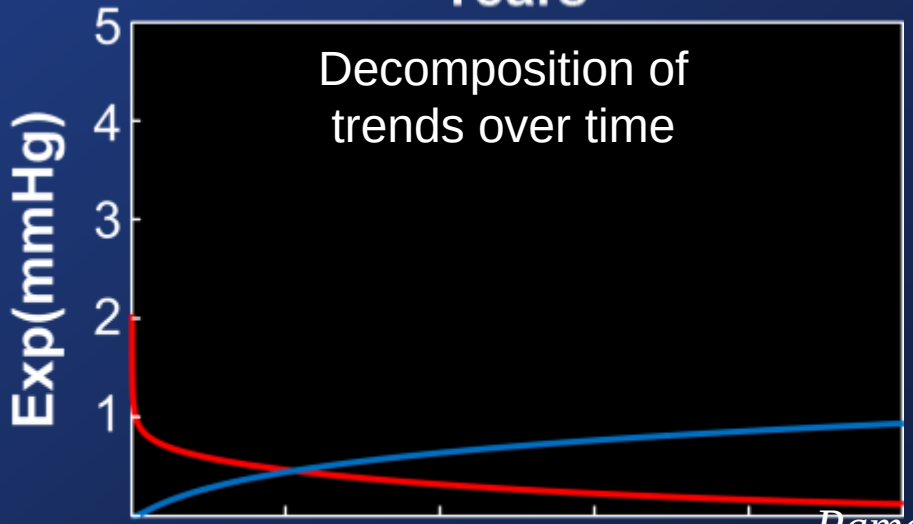
- 39% at 5 years

AV Mean Gradient Population Trends: Early (0-3 m) and Mid term (3 m-5 yrs)

PARTNER 1 trial echo hemodynamic trends at 5 years







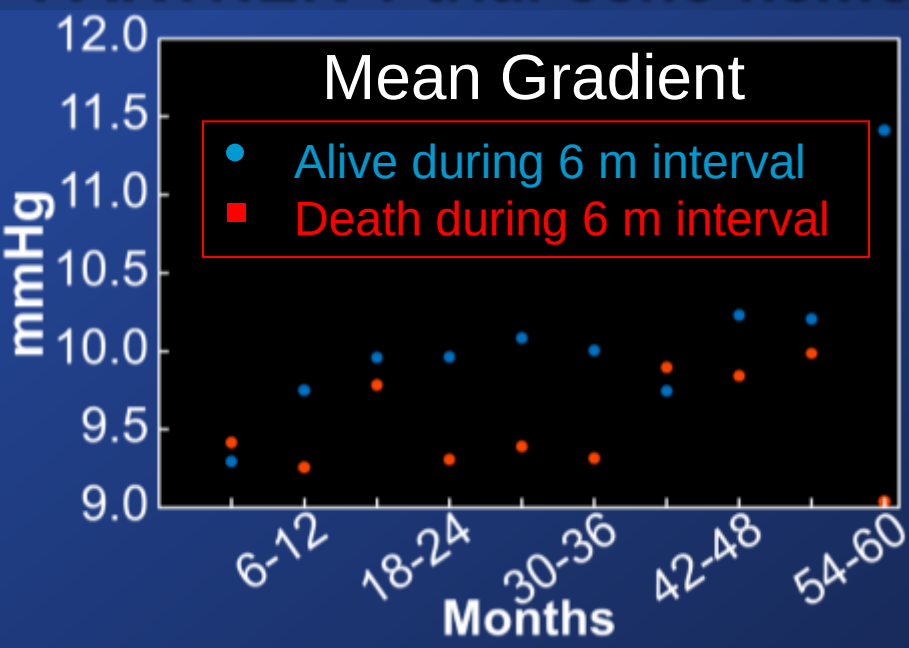
Early change (0-3mo):
12.1 to 9.2 mmHg

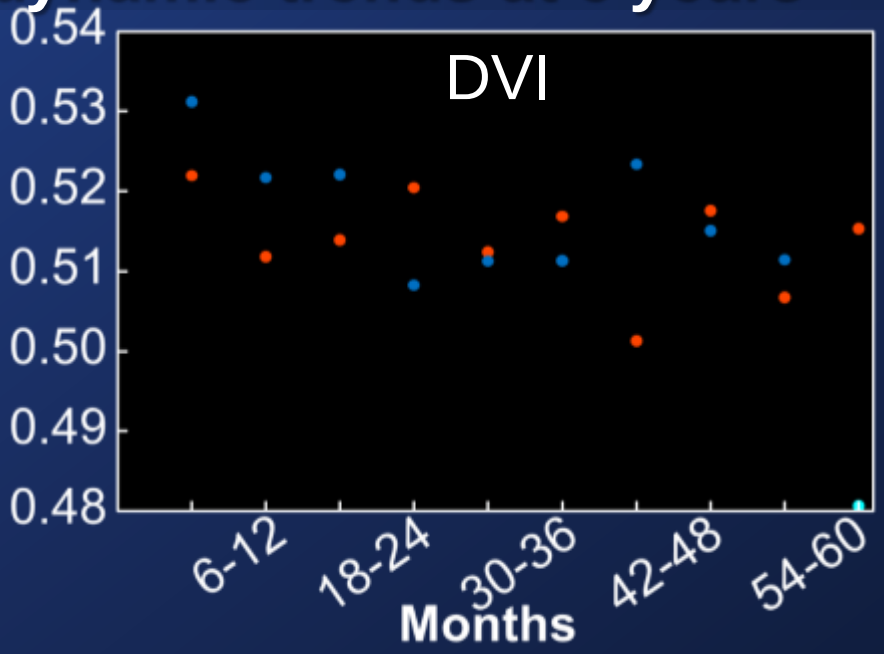
Late change (3 m-5y):
9.2 to 10.3 mmHg
Slope: 0.0018± 0.0039

