Transcatheter heart valve thrombosis

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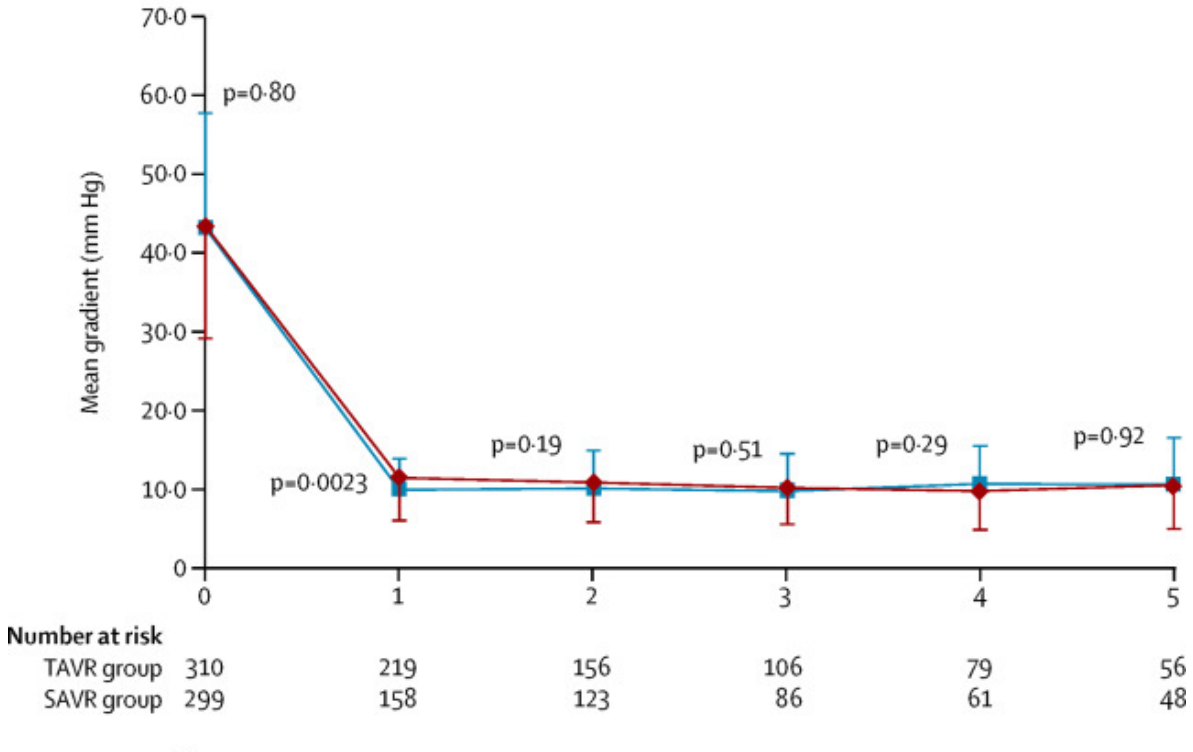
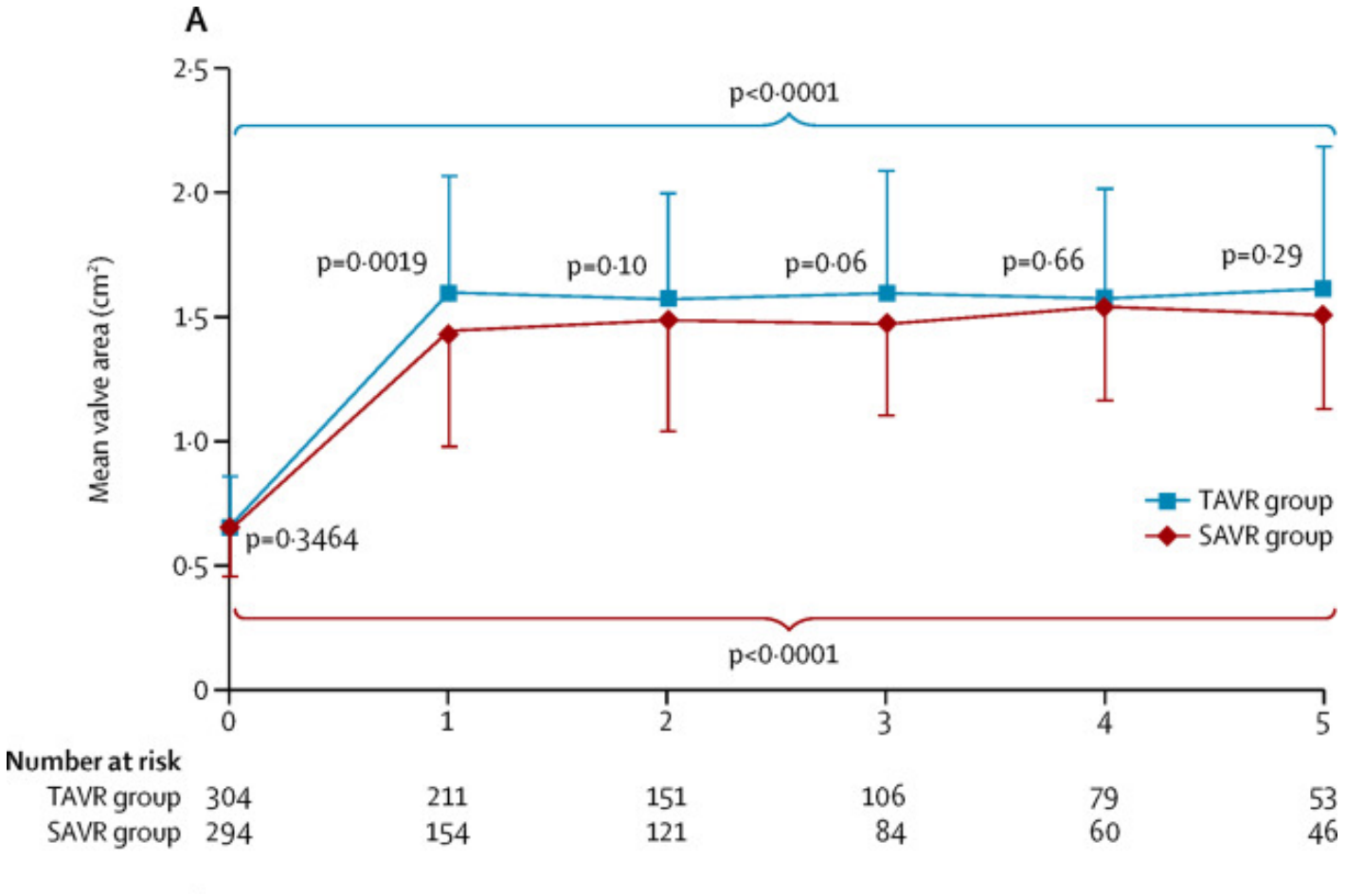
When everything was simple: AV mean gradient after TAVR



