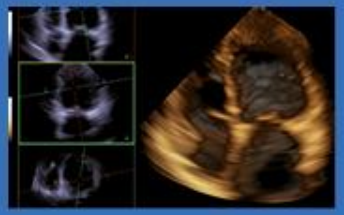
EuroValve
January 26-27, 2017

# Subclinical valve thrombosis post TAVR: should we panic or calm down?

**J. Kefer, MD, PhD, FESC**
**Interventional Cardiology**
**Head of the Cardiac Cath Laboratory**
**Cliniques Universitaires Saint-Luc**
**Brussels, Belgium**

Cliniques universitaires SAINT-LUC UCL BRUXELLES

www.eurovalvecongress.com



EuroValve

January 26-27, 2017

# Faculty disclosure

***Joelle Kefer***

*I disclose the following financial relationships:*

**Consultant** – proctorship for StJude Medical
**Receive grant/research support** from Abbott Vascular
**Receive grant/research support** from Edwards Lifesciences

Images and Case Reports in Interventional Cardiology

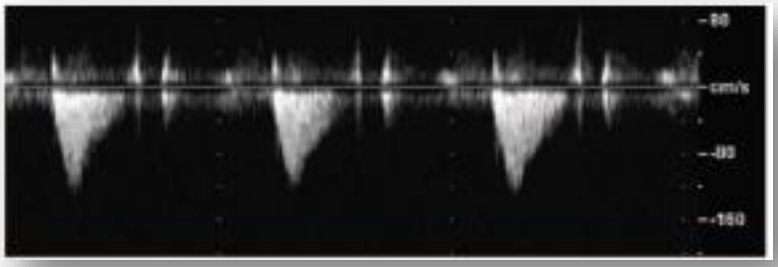
SPAIN

# Thrombotic Aortic Restenosis After Transapical Sapien Valve Implantation

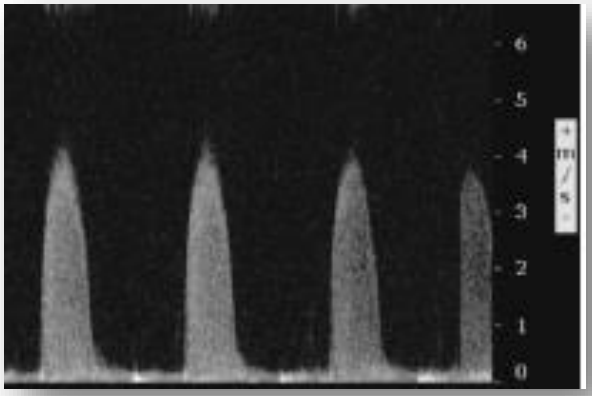
Joelle Kefer, MD, PhD; Parla Astarci, MD; Jean Renkin, MD, PhD; David Glineur, MD; Sophie Pierard, MD; Stephanie Seldrum, MD; Jean-Louis Vanoverschelde, MD, PhD

4 months after an uneventful and successful Sapien 26 mm implantation, NSTEMI and dyspnea III.