Pamela Douglas. TCT 2016 Late Breaking Presentation

Last Mean Gradient and DVI by Vital Status/Reintervention q 6 mo

PARTNER 1 trial echo hemodynamic trends at 5 years





- Relationship btwn last mean gradient and survival changed over time
  - Mean gradients were higher among survivors up to 3 years of f/u
- No time-varying relationship between last DVI and survival
- These findings suggested a relationship between adverse events and low flow/ low output states

Centre for
Heart Valve Innovation
St. Paul's Hospital, Vancouver

2016 | euro PCR

- 45

First look at long-term durability of transcatheter heart valves:

Assessment of valve function up to 10-years after implantation

Danny Dvir, St. Paul's Hospital, Vancouver, Canada.

Structural valve degeneration (VARC2)

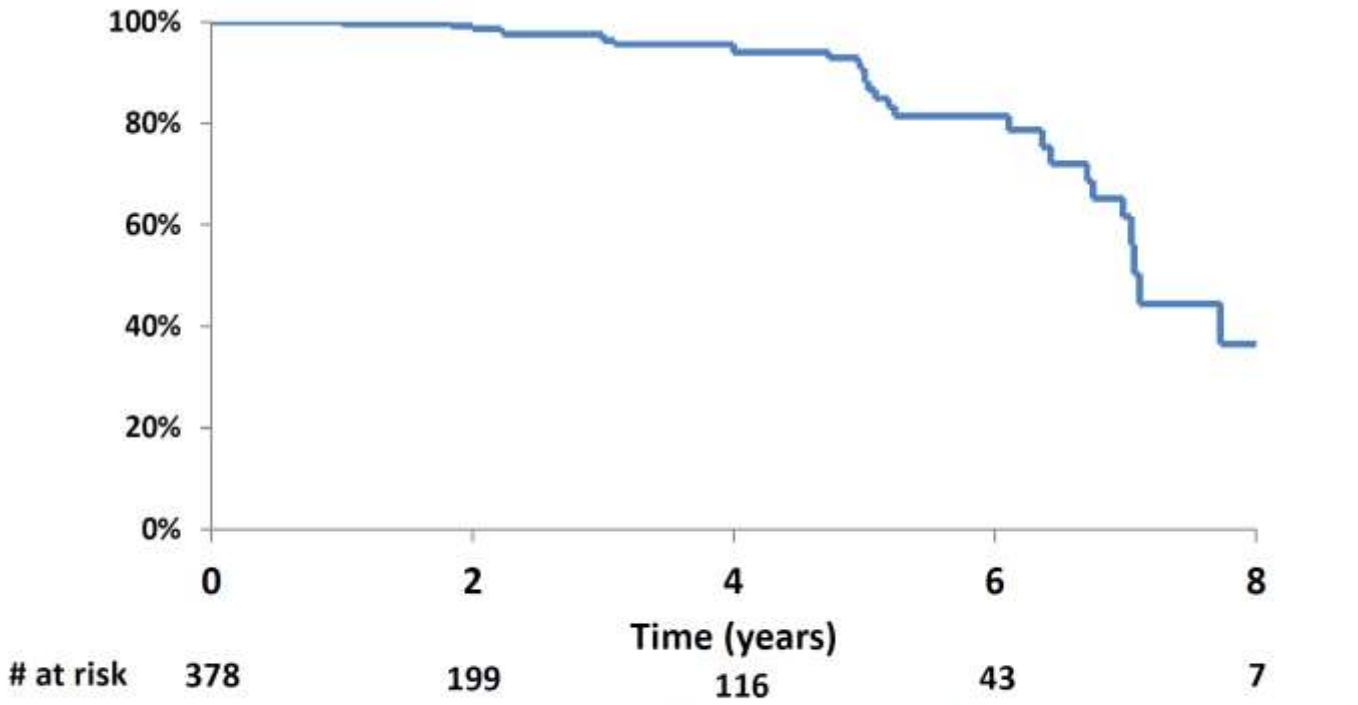
At least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis

First look at long-term durability of transcatheter heart valves:
Assessment of valve function up to 10-years after implantation

Danny Dvir, St. Paul's Hospital, Vancouver, Canada.

2016 euro PCR

Freedom from THV degeneration



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 degeneration per study definition.

Structural Valve Deterioration - from a TAVR perspective

- During EuroPCR (D. Dvir), SVD 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."