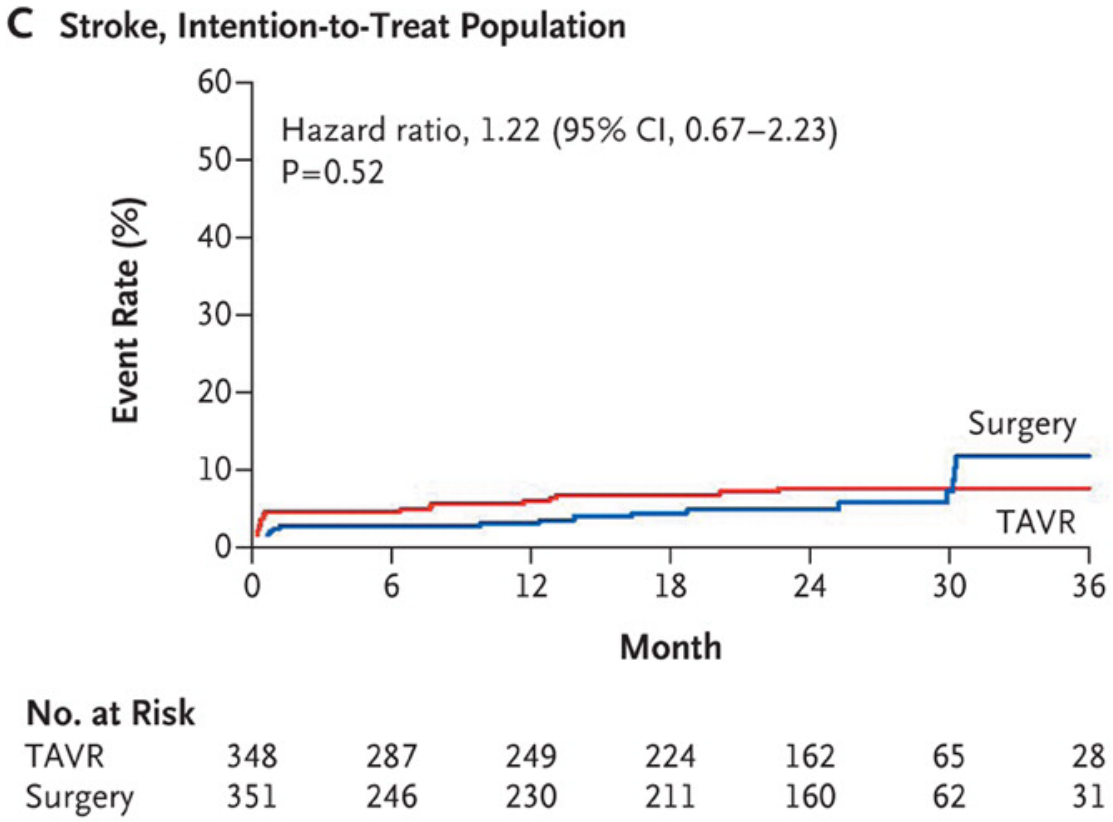
PARTNER 1-cohort A Mack et al. Lancet et al 2015

When everything was simple: EROA after TAVR



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

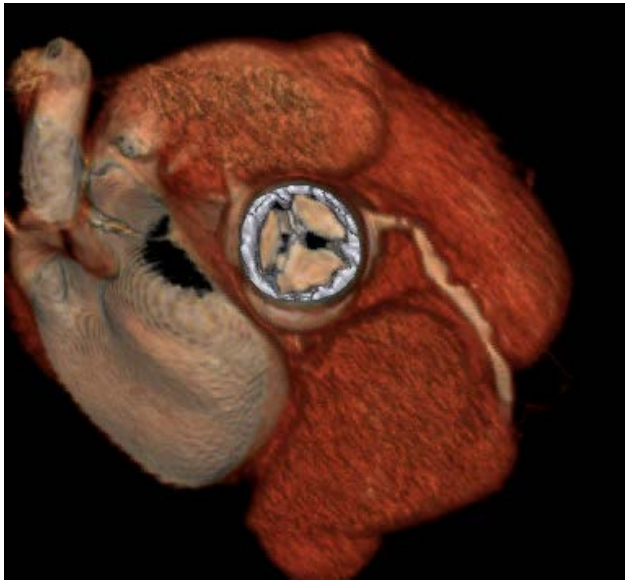
TIA stroke rate

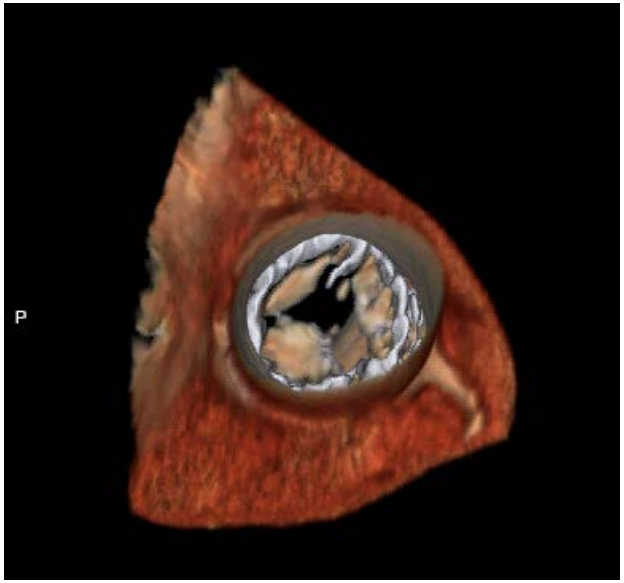


"Between 1 and 2 years, 8 strokes occurred (4 in the TAVR group and 4 in the surgery group) and 3 transient ischemic attacks (2 in the TAVR group and 1 in the surgery group)."

PARTNER 1-cohort A Kodali et al. NEJM 2012

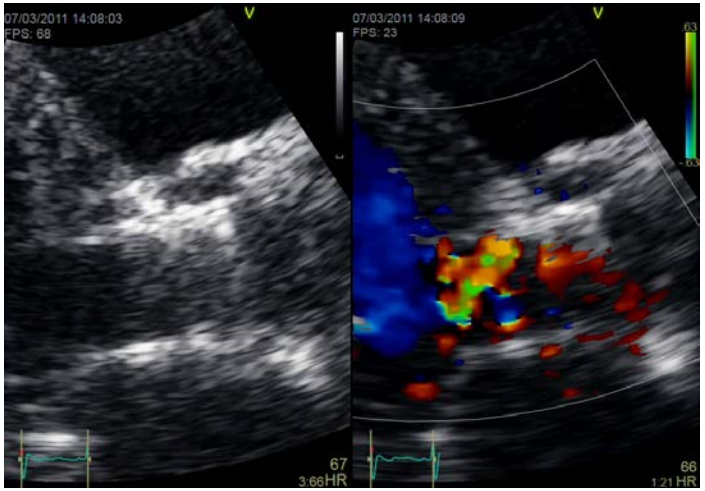
CT post-TAVR however showed….