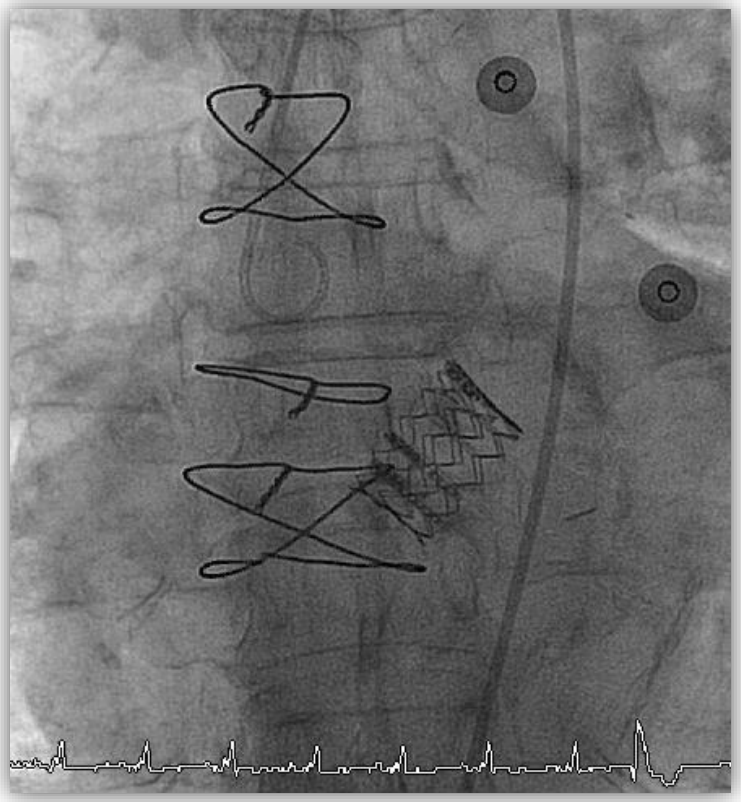
Echo TT @ discharge : Peak Vel 1 m/sec



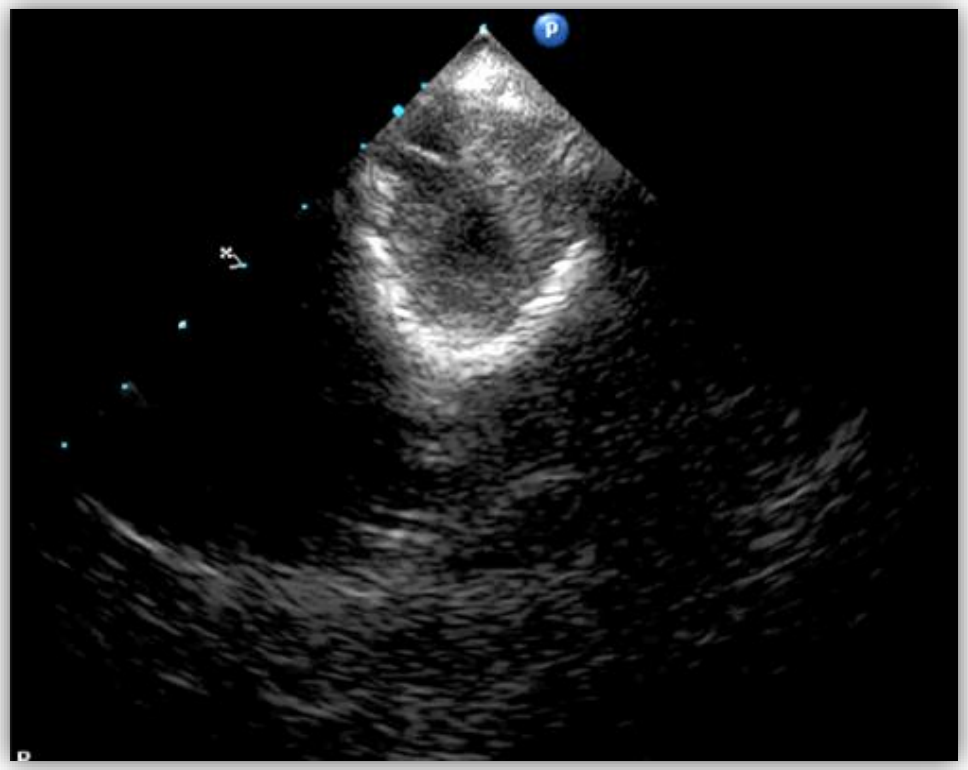

ICE @ 4 months : Peak Vel 4 m/sec



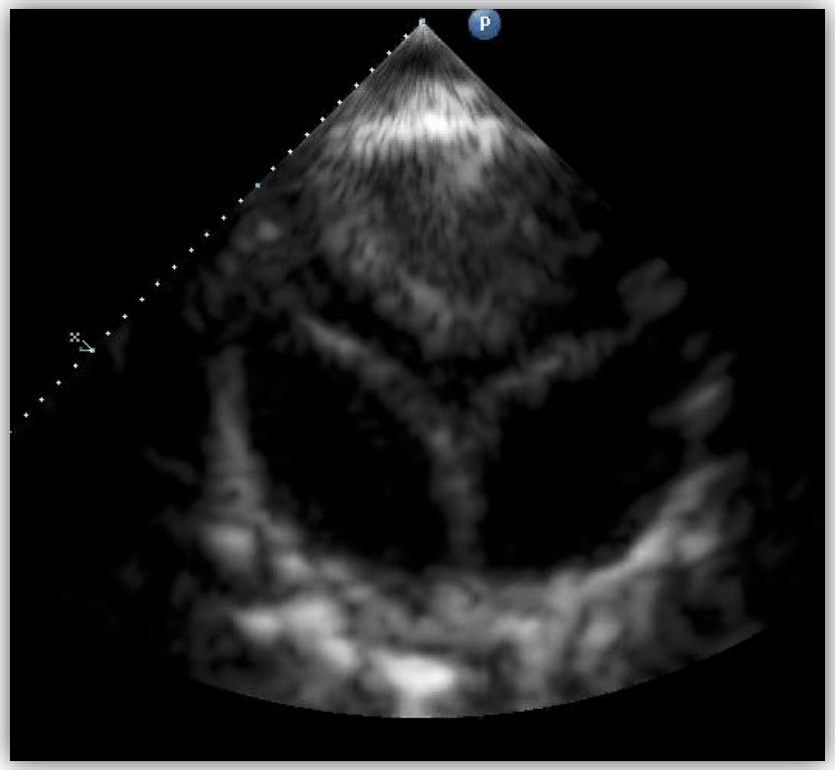

Cath @ 4 months



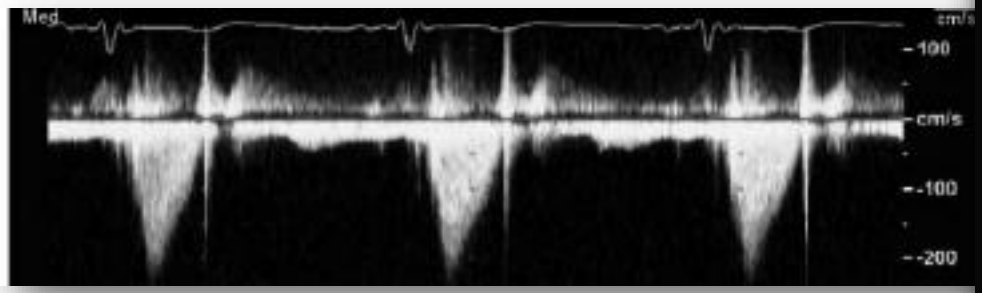
Thickened leaflets
Reduced motion

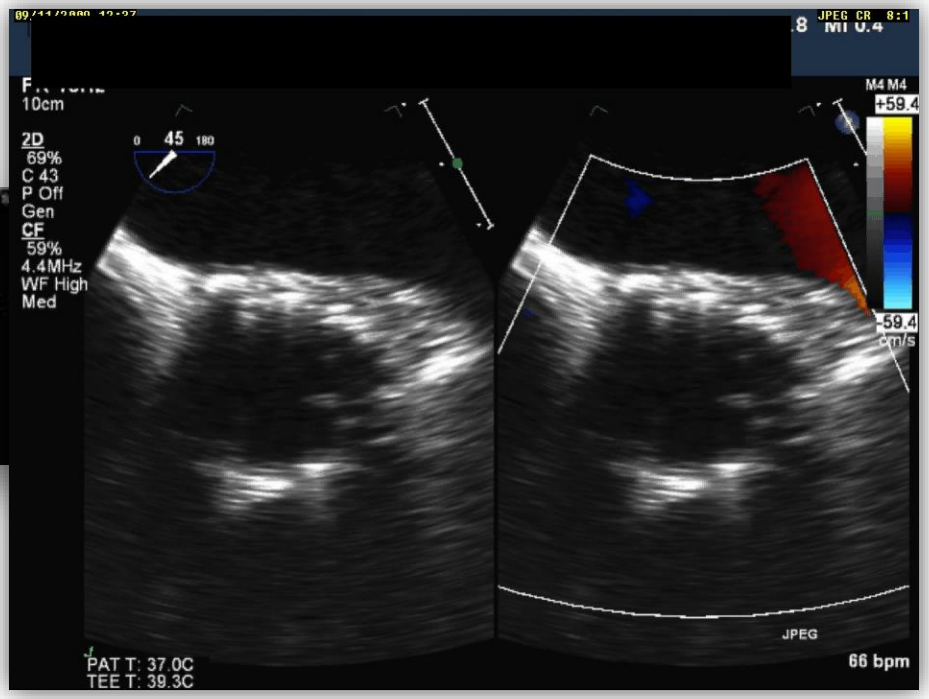


Thin leaflets
Normal motion



# Recovery after 1 months ACO



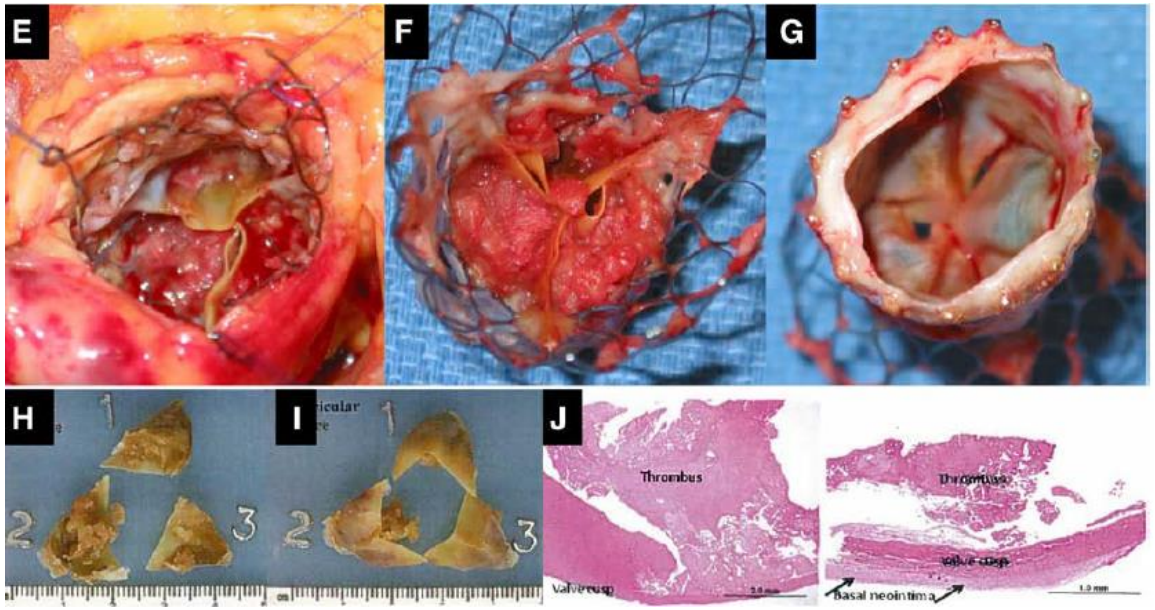

Echo after ACO : Peak Vel 2 m/sec

Thrombotic aortic restenosis after transcatheter aortic valve replacement with the Sapien valve is an uncommon situation, not yet well described, which can be successfully treated by anticoagulant therapy. (*Circ Cardiovasc Interv*. 2010;3:289-292.)

# Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

Azeem Latib, MD*; Toru Naganuma, MD*; Mohamed Abdel-Wahab, MD; Haim Danenberg, MD; Linda Cota, MD; Marco Barbanti, MD; Helmut Baumgartner, MD; Ariel Finkelstein, MD; Victor Legrand, MD; José Suárez de Lezo, MD; Joelle Kefer, MD; David Messika-Zeitoun, MD; Gert Richardt, MD; Eugenio Stabile, MD; Gerrit Kaleschke, MD; Alec Vahanian, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; John G. Webb, MD; Vasileios F. Panoulas, MD; Francesco Maisano, MD; Ottavio Alfieri, MD; Antonio Colombo, MD

*Circ Cardiovasc Interv. 2015 Apr;8(4)*




- ✓ 26 cases on 4266 TAVI in 12 centres : 0.6%
- ✓ Sapien/ Sapien XT and Corevalve
- ✓ Median time : 181 days after TAVI
- ✓ No thrombogenic diathesis, no discontinuation of DAPT
- ✓ Echo : increased gradient, thickened leaflets, thrombus
- ✓ Restoration of normal THV function within 2 months of ACO

Symptomatic THV thrombosis exists, noted in up to 1%, associated with high transvalvular gradients @ echo.

ORIGINAL ARTICLE

N Engl J Med 2015;373:2015-24.

# Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

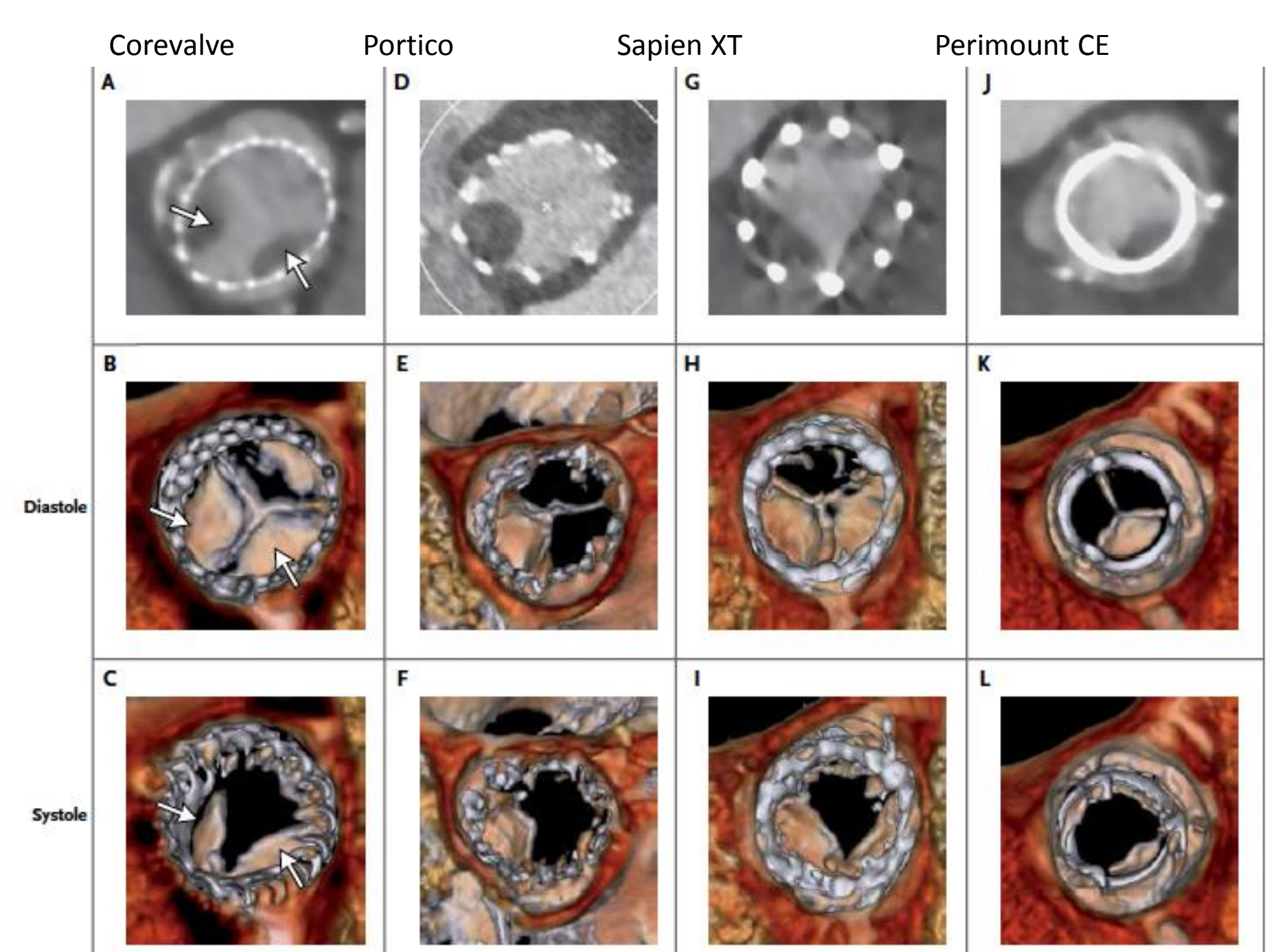
R.R. Makkar, G. Fontana, H. Jilaihawi, T. Chakravarty, K.F. Kofoed, O. de Backer, F.M. Asch, C.E. Ruiz, N.T. Olsen, A. Trento, J. Friedman, D. Berman, W. Cheng, M. Kashif, V. Jelnin, C.A. Kliger, H. Guo, A.D. Pichard, N.J. Weissman, S. Kapadia, E. Manasse, D.L. Bhatt, M.B. Leon, and L. Søndergaard

# PORTICO IDE Study

- ✓ RCT Portico versus commercial valves in US
- ✓ 4-dimensional volume rendered CT detected a reduced leaflet motion (RLM) in one patient with stroke
- ✓ 55 patients undergoing 4D-CT @ 30d after TAVI, were investigated
- ✓ 40% have a RLM, in all subgroups of devices
- ✓ All have hypoattenuating opacities @ 2D-CT, at the base of the valve leaflets
- ✓ Low mean gradient @ TT echo : 9 mmHg
- ✓ RLM less prevalent in patients receiving warfarin (vs DAPT)

# Pooled RESOLVE and SAVORY registries

- ✓ 132 patients in 2 centres : 4D-scan after TAVI
- ✓ RLM : 13% (14% TAVR ; 7% after SAVR)


Corevalve
Portico
Sapien XT
Perimount CE
A
D
G
J
B
E
H
K
C
F
I
L
Diastole
Systole

