

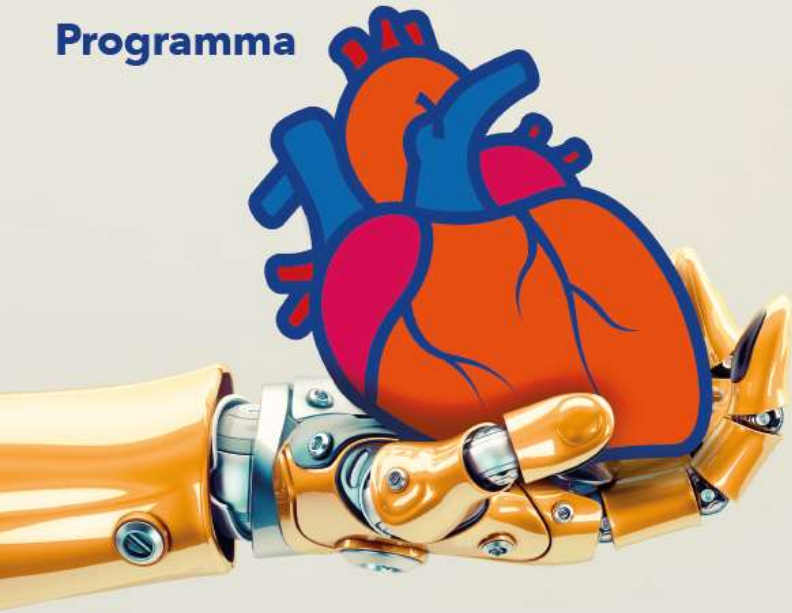
17° Meeting



CardioLUCCA

Heart Brings Heart 2023

Programma



Lucca, 22-24 Giugno 2023

Centro Congressi Auditorium San Francesco

Il rischio di stroke e le scelte antitrombotiche dopo TAVI



June, 2023

Renato Valenti

**Cardiologia Interventistica d'Urgenza
Azienda Ospedaliero-Universitaria Careggi
Firenze**



17° Meeting

CardioLucca
Heart Brings Heart **2023**



Lucca,
22-24 Giugno
2023

Centro Congressi
Auditorium San Francesco

Nothing to disclose for this presentation

but

**I believe in pharmaco-invasive treatments
and in “individualized” precision medicine**



Thrombotic and Bleeding Risk in TAVI Patients

Thrombotic Risk



Stroke



Prosthetic Valve
Thrombosis



Myocardial Infarction



New-onset
Atrial fibrillation

Bleeding Risk



Patient

- ✓ Age
- ✓ Antithrombotic therapy
- ✓ Anemia
- ✓ Bleeding history
- ✓ diathesis