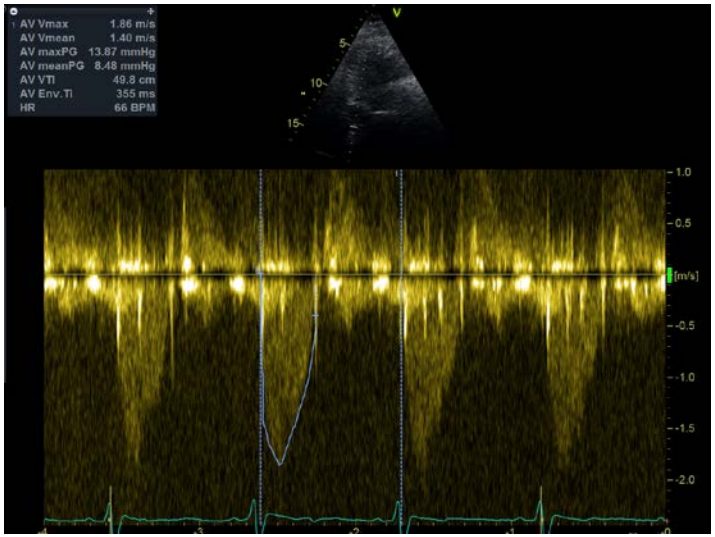




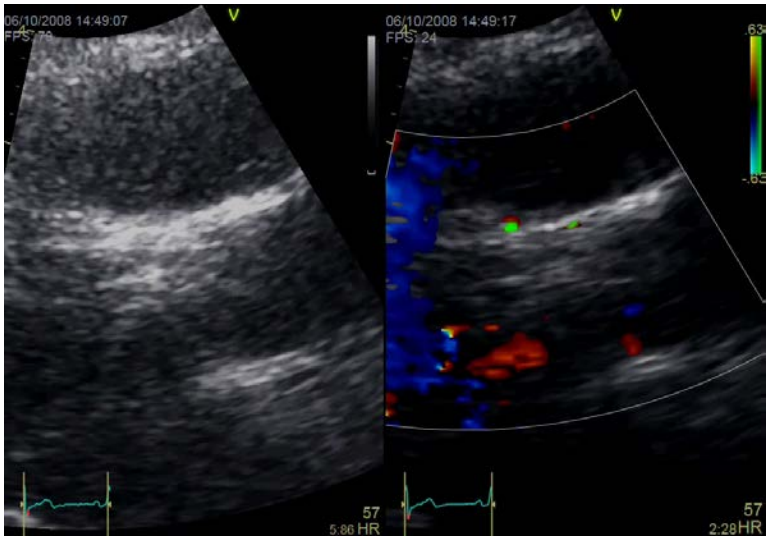
hypo-attenuated leaflet thickening (HALT)
with or without restricted leaflet motion (HAM)
(2D and 4D) – suggesting thrombosis ..

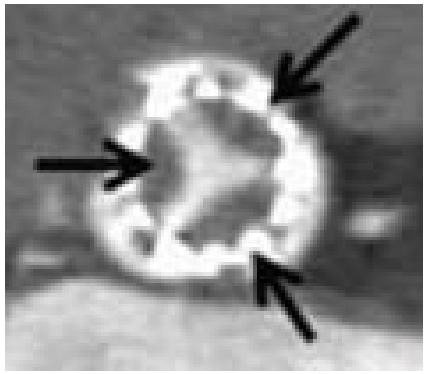
Normal:
CT vs Echo (mean 8 mmHg)

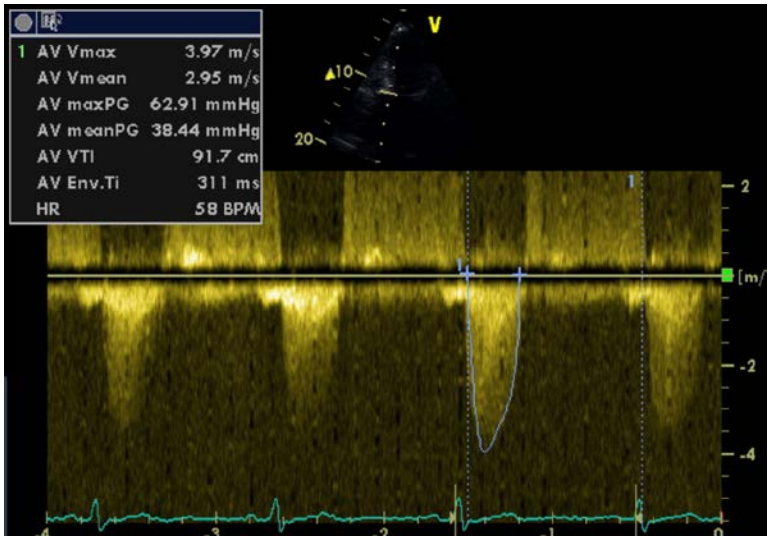




Abnormal:
CT vs Echo (mean 38 mmHg)







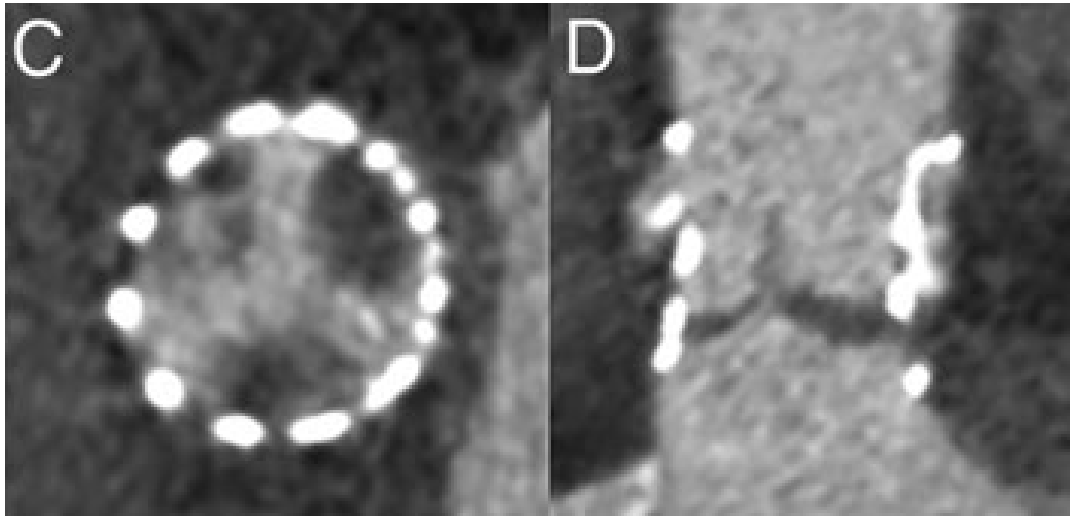
One of the first studies

- N = 156, 46% male
- TAVI with SAPIEN 3 THV

- CT – 5 days (median) after TAVI
  - HALT 10.3% of patients
- Echo – 5 days (median) after TAVI
  - mean gradient 8±3.5 mmHg