# Outcome of patients with RLM

**Table 3. Clinical Outcomes.**

| Outcome | Normal Leaflet Motion | Reduced Leaflet Motion | P Value* |
|---|---|---|---|
| | *number of patients* | | |
| **PORTICO IDE study** | | | |
| Patients in study | 33 | 22 | |
| Death† | 1 | 2 | 0.56 |
| Myocardial infarction‡ | 1 | 1 | >0.99 |
| Stroke or transient ischemic attack§ | 0 | 2 | 0.16 |
| Stroke | 0 | 2 | 0.16 |
| Transient ischemic attack | 0 | 0 | >0.99 |
| **Pooled registries** | | | |
| Patients in group | 115 | 17 | |
| Death | 0 | 0 | >0.99 |
| Myocardial infarction | 0 | 0 | >0.99 |
| Stroke or transient ischemic attack¶ | 1 | 3 | 0.007 |
| Stroke | 1 | 0 | >0.99 |
| Transient ischemic attack | 0 | 3 | 0.002 |

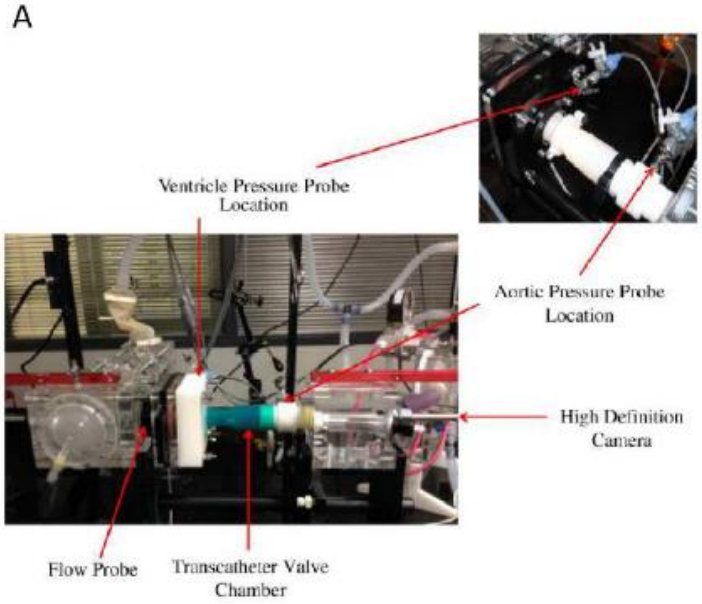
# Possible subclinical leaflets thrombosis

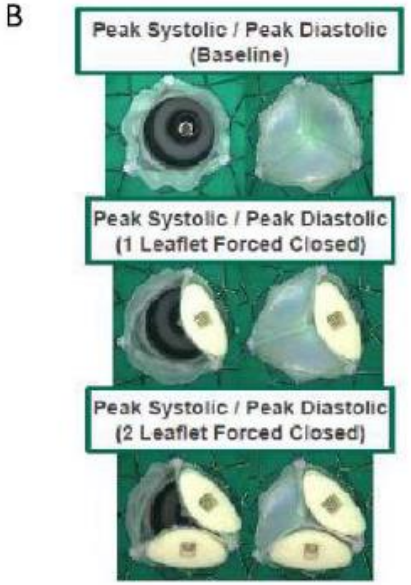
- ✓ Reduced aortic valve leaflet motion
- ✓ Incidental finding by 4D-CT scan (hypoattenuated leaflets thickening)
- ✓ Hemodynamically subclinical at the time of detection
- ✓ Occured with several types of prostheses (SAVR and TAVR)
- ✓ Lower prevalence among patients ACO
- ✓ High rate of recovery after warfarin
- ✓ No histological confirmation

# Possible subclinical leaflets thrombosis

- ✓ Missed by TT echo
- ✓ RLM does not provide elevated gradient

Pulse duplicator model



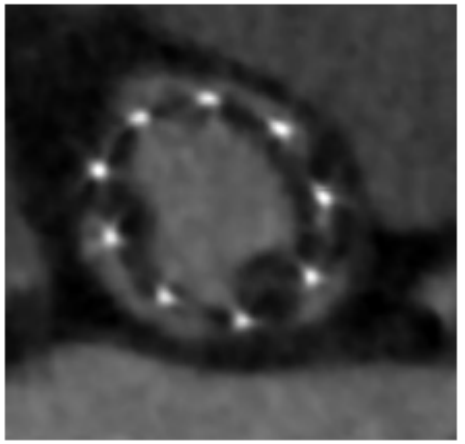




The forced closure of one (or two) leaflet of a transcatheter aortic valve was associated with only a minor increase of transvalvular gradient (normal range of the aortic bioprostheses).

# HALT & HAM definitions

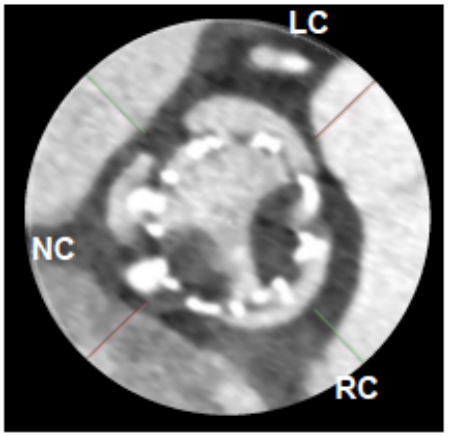
## HALT: Hypo-Attenuating Leaflet Thickening

- Involving the periphery and base of the leaflet and extend to varying degrees to the edges of the leaflet



## HAM: Hypo-Attenuation affecting Motion

- Reduction in leaflet motion *in the presence of HALT*
- A reduction in leaflet excursion of more than 50% was considered significant