Our proposed definition to detect early signs of SVD:

- Mean GR ≥ 20mmHg **AND** increase > 10mmHg from 30-Day echo

OR

- AR ≥ 3 (Moderately severe /Severe) not present at 30-Day

Helene Eltchaninoff. TCT 2016

CHU Rouen data on valve degeneration

Freedom from SVD in Rouen - Using TAVR definition

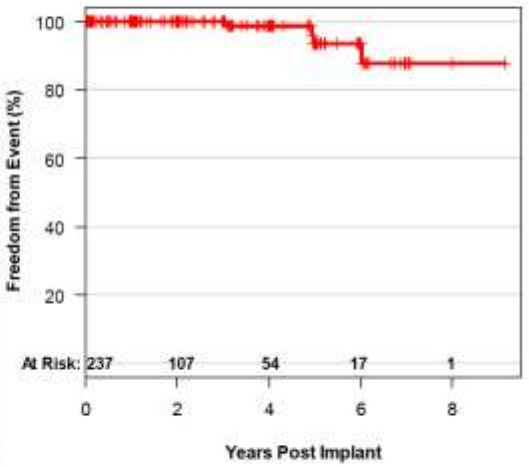
- 242 TAVR from FIM (2002) to 2011 (> 5 yrs FU)
- PVT/Cribier-Edwards (not commercialized), SAPIEN and SAPIEN XT valves
- Annual pre-planned clinical and echocardiographic FU
- No Echo Lab (results based on reports)

Freedom from SVD according to this definition

- 4 patients excluded (lost of FU)

SVD: n=4 (1.7%)

- **3 patients** with mean GR ≥ 20mmHg AND an increase > 10 mmHg from 30-D echo, including 1 patient with *severe anemia* (cancer)
- **1 patient** with reintervention (V-in-V)



Helene Eltchaninoff. TCT 2016

Vancouver data on valve degeneration

266 patients with available follow-up

Structural valve degeneration in 5 out of 266 cases

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%

1. *predominantly: stenosis in 3, regurgitation in*
2. *EOA <0.8cm² or indexed EOA <-0.5cm²A<0.5cm2/*
3. *SAVR in 3 patients, 2 of whom died peri-operatively*

John Webb. TCT 2016

Key Messages

- Impact of Reduced Leaflet motion/Sub clinical leaflet thrombosis on valve durability remains to be elucidated. In the short term at 1 year majority of patients do not have elevated gradients
- Best data available comparing TAVR and SAVR shows comparable durability at 5 years
- Uniform and clinically meaningful definitions of Valve degeneration need to be established to meaningfully compare and report durability
- Data presented on TAVR durability at 5 years are reassuring (lower gradients had greater mortality –LV function not Valve dysfunction was predictor of mortality!)
- Data on durability beyond 5 years from Vancouver and Rouen are limited but raise no major alarms
- Competing mortality risk in populations studied thus far make interpretation of TAVR durability challenging. Studies of TAVR in younger and healthier patients with longer life expectancy will provide best data on this issue

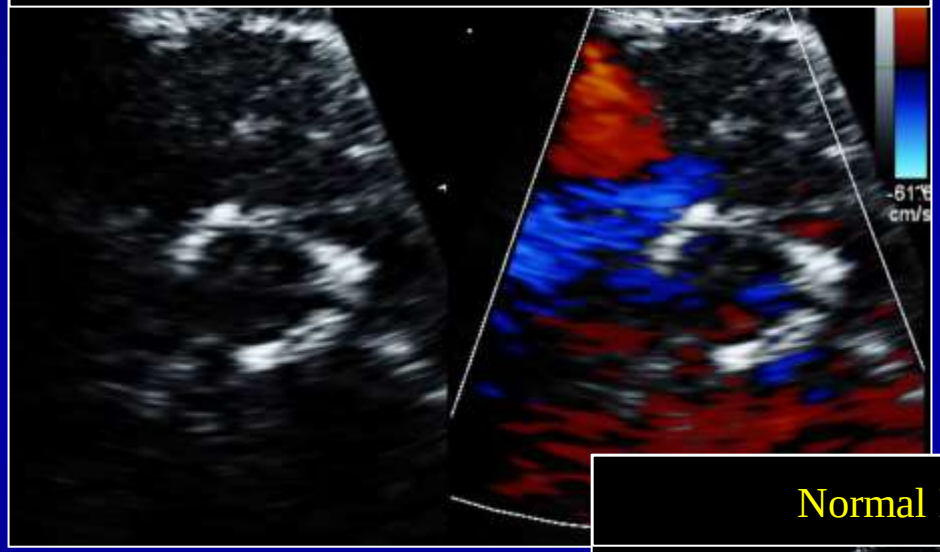
87 y/o female transferred to CSMC from Tenessee for higher level of care

Past medical history

- Transapical TAVR with 26mm Sapien-XT in 2013
- LM bifurcation stenosis (95%)
- Acute on chronic diastolic heart failure, NYHA III-ambulatory IV