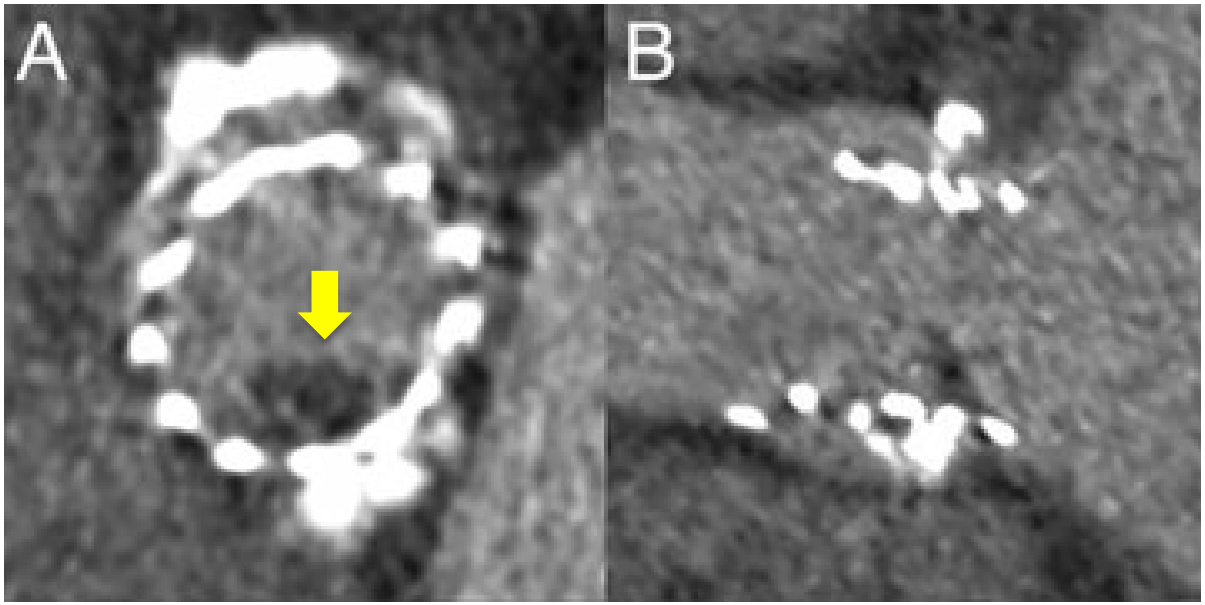
Pache et al Eur Heart J 2016

Some show:
Matched anatomy and (dys)function



Mean gradient 25 mmHg

But most show:
Mismatch anatomy and function



Mean gradient 11 mmHg

What is in the literature? – 12 studies

Author (year)	No	Prevalence of thrombosis on MDCT (time)	Prevalence of thrombosis on Echo (time)	Mean gradient (mmHg) - EOA (cm^2)
Latib et al (2015)	4266	NA	0.61% (median 181 days)	40.5±14.0 - NA
Pache et al (2016)	156	10.6% (median 5 days)	NA (median 5 days)	8±3.5 - NA
Leetmaa et al (2016)	140	4% (1-3 months)	NA (1-3 months)	19.2 – 1.44
Del Trigo et al (2016)	1521	NA	4.5% (4 years)	26.1±11 - NA
Hansson et al (2016)	405	7% (1-3 months)	NA (1-3 months)	10±7 - 1.5±0.5
Makkar et al (2015)	55	40% (median 32 days)	NA (30 days)	9.2±4.9 - NA
Makkar et al (2015)	132	13% (median 86 days)	NA (30 days)	8.4±2.9 - NA
Yanagisawa et al (2017)	70	14.3% (1 year)	NA (1 year)	8.3±0.8 - 1.03±0.25
Chakravarty et al (2017)	752	13% (median 58 days)	6% (median 58 days)	13.8±10.0 - NA
Vollema et al (2017)	434	12% (median 35 days)	3% (3years)	9.3±4.7 - 1.99±0.56
Jose et al (2017)	642	9/10 (NA)	2.8% (median 181 days)	34±14 - 1.06±0.46
Sondergaard et al (2017)	61	11% (140±152 days)	NA	7.0±3.2 - NA

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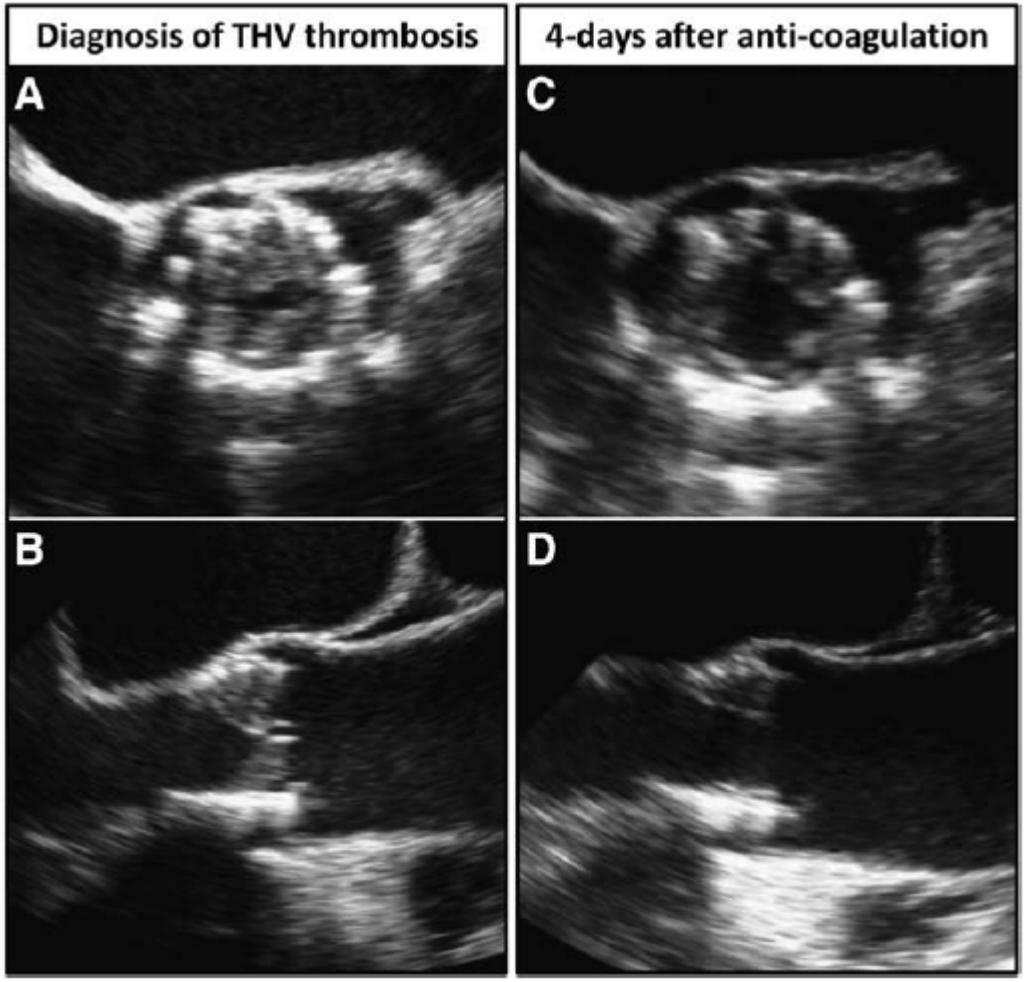
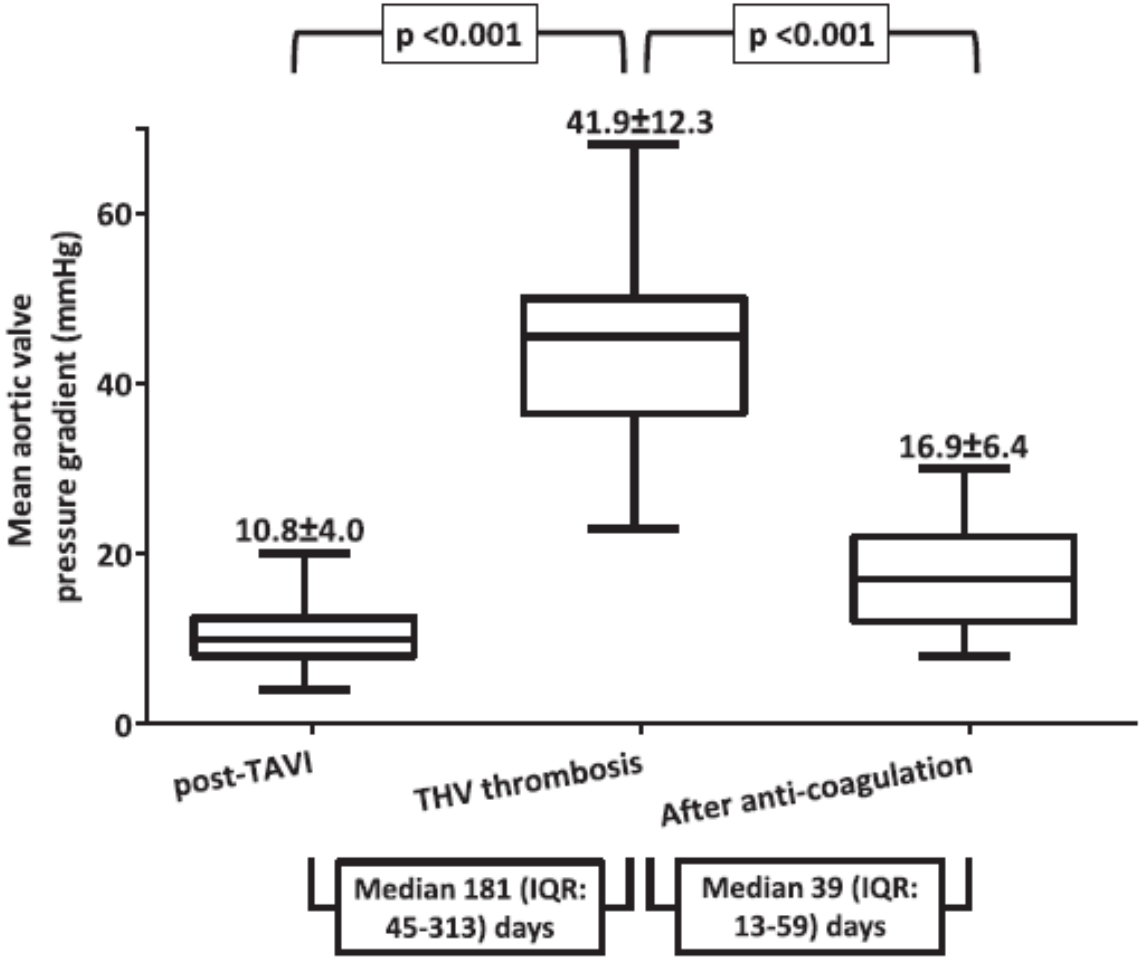
N = 4266 ☞ 26 (0.61%) THV thrombosis



