πρώιμη θρόμβωση των γλωχίνων -
διάγνωση και θεραπεία

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Α’ Παν/κή Καρδ/κή Κλινική, ΓΝΑ Ιπποκράτειο
81 y/o female with severe aortic stenosis treated with TAVR
Severe elevation in gradients on POD# 1
Cardiac CT revealed extensive aortic valve thrombus

1 Day Post-TAVR mean gradient = 38 mmHg

4D VR showing leaflet motion
Leaflet thrombus
• **leaflet thrombosis** is a recently recognized and important mechanism of trans-catheter heart valve failure.\(^1-3\)

• It is **not known** whether leaflet thrombosis after transcatheter aortic valve replacement (TAVI) has **serious** clinical consequences.

**Timing**
- Acute (0-3 days)
- Subacute (3 days to 3 months)
- Late (3 months to 1 year)
- Very late (> 1 year)
LETTERS TO THE EDITOR

TAVR and Thrombosis

Transcatheter aortic valve replacement (TAVR) is a rapidly proliferating technology with the potential to become the dominant treatment strategy for aortic valve stenosis in patients who are at excessive or high operative risk (1). Antithrombotic therapy in the setting of TAVR has been empirically determined, with the most commonly recommended treatment consisting of unfractionated heparin during the procedure followed by dual antiplatelet therapy with aspirin (indefinitely) and clopidogrel (1 to 6 months) (2). Transcatheter heart valve (THV) thrombosis occurs in approximately 1% of patients after transcatheter aortic valve replacement, with a mean time to diagnosis of 9 ± 7 months (range 1 to 24 months) (3,4).

Several mechanisms that could potentially increase the risk of THV thrombosis have been proposed: 1) incomplete THV apposition to the aortic wall may delay endothelialization; 2) the metallic THV frame could potentially provide a site for thrombosis; 3) incomplete THV expansion can create leaflet folds and potential recesses for thrombus formation; and 4) the elderly TAVR population is more likely to have coexisting prothrombotic conditions (e.g., cancer) (4).

There is a case of asymptomatic thrombosis on the frame of the prosthetic valve. A 78-year-old female patient with symptomatic severe aortic stenosis...
Bioprosthetic valve dysfunction

- Structural Valve Deterioration: Intrinsic permanent changes of the prosthetic valve (i.e., calcification, leaflet fibrosis, tear or flail) leading to degeneration and/or haemodynamic dysfunction.
- Nonstructural Valve Deterioration: Any abnormality not intrinsic to the prosthetic valve itself (i.e., intra- or para-prosthetic regurgitation, prosthesis malposition, patient-prosthesis mismatch, late embolization) leading to degeneration and/or dysfunction.
- Thrombosis: Thrombus development on any structure of the prosthetic valve, leading to dysfunction with or without thrombo-embolism.
- Endocarditis: Infection involving any structure of the prosthetic valve, leading to perivalvular abscess, dehiscence, pseudoaneurysms, fistulae, vegetations, cusp rupture or perforation.

Capodanno et al Eur Heart J. 2017; 38:3382-90
sub-clinical leaflet thrombosis

- observed in all types of bio-prosthetic aortic valves
- not associated with symptoms or high trans-valvular gradient
- (N)OAC may prevent and resolve leaflet thrombosis
- uncertain association with stroke/TIA and valve durability

Makkare et al. NEJM. 2015;373:2015-24
Prevalence of subclinical leaflet thrombosis

Reduced leaflet motion in 106/890 (11.9%) patients

- Transcatheter valves: 13.4% (101 out of 752)
- Surgical valves: 3.6% (5 out of 138)

$P = 0.001$

4x in TAVI

Definitions

HALT

- Hypo-Attenuating Leaflet Thickening
  - Involves the periphery and bases of leaflets
  - May extend into leaflet edges

HAM

- Hypo-Attenuation Affecting Motion
  - Reduction in leaflet motion in the presence of HALT
  - Significant if there is >50% reduction in leaflet excursion

Makkar & Chakravarty, JACC Cardiovasc Interv. 2018 Jun 25;11(12):1172-74
Spectrum of transcatheter aortic valve thrombosis

- **Normal aortic valve**
- **HALT +ve, normal leaflet motion**
- **HALT +ve, reduced leaflet motion, normal AV gradients**
- **HALT +ve, reduced leaflet motion, elevated AV gradients**

**HALT**

**Systole**

**Diastole**

**Aortic valve gradients**
485 patients

asymptomatic - incidental on CT - valve thrombosis

untreated early leaflet thrombosis did not affect death, stroke, and rehospitalization

**OCEAN-TAVI registry**

symptomatic leaflet thrombosis

- acute- or subacute onset of heart failure, or
- stroke/TIA symptoms

with......

direct visualization of leaflet thrombosis on echocardiogram or
increase in mean gradient > 10 mmHg with no thrombus visible or
regression of elevated mean gradient after oral anticoagulation therapy or
reduced leaflet motion or hypoattenuated leaflet thickening on CT angiogram or
thrombosis at autopsy or via examination of tissue during reoperation

Blue arrows indicate thrombotic mass on transesophageal echocardiographic images (top). Yellow arrows indicate hypoattenuated areas on computed tomographic images (bottom).
1.47 per 100 patient-years

What were the important predictors of clinical valve thrombosis?