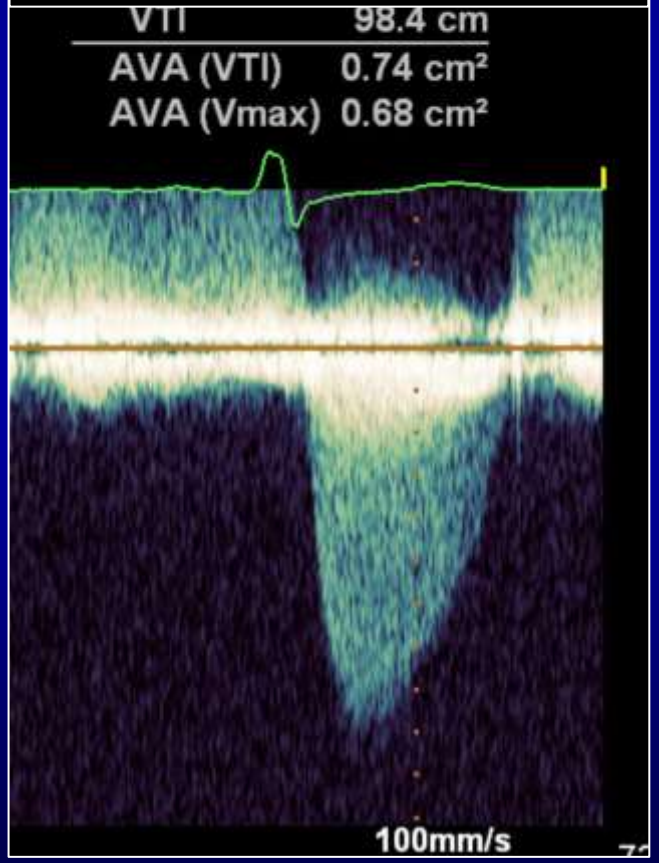
Degenerative 23mm Sapien-XT valve

Mild AR

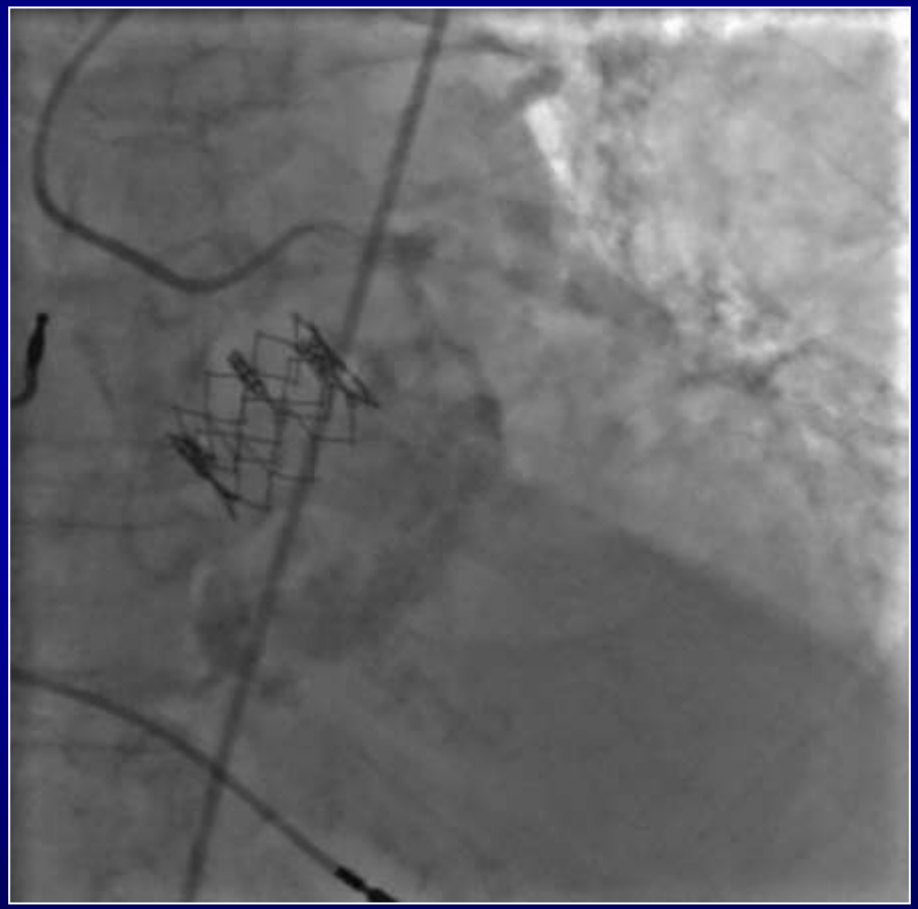