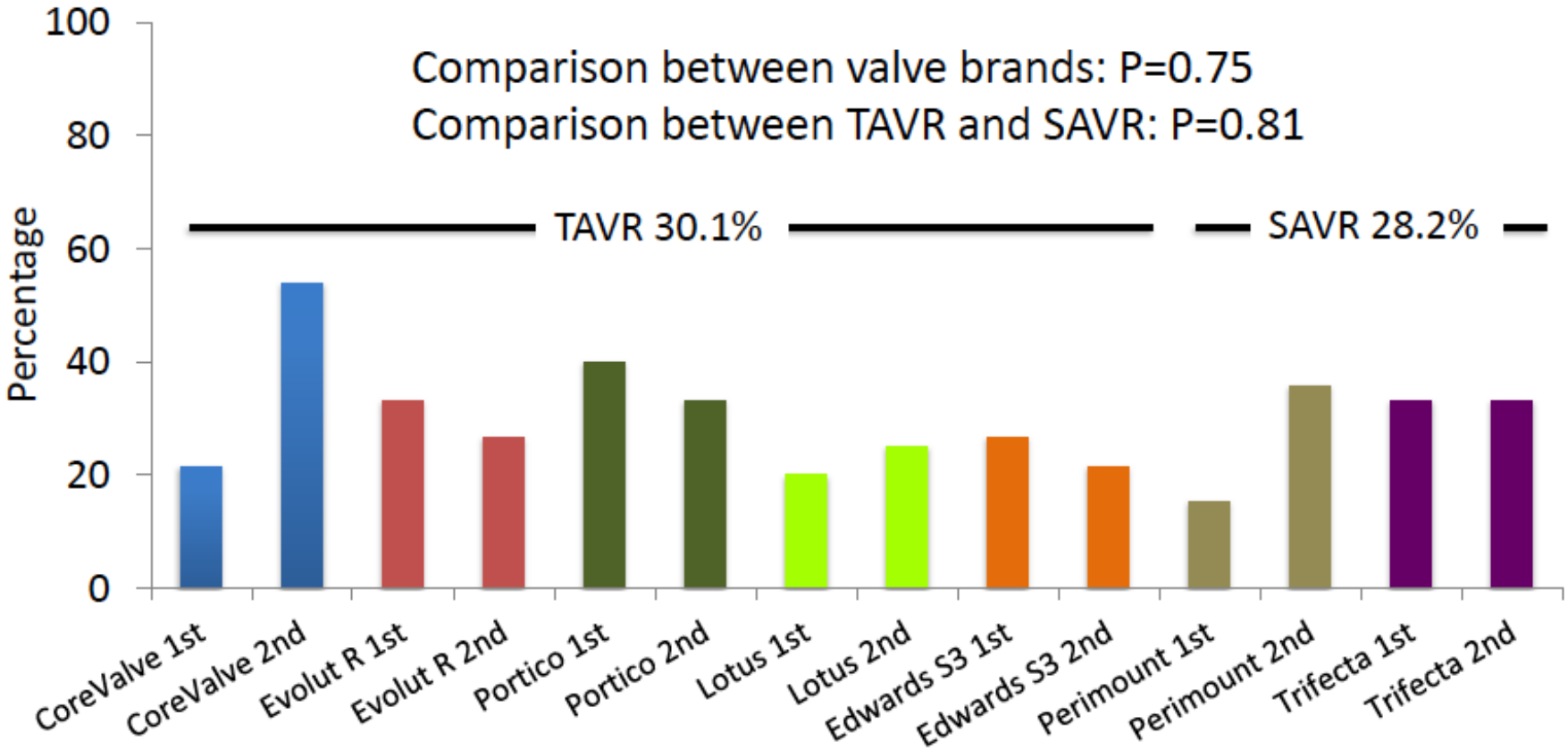

Sondergaard L, TVT 2016

# The SAVORY registry in Copenhagen:

- 105 patients who underwent TAVR or SAVR

## Prevalence of HALT

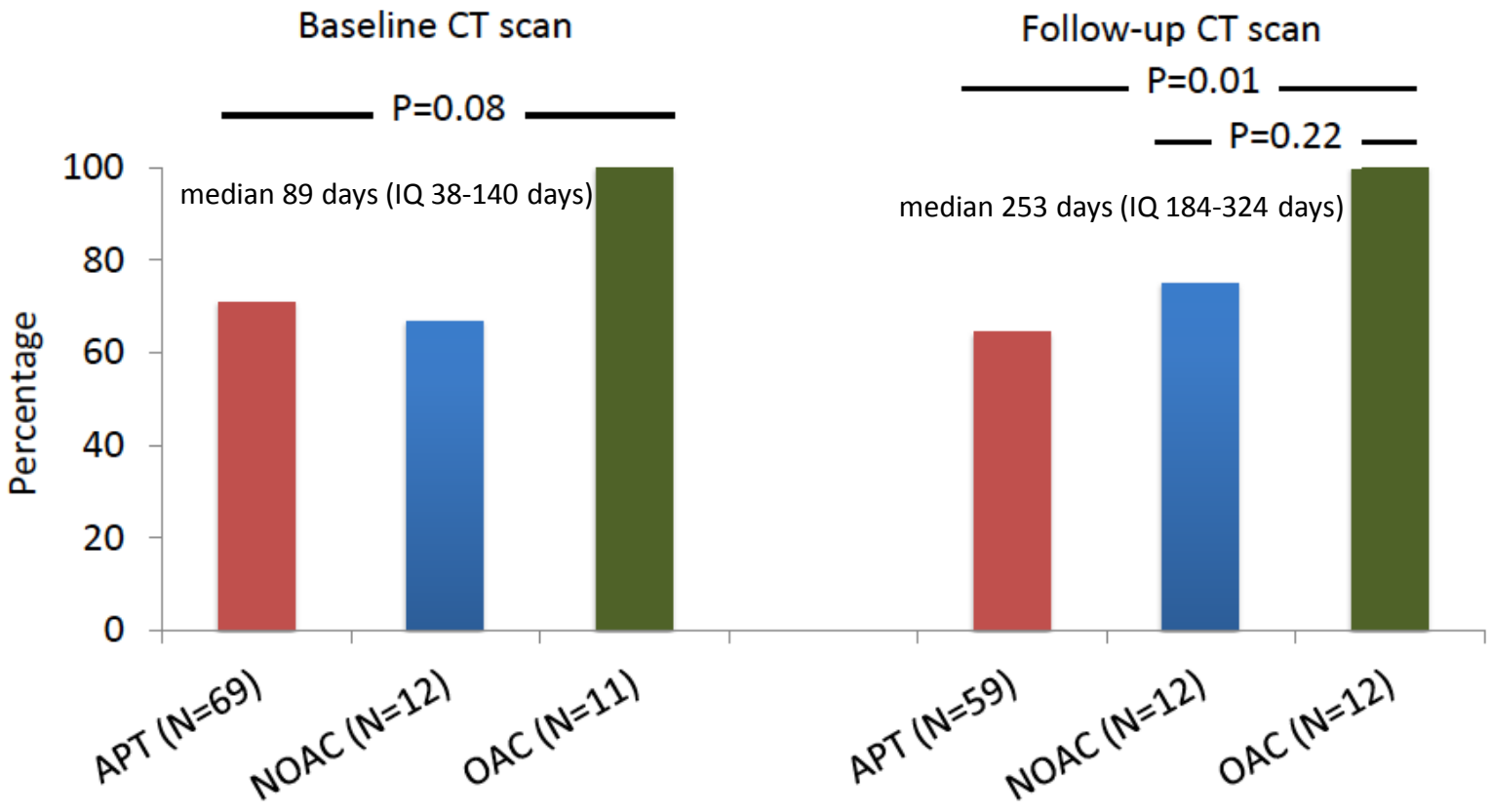
*baseline and follow-up scan*




Sondergaard L, TVT 2016

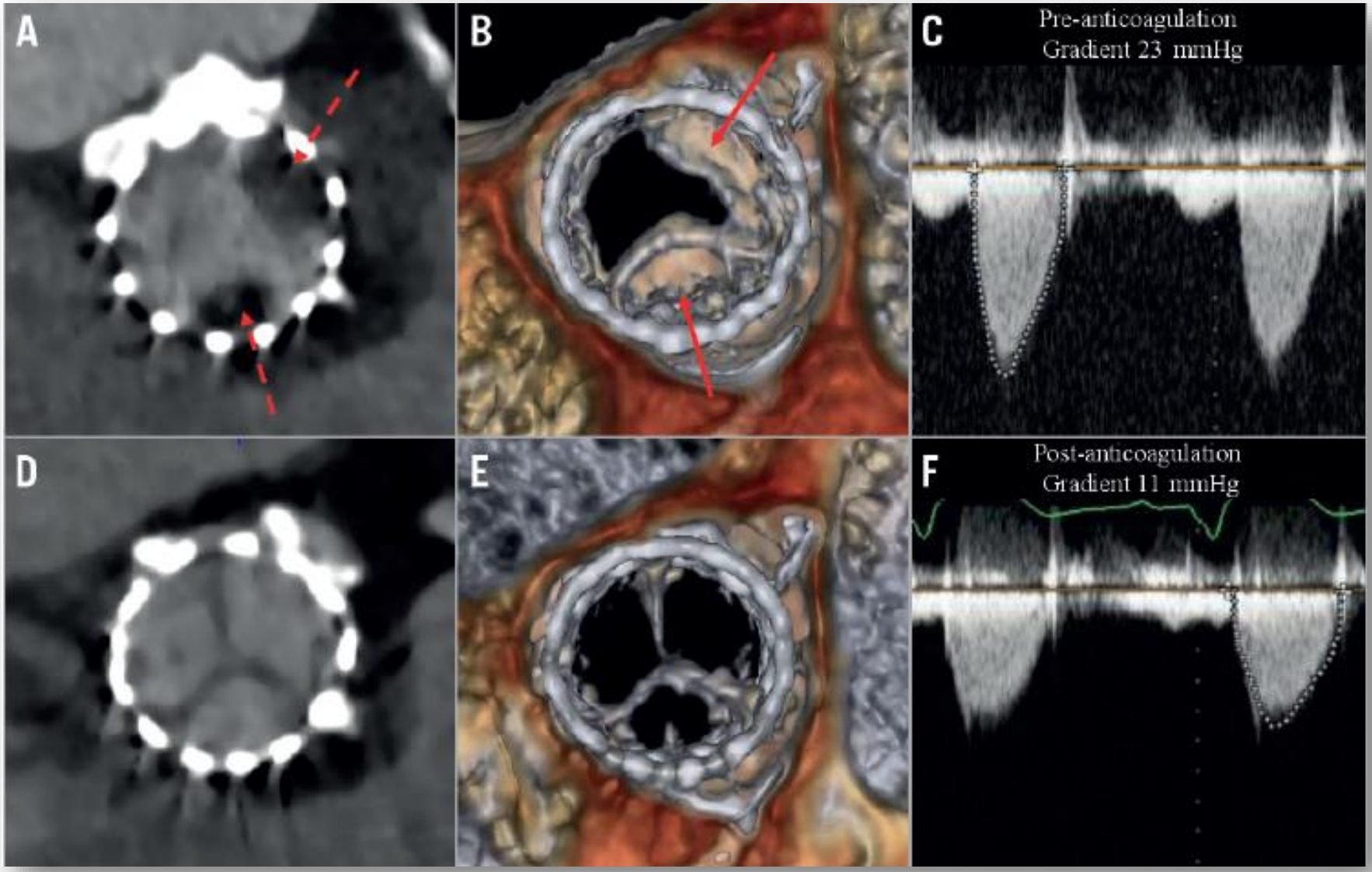
VKA seems to prevent and resolve this phenomenon, whereas APT and NOAC do not

# Medication & freedom from HALT




Sondergaard L, TVT 2016

# Resolution of HALT and RLM after warfarin




*Makkar et al. EuroIntervention 2016*

# Clinical implications

- ✓ No RLM or HALT in anticoagulated patients
- ✓ Restoration of normal THV after warfarin
- ✓ Should we give ACO in all patients after TAVI?
- ✓ Risk of bleeding
- ✓ No robust evidence for ACO after SAVR

| | | |
|---|---|---|
| Oral anticoagulation may be considered for the first three months after implantation of an aortic bioprosthesis. | IIb | C |

2012 ESC guidelines

**CLASS IIb**

1. **Anticoagulation, with a VKA, to achieve an INR of 2.5 may be reasonable for the first 3 months after bioprosthetic AVR (276). *(Level of Evidence: B)***