- Median time to diagnosis 181 days
- 65% worsening dyspnea
- 31% subclinical (asymptomatic)
- **No neurological events**
- **No thromboembolic events**
- Mean aortic valve gradient 40.5±14.0 mmHg
- Anticoagulation effective treatment

Latib et al. Circ Cv Intervent 2015

Gradient vs anti-coagulation

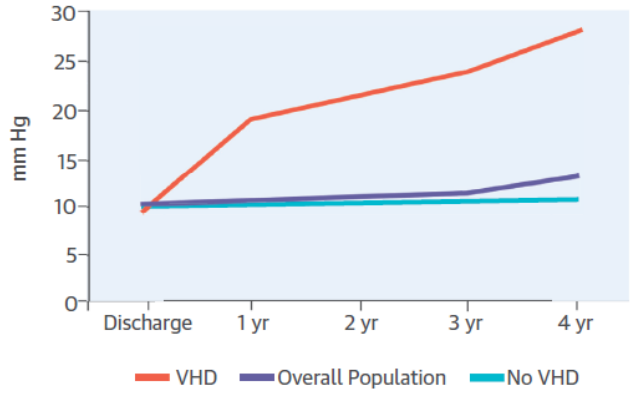


Latib et al. Circ CV Intervent 2015

N = 1521 ☞ 68 (4.5%) Valve hemodynamic deterioration (VHD)

- Assessed with echocardiography.
- VHD was defined as a ≥10 mmHg increase in transprosthetic mean gradient during follow-up compared with discharge assessment.
- Follow-up 4 years

Progression of Transvalvular Mean Gradients Following TAVR



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

Del Trigo et al. JACC 2016

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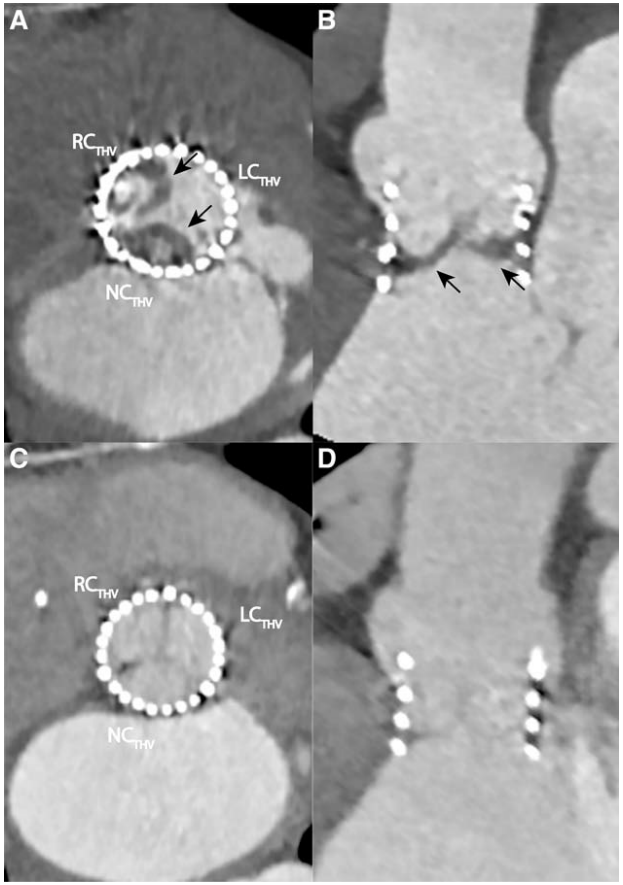
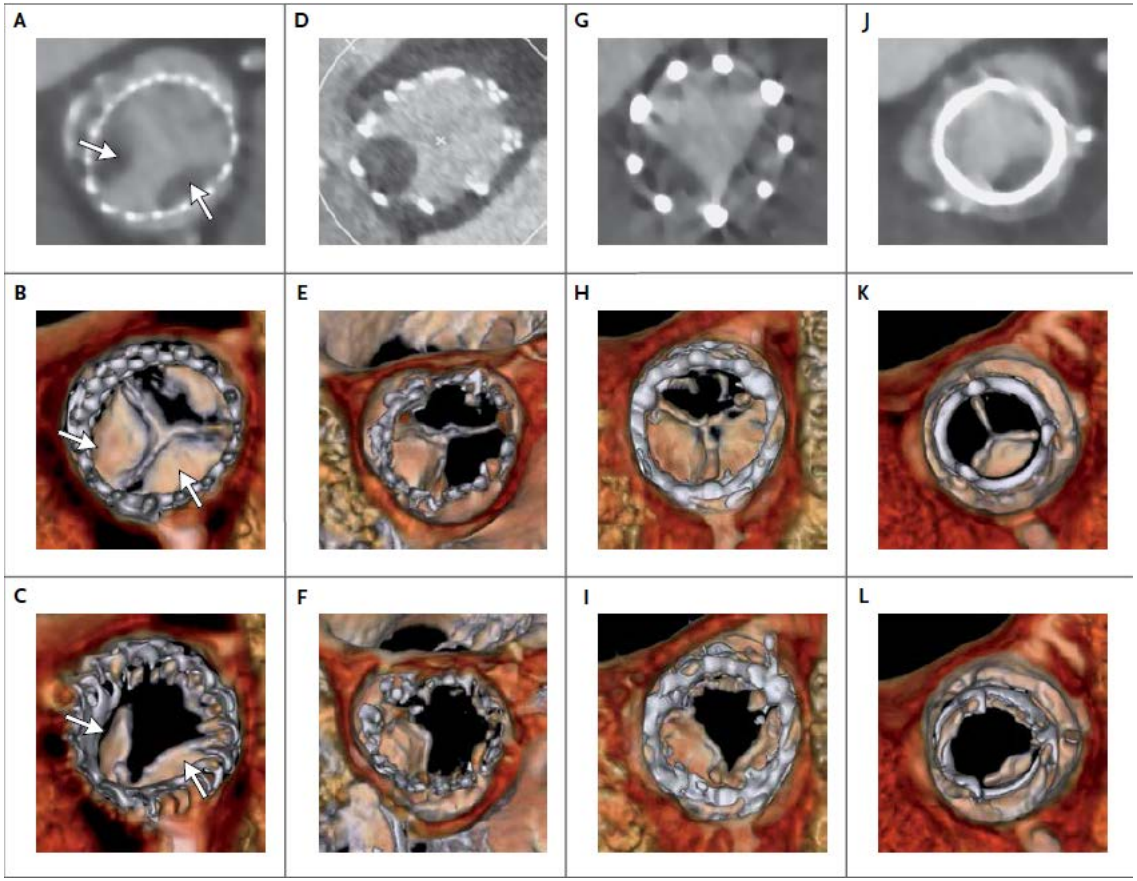
N = 140 ☞ 5 (4%) THV thrombosis