- Balloon-expandable valves
- Valve-in-valve TAVR
- Use of antiplatelet therapy alone

**TABLE 3** Predictors of Clinical Transcatheter Valve Thrombosis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.7 (0.2-2.1)</td>
<td>0.53</td>
</tr>
<tr>
<td>Age &gt;80 yrs</td>
<td>0.8 (0.3-2.2)</td>
<td>0.65</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>1.1 (0.3-4.5)</td>
<td>0.85</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.8 (0.4-7.1)</td>
<td>0.43</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>0.2 (0.1-1.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Obesity (BMI &gt;30 kg/m²)</td>
<td>4.6 (1.6-13.1)</td>
<td>0.005</td>
</tr>
<tr>
<td>Presence of coronary artery disease</td>
<td>0.8 (0.3-2.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>Antiplatelet therapy alone</td>
<td>79.1 (3.1-1,994.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Use of balloon-expandable valve</td>
<td>8.0 (2.1-29.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>Valve-in-valve procedure</td>
<td>17.1 (3.4-84.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pre-dilatation</td>
<td>0.9 (0.3-2.8)</td>
<td>0.81</td>
</tr>
<tr>
<td>Post-dilatation</td>
<td>1.2 (0.3-4.7)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Anticoagulation post-TAVR

DAPT
- Lower bleeding risk
- Higher risk of HALT and HAM
- Risk of impaired hemodynamics
- Higher patient acceptance and compliance

(N)OACs
- Lower risk of HAM
- Improved hemodynamics
- Higher bleeding risk
- Lower patient acceptance
# Antithrombotic Therapy for Prosthetic Valves

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin 75 -100 mg per day</strong> is reasonable in all patients with a bioprosthesis aortic or mitral valve</td>
<td>IIA</td>
</tr>
<tr>
<td><strong>Anticoagulation with a VKA</strong> to achieve an INR ~2.5 is reasonable for min 3 and max 6 months after surgical bioprosthesis MVR or AVR in patients at low risk of bleeding</td>
<td>IIA</td>
</tr>
<tr>
<td><strong>Clopidogrel 75 mg daily</strong> may be reasonable for the first 6 months after TAVR in addition to life-long aspirin 75 -100 mg daily</td>
<td>IIB</td>
</tr>
</tbody>
</table>

2017 AHA/ACC Guidelines for VHD

[2017 AHA/ACC Guidelines for VHD](#)
Prevalence of subclinical leaflet thrombosis

Reduced leaflet motion in 106/890 (11.9%) patients

Transcatheter valves 13.4% (101 out of 752)

Surgical valves 3.6% (5 out of 138)

P=0.001

Impact of anticoagulation on reduced leaflet motion

Resolution in all patients treated with NOACs and warfarin
Persistence/progression in 20/22 not treated

Chakravarty et al., Lancet, 2017
# Anticoagulation vs. DAPT

<table>
<thead>
<tr>
<th></th>
<th>Index CT</th>
<th>Follow-up CT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DAPT continued after index CT</strong></td>
<td><img src="#" alt="Image A" /></td>
<td><img src="#" alt="Image Progression" /></td>
</tr>
<tr>
<td><strong>Warfarin initiated after index CT</strong></td>
<td><img src="#" alt="Image B" /></td>
<td><img src="#" alt="Image Resolution" /></td>
</tr>
<tr>
<td><strong>Rivaroxaban initiated after index CT</strong></td>
<td><img src="#" alt="Image C" /></td>
<td><img src="#" alt="Image Resolution" /></td>
</tr>
<tr>
<td><strong>Apixaban initiated after index CT</strong></td>
<td><img src="#" alt="Image D" /></td>
<td><img src="#" alt="Image Resolution" /></td>
</tr>
</tbody>
</table>
Prosthetic Valve Thrombosis

Suspected Prosthetic Valve Thrombosis

Fibrinolytic Rx if persistent valve thrombosis after IV heparin therapy

Emergency Surgery

CT or fluoroscopy to evaluate valve motion

TTE to evaluate hemodynamic severity

Left-sided prosthetic valve thrombosis

TEE for thrombus size

NYHA class III-IV symptoms

Mobile or large (≥0.8 cm²) thrombus

Recent onset (<14 d)
NYHA class I-II symptoms
Small thrombus (<0.8 cm²)

Emergency Surgery

Emergency Surgery

Fibrinolytic Rx if persistent valve thrombosis after IV heparin therapy*

Class I

Class IIa

Emergency Surgery

TTE for thrombus size

NYHA class I-II symptoms

Small thrombus (<0.8 cm²)

Fibrinolytic Rx if persistent valve thrombosis after IV heparin therapy*
OAC in case of subclinical leaflet thrombosis?

- No evidence of clinical impact of subclinical leaflet thrombosis
- The phenomenon may spontaneously regress
- Duration of oral anti-coagulation?
- Will it protect against new repeated leaflet thrombosis?
- Life-long oral anti-coagulation will impact the advantage of bioprosthetic compared to mechanical aortic valves!

Should all TAVR patients undergo CT scan?

NO!

- Subclinical leaflet thrombosis can appear early and late after, so when is the best time for CT scan?
- Multiple CT scans are a risk for the patient due to radiation and contrast burden
- CT scan may be considered in case of stroke/TIA after TAVR
diagnose with TOE & CT

treat for sure if symptoms, with (N)OACs

surgery? (high risk patients before TAVI)
ευχαριστώ !