2. **Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to life-long aspirin 75 mg to 100 mg daily. *(Level of Evidence: C)***

2014 ACC/AHA guidelines

# Absence of ACO at discharge predicts elevated gradients after TAVI

## Incidence, Timing, and Predictors of Valve Hemodynamic Deterioration After Transcatheter Aortic Valve Replacement

### Multicenter Registry

Maria Del Trigo, MD,[a] Antonio J. Muñoz-Garcia, MD,[b] Harindra C. Wijeysundera, MD,[c] Luis Nombela-Franco, MD,[d] Asim N. Cheema, MD,[e] Enrique Gutierrez, MD,[f] Vicenç Serra, MD,[g] Joelle Kefer, MD, PHD,[h] Ignacio J. Amat-Santos, MD,[i] Luis M. Benitez, MD,[j] Jumana Mewa, MD,[c] Pilar Jiménez-Quevedo, MD, PHD,[d] Sami Alnasser, MD,[e] Bruno Garcia del Blanco, MD,[g] Antonio Dager, MD,[j] Omar Abdul-Jawad Altisent, MD,[a] Rishi Puri, MBBS, PHD,[a] Francisco Campelo-Parada, MD,[a] Abdellaziz Dahou, MD,[a] Jean-Michel Paradis, MD,[a] Eric Dumont, MD,[a] Philippe Pibarot, DVM, PHD,[a] Josep Rodés-Cabau, MD[a] (J Am Coll Cardiol 2016;67:644-55)

VHD = > 10 mmHg increase of gradient at echo Fup
4.5% @ 20 months

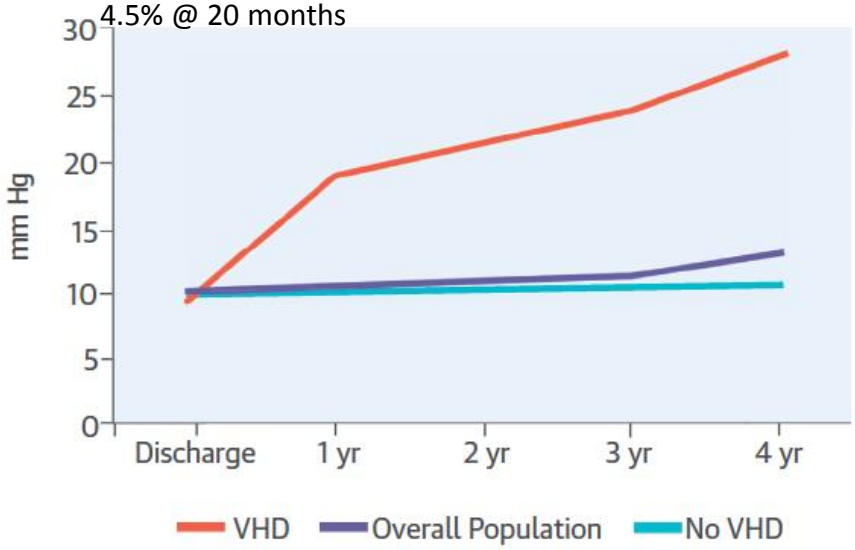
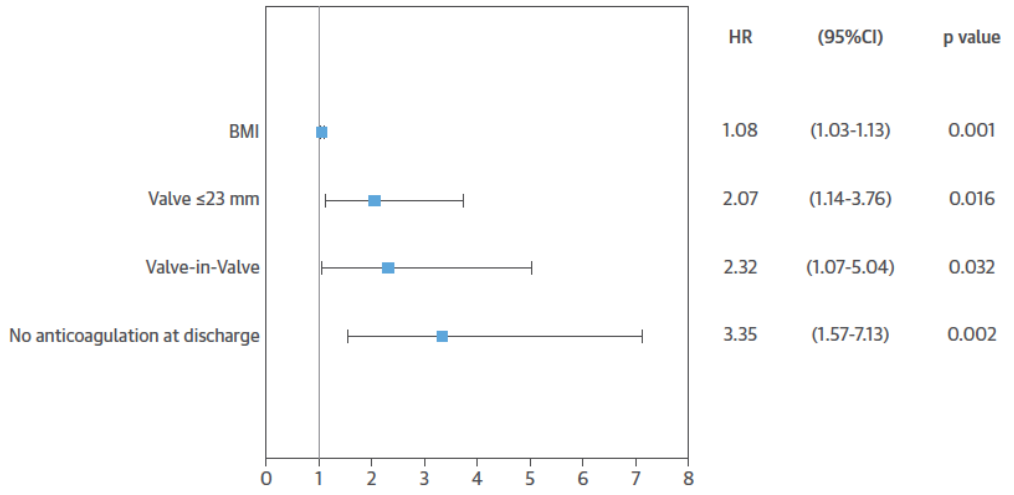