- MDCT performed within 1-3 months of TAVI
- N = 1 heart failure symptoms
- N= 4 subclinical (asymptomatic)
- **No neurological events**
- **No thromboembolic events**
- Mean aortic valve gradient <20 mmHg in all
- Anticoagulation effective treatment

Leetmaa et al. Circ Cv Intervent 2015

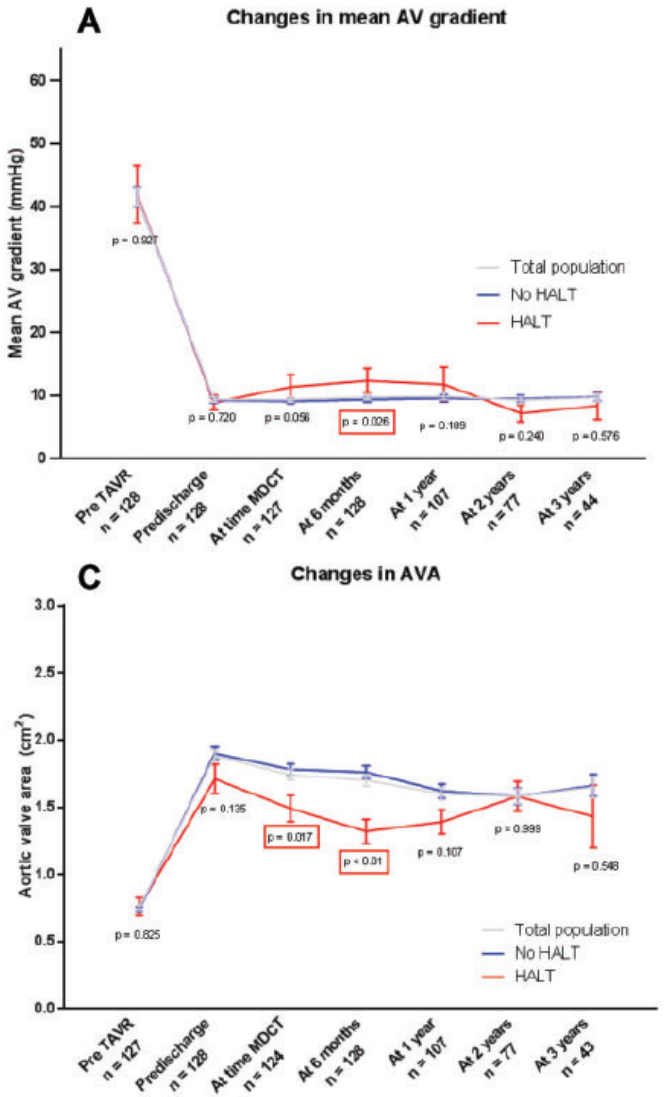
N = 55 TAVI clinical trial ☞ 22 (40%)
N = 132 registry (TAVR or SAVR) ☞ 17 (13%)
THV thrombosis



- Median time to MDCT:
  - 32-86 days
- Mean gradient <20 mmHg in all patients
- Anticoagulation effective treatment