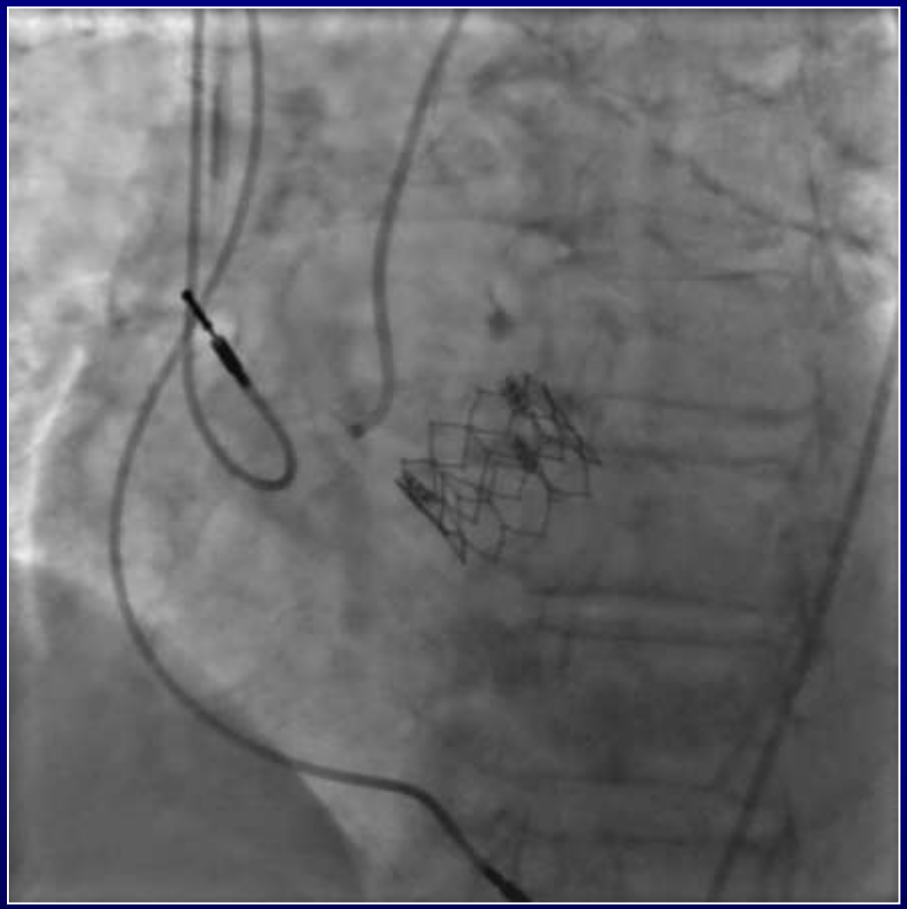
Normal EF

4 years post-TAVR
Mean aortic valve gradient
45mmHg