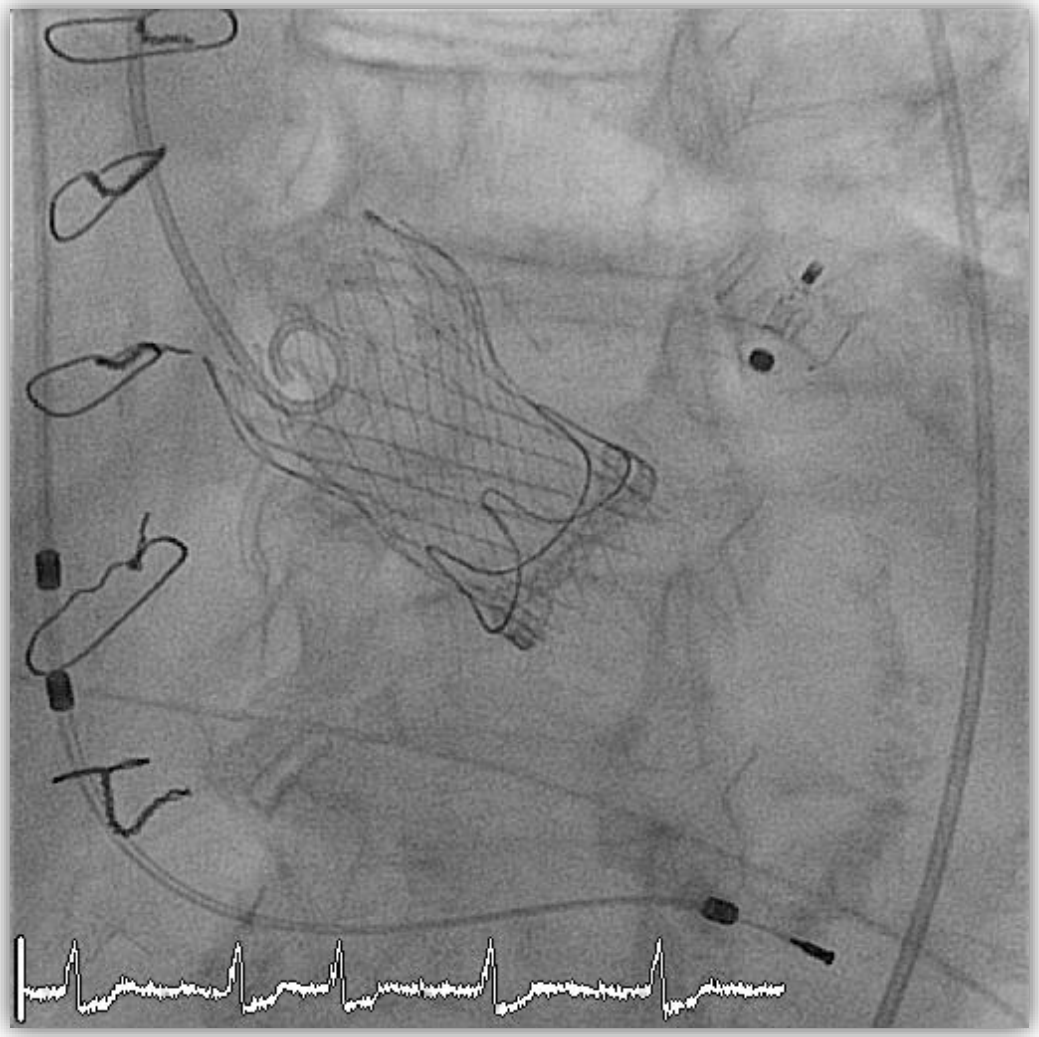

**FIGURE 2** Predictors of Transcatheter VHD Post-TAVR



# ACO in all patients after TAVI ?
# NO

- AF present in ± 1/3 of patients TAVI
- Independently associated with CV morbi and mortality
- Driven by increased risk of bleeding relating to OAC (Vavuranakis et al. Curr Pharm Des 2016)
- PARTNER 1B : 1-yr mortality was quadrupled in AF patients experienced major bleedings

# TAVI and LAAO + SAPT



# CT–scan in all patients after TAVI ?

# NO

- ✓ Risk of radiation
- ✓ Risk of contrast-induced renal failure

- ✓ Ongoing substudies : 4DCT GALILEO

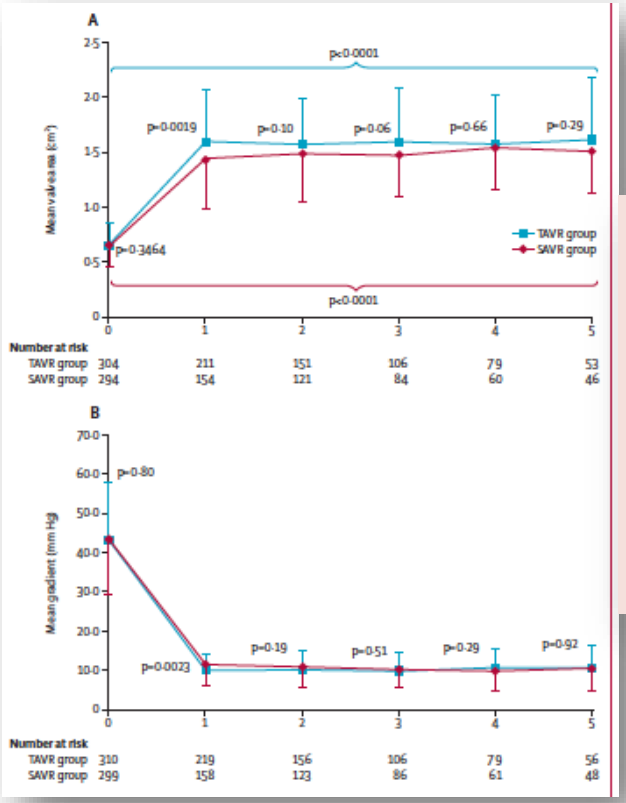
# Ongoing studies on antiplatelet/(N)OAC after TAVI

- ✓ ATLANTIS : Anti-Thrombotic Strategy After Trans-Aortic Valve Implantation for Aortic Stenosis
- ✓ AVATAR : Anticoagulation Alone Versus Anticoagulation and Aspirin Following Transcatheter Aortic Valve Interventions
- ✓ GALILEO : Global Study Comparing a Rivaroxaban-Based Antithrombotic Strategy to an Antiplatelet-Based Strategy After Transcatheter Aortic Valve Replacement to Optimize Clinical Outcomes
- ✓ POPular-TAVI : Antiplatelet Therapy for Patients Undergoing Transcatheter Aortic Valve Implantation

