Transcatheter heart valve thrombosis

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Leiden, The Netherlands
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When everything was simple: AV mean gradient after TAVR

When everything was simple: EROA after TAVR

“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
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

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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 \( \geq 68 \ (4.5\%) \) Valve hemodynamic deterioration (VHD)

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

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

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:**
  - 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

10-15%  
HALT - CT

3-5%  
Echocardiography

5-7%  
Stroke/TIA
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

N = 1509

Stratum 1
Indication for anticoagulation
R 1:1
SOC* - VKA
Apixaban 5 mg twice daily
2.5 mg twice daily in select patients*
SOC-DAPT/ SAPT
12-mo follow-up

Stratum 2
No indication for anticoagulation
R 1:1

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

Day 1
N = 1520

Rivaroxaban 10 mg daily AND aspirin 75-100 mg daily → Rivaroxaban 10 mg daily

3 mo: Drop one antiplatelet

Clopidogrel 75 mg daily AND aspirin 75-100 mg daily → Aspirin 75-100 mg daily

Min 360 d Max 730 d

Follow-Up Period 30 d

2-7 d post-TAVR

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