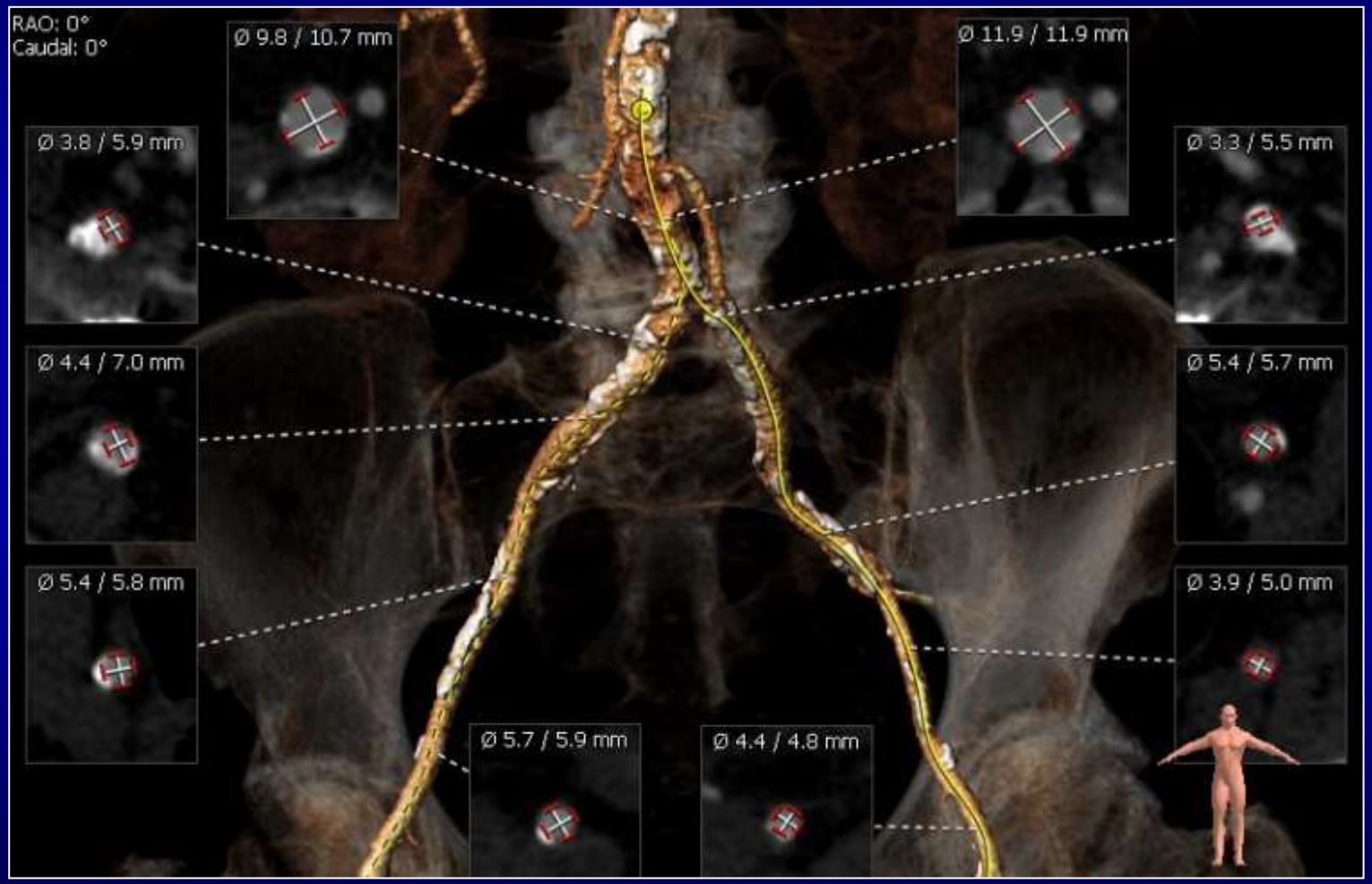


Baseline angiogram
Severe LM bifurcation stenosis

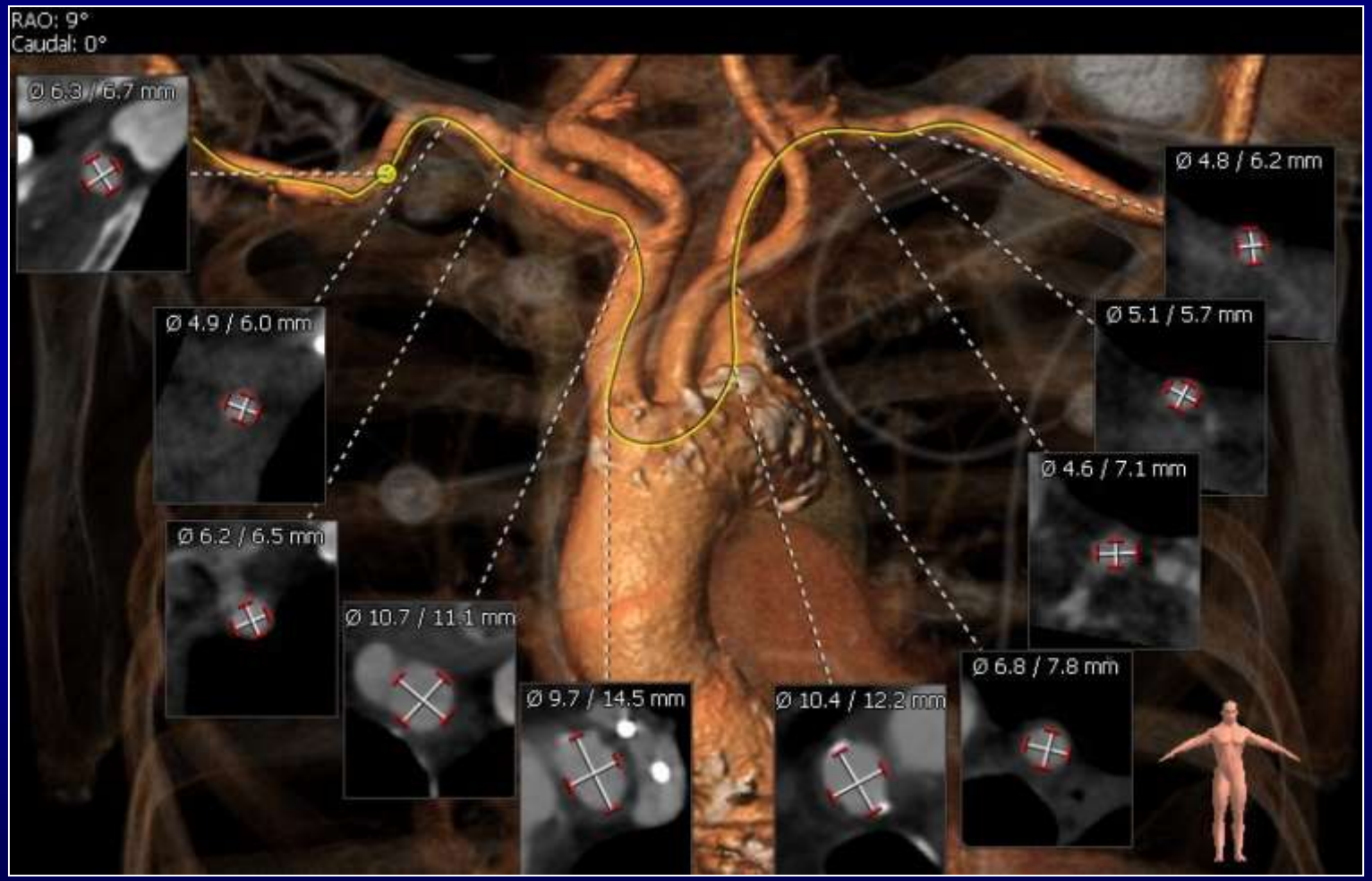