# Reassuring long term data

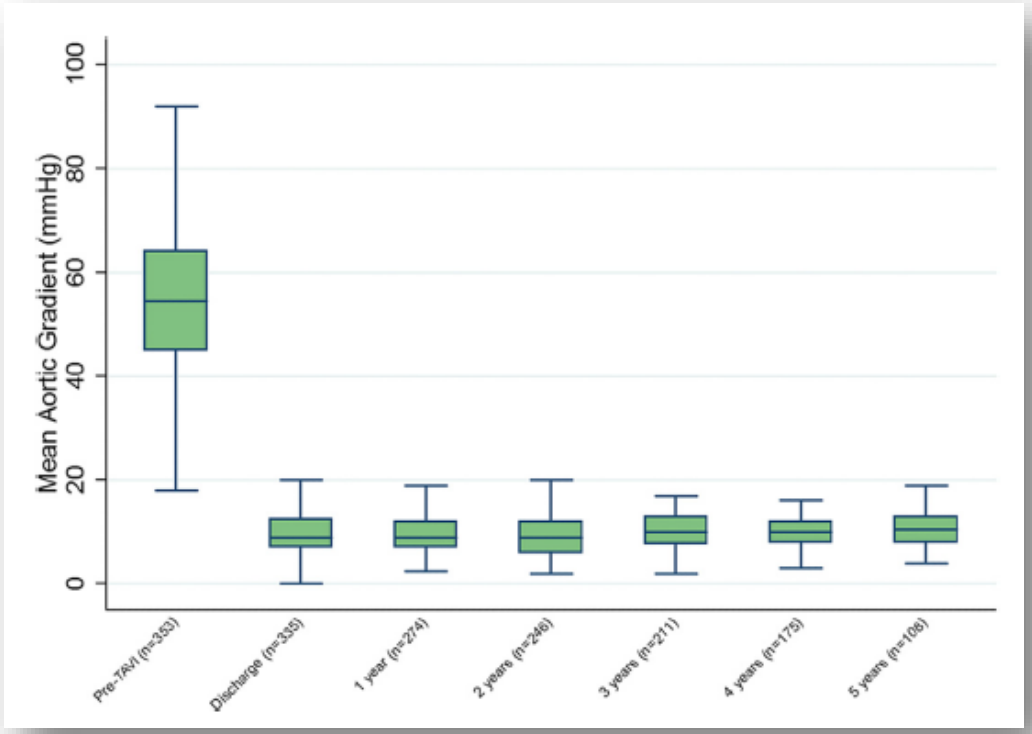
## 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial

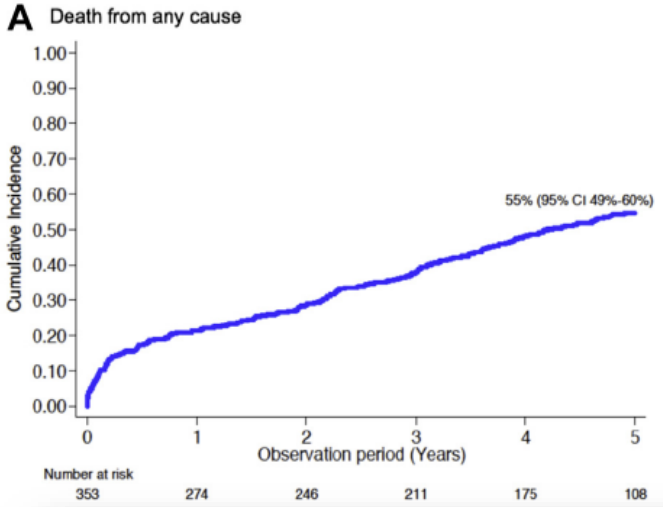
*Lancet* 2015; 385: 2477–84

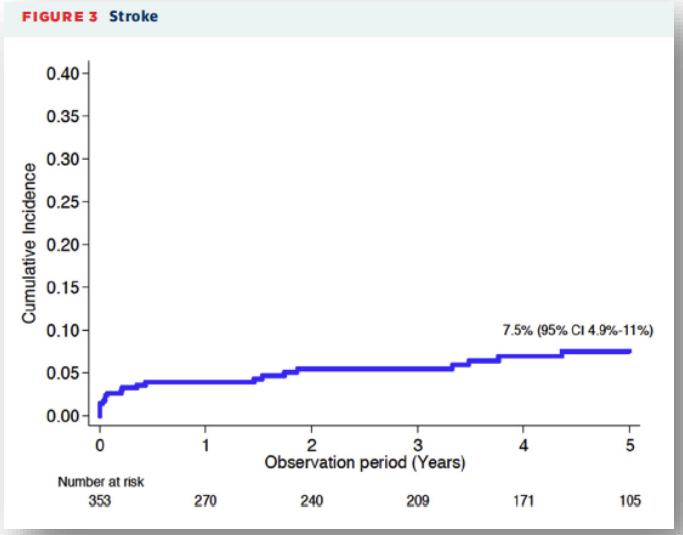



| | At 1 year | | At 5 years | | |
|---|---|---|---|---|---|
| | TAVR group (n=348) | SAVR group (n=351) | TAVR group (n=348) | SAVR group (n=351) | Log-rank p value |
| Death | | | | | |
| From any cause | 84 (24·2%) | 89 (26·8%) | 229 (67·8%) | 198 (62·4%) | 0·76 |
| From cardiovascular causes | 46 (14·0%) | 40 (13·0%) | 147 (53·1%) | 123 (47·6%) | 0·67 |
| Repeat hospital admission | 59 (18·5%) | 51 (17·7%) | 108 (42·3%) | 81 (34·2%) | 0·17 |
| Death from any cause or repeat hospital admission | 121 (34·9%) | 125 (37·7%) | 265 (77·8%) | 228 (71·3%) | 0·49 |
| Stroke or transient ischaemic attack | | | | | |
| All | 28 (8·6%) | 13 (4·3%) | 42 (15·9%) | 33 (14·7%) | 0·35 |
| Stroke | 20 (6·0%) | 10 (3·2%) | 29 (10·4%) | 26 (11·3%) | 0·61 |
| Transient ischaemic attack | 8 (2·6%) | 4 (1·5%) | 14 (6·3%) | 8 (3·8%) | 0·30 |
| Stroke or death from any cause | 95 (27·4%) | 95 (28·6%) | 236 (69·8%) | 200 (62·9%) | 0·39 |

# 5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis




(J Am Coll Cardiol Intv 2015;8:1084–91)

# Should we panic or calm down ?

- ✓ We treated patients with AS at high risk
- ✓ We dont treat CT-scan images
- ✓ 5-yr clinical outcome of patients treated by Sapien/Corevalve is reassuring
- ✓ Subclinical leaflets thrombosis is observed in all types of aortic bioprostheses
- ✓ Not associated with symptoms, clinical events or high gradients

- ✓ Stay calm and wait the results of the ongoing trials
- ✓ Role of APT/ACO treatment is uncertain

# Reduced Leaflet Motion in Bioprosthetic Aortic Valves — The FDA Perspective

John C. Laschinger, M.D., Changfu Wu, Ph.D., Nicole G. Ibrahim, Ph.D., and Jeffrey E. Shuren, M.D., J.D.

N ENGL J MED 373;21 NEJM.ORG NOVEMBER 19, 2015

We at the FDA believe that the available clinical evidence supports the conclusion that these valves remain safe and effective and that findings to date concerning reduced leaflet motion have not changed the overall favorable benefit–risk balance for these valves when they are used for their approved indications.