Makkar et al. New Engl J Med 2016

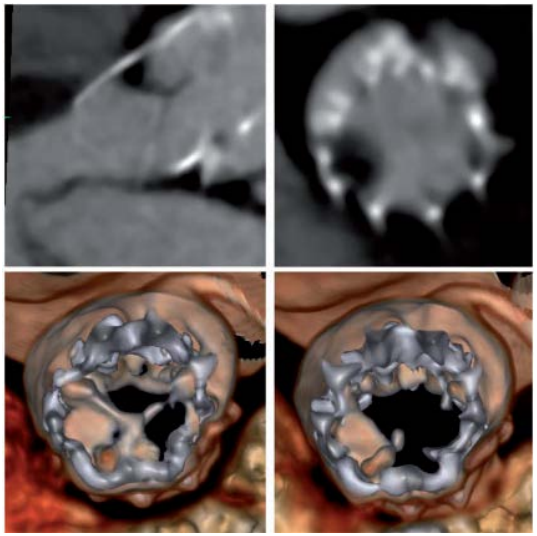
N = 128 ☞ 16 (12%) THV thrombosis

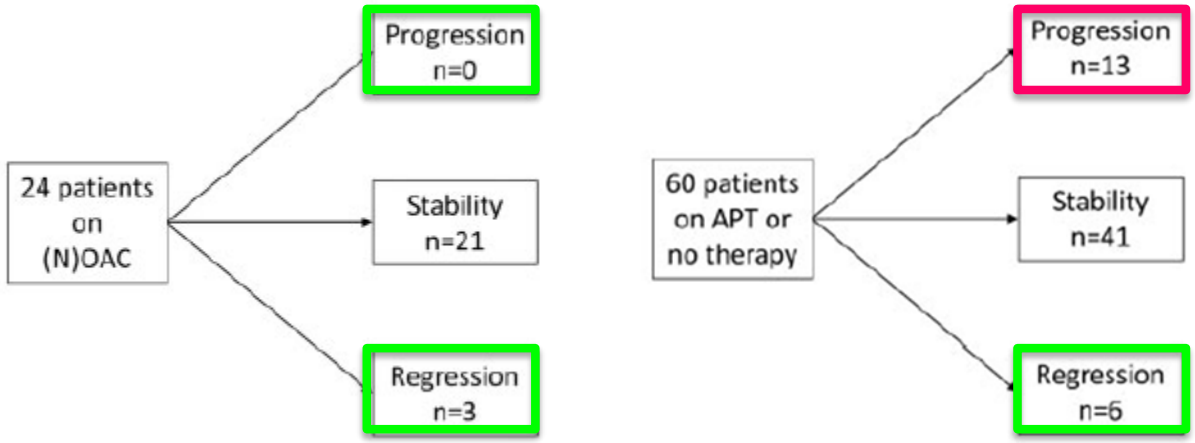


- Assessed with MDCT
  - median follow-up of 35 days
- Mostly asymptomatic (1 patient with heart failure)
- Mean gradient 9.3±4.7 mmHg
- **No association with increased risk of TIA and all strokes**

Vollema et al. Eur Heart J 2017

COHORT OF THV ☞ 11% THV thrombosis
scan 1 = 140 (STD 152) days – scan <12 MONTHS





First important observation: progression absent in all patients using anticoagulation.

Second important observation: 61.9% of patients - normal valves at both 4D CT scans despite absence of oral anticoagulation.
Third important observation: stability also noted in 41 patients using antiplatelet therapy (or no therapy).

Implying that anticoagulation may not be warranted in all patients, but should be personalized to patients who need it.

Sondergaard et al. Eur Heart J 2017

The definitions

- **Echocardiography:**

- Zoghbi et al (JASE 2009): definition for surgical bioprosthetic valve prostheses
- Possible stenosis: mean gradient 20-35 mmHg
- effective orifice area (indexed for body surface area) 1.2-0.8 cm2.

- Significant stenosis: mean gradient >35 mmHg
- effective orifice area (indexed for body surface area) <0.8 cm2.

- expanded by Lancellotti et al (EHJCVI 2016):
- possible obstruction: increase in mean gradient at follow-up between 10-19 mmHg
- significant obstruction: increase in mean gradient at follow-up ≥20 mmHg.

The definitions

- **CT:**

- hypo-attenuated leaflet thickening
  (HALT) – 2D
- with or without restricted leaflet motion
  4D

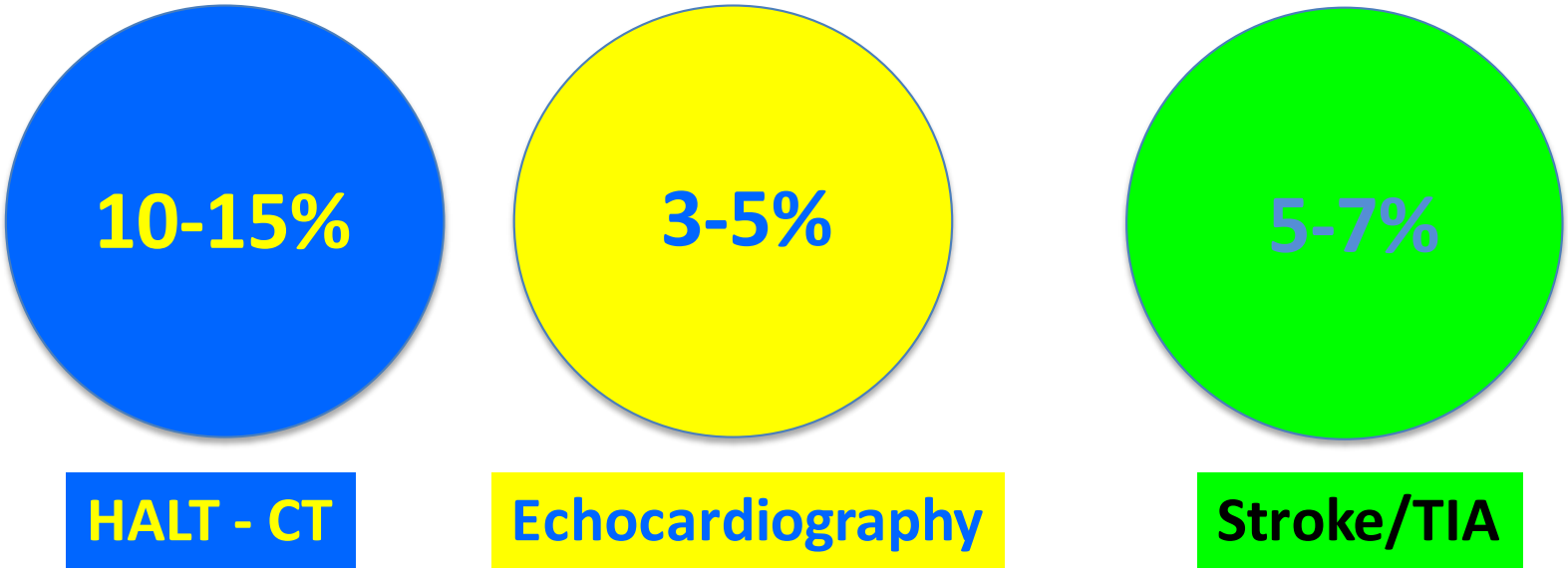
Need for better definitions

- *Dangas et al recently stated that prosthetic heart valve dysfunction can be seen as "a continuum of the same pathological process"*
- *with early thrombus formation (CT),*
- *later fibrotic pannus formation (echo),*
- *followed by degeneration / dysfunction (echo)*

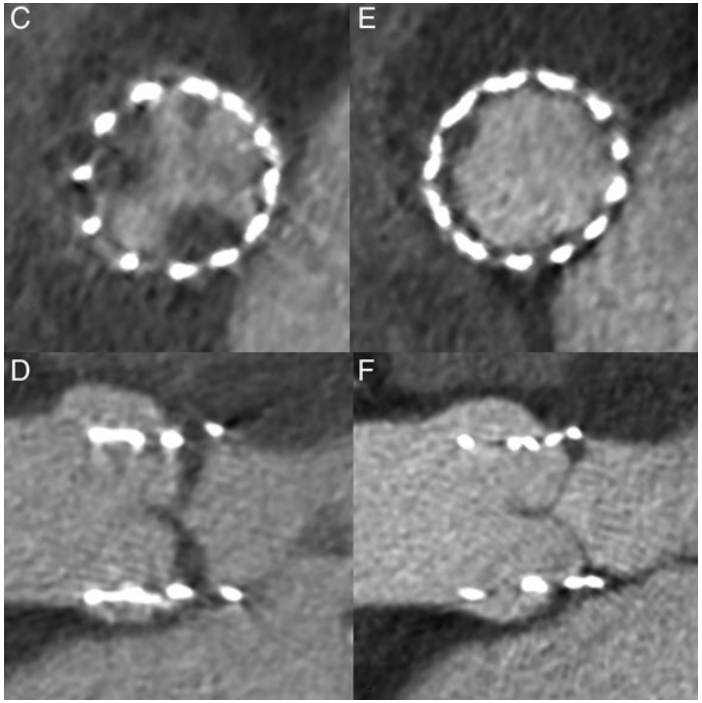
- *JACC 2016*

Open questions:

Correlation between thrombosis rate based on imaging vs. stroke rate



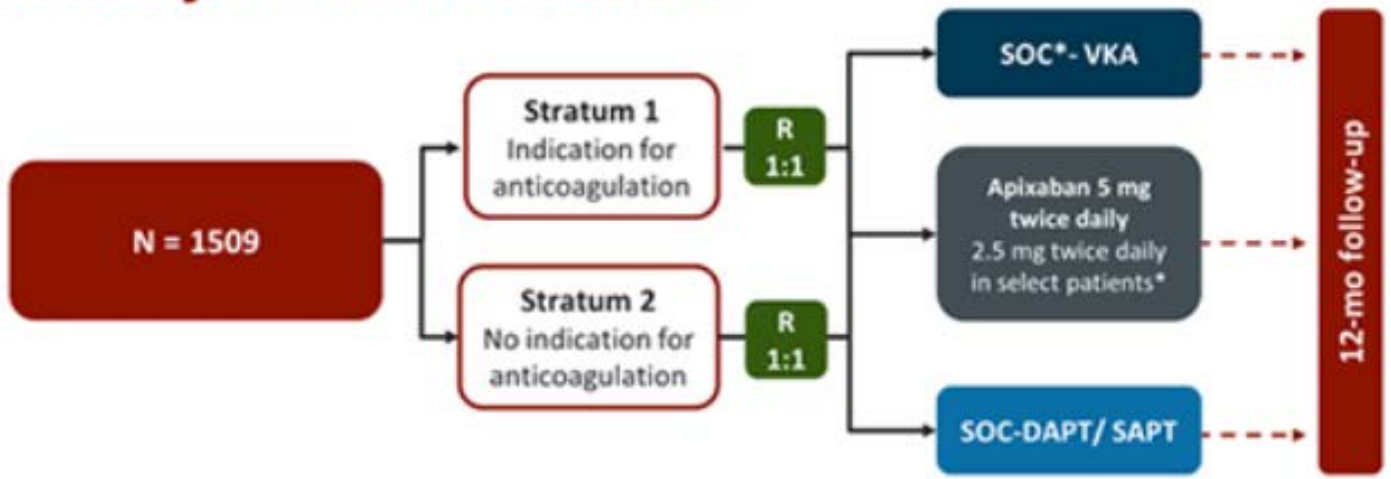
Open questions: Resolution after anticoagulation



- Everyone anticoagulation? How long? When to start? (but a significant number of patients has indication)
- Imaging surveillance? When? How often? Which technique?

ATLANTIS Trial Design

Apixaban in Patients Who Underwent a Clinically Successful TAVI Procedure



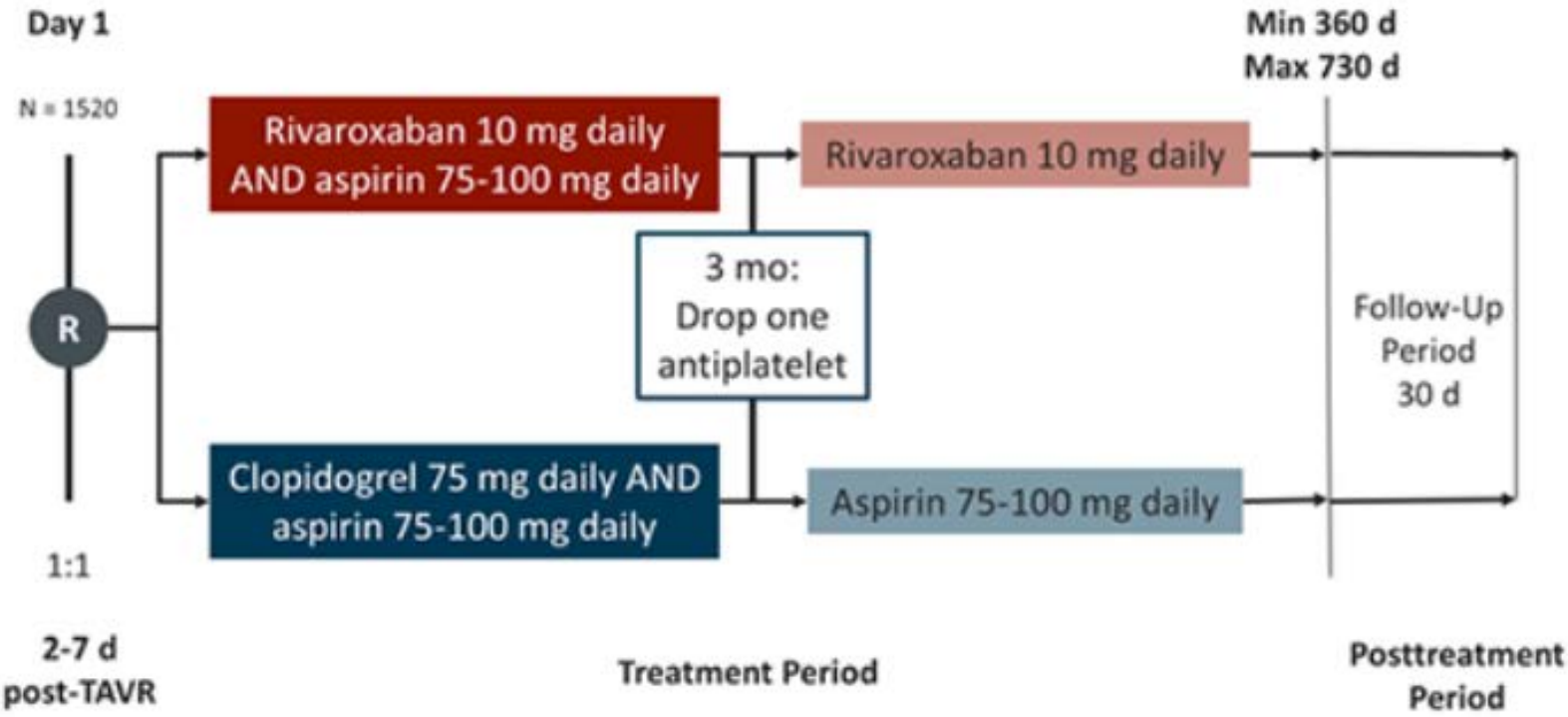
Primary endpoint: Composite of death, MI, stroke/TIA/systemic emboli, intracardiac or bioprosthesis thrombus, episode of DVT/PE, major bleeding, over 6 months of follow-up.

*2.5 mg twice daily if CrCl 15 to 29mL/min or if 2 of the following criteria: age ≥ 80 y, weight ≤ 60 kg, or Cr ≥ 1.5 mg/dL (133 µmol).

ClinicalTrials.gov. NCT02664649.

Source: https://www.medscape.org/viewarticle/864130_transcript

GALILEO Trial Design



- Primary efficacy endpoint: Composite of death, stroke, MI, symptomatic valve thrombosis, systemic thromboembolism, or major VTE

ClinicalTrials.gov. NCT02556203.

Source: https://www.medscape.org/viewarticle/864130_transcript