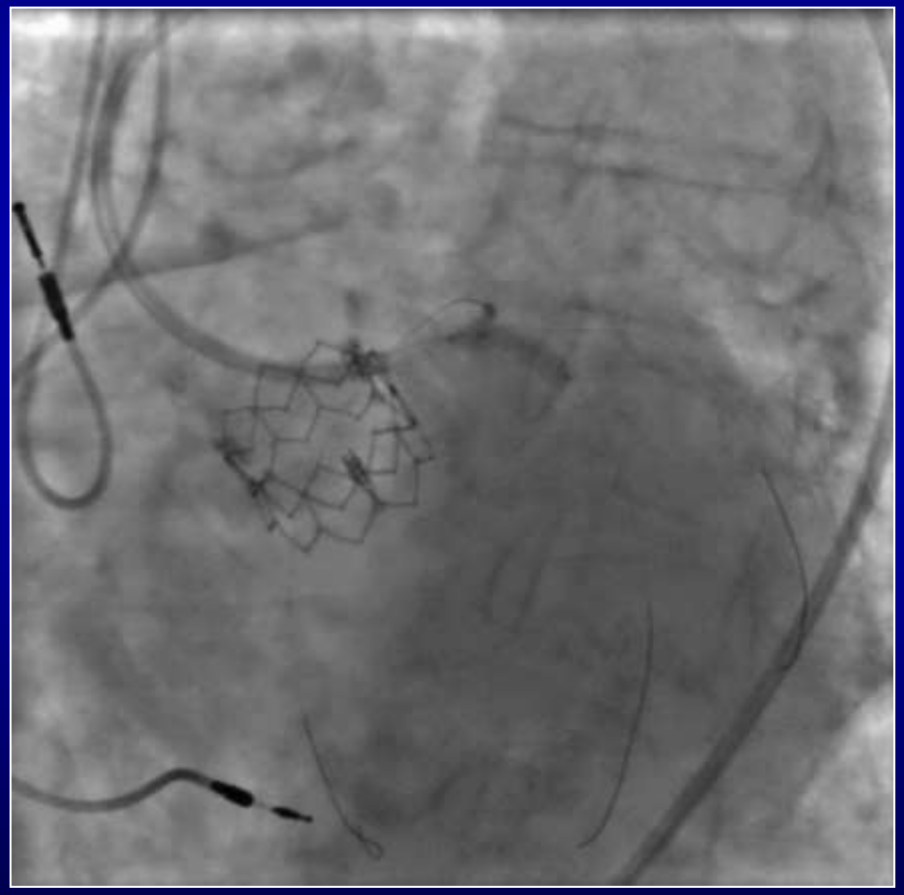
Vascular access not suitable for transfemoral TAVR

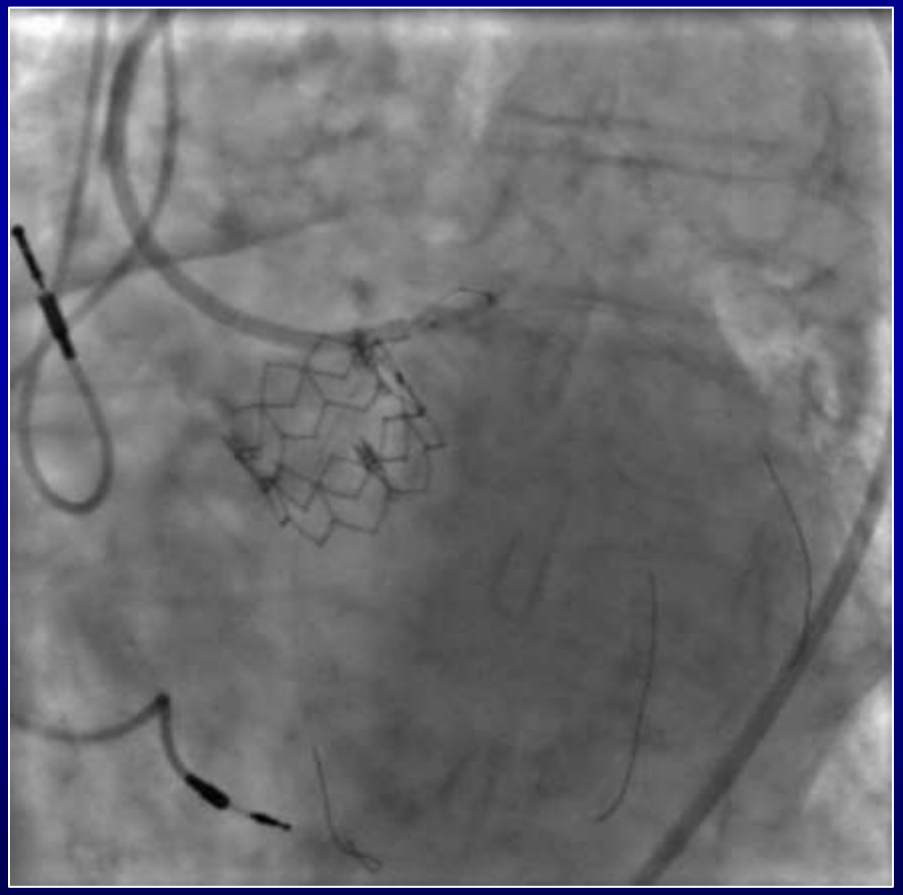


Plan for subclavian approach



3.0x12mm Xience DES to the LCx





3.5x18mm Xience DES LM→LAD

Final result

Subclavian access obtained after PCI

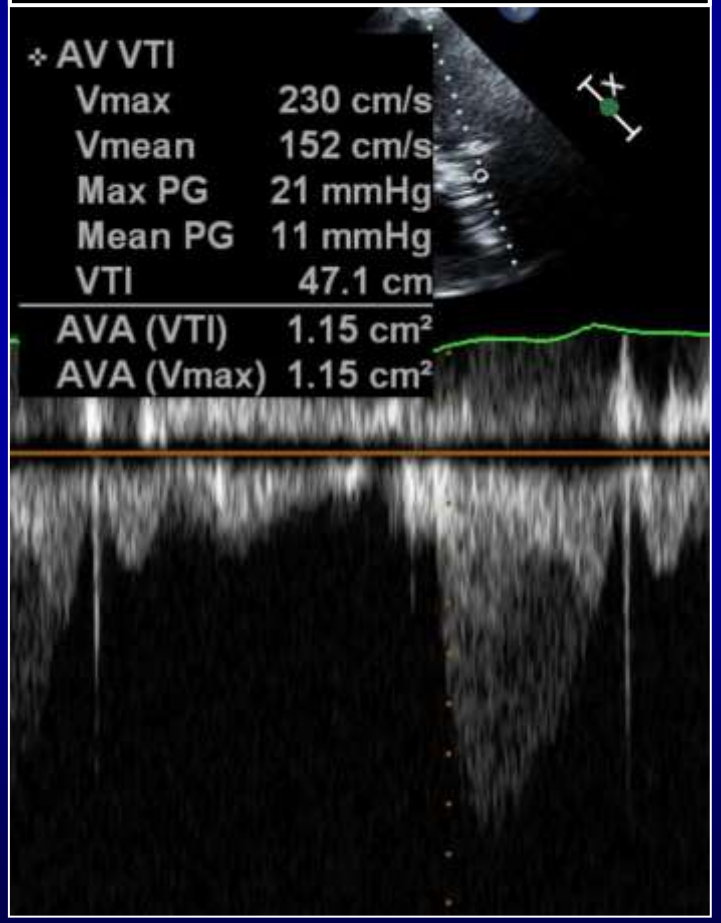
- 14 French sheath advanced through the right subclavian artery

26mm Sapien 3 valve deployed in the usual standard manner

Echo gradients

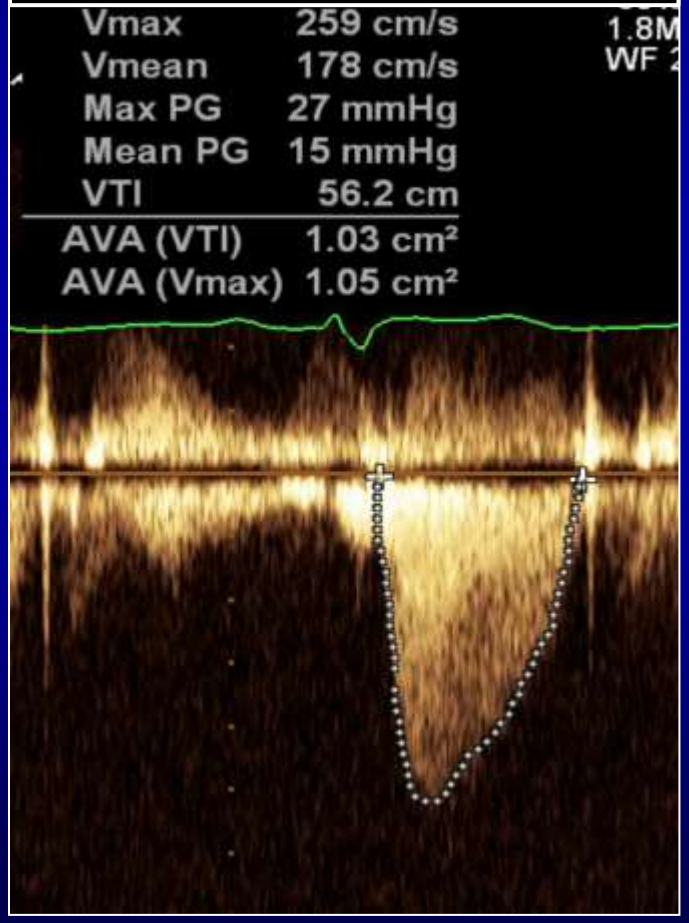
Day 1

Mean gradient 11mmHg



2 weeks

Mean gradient 15mmHg



CT performed 2 weeks post-TAVR

Reduced leaflet motion and hypoattenuating opacities suggestive of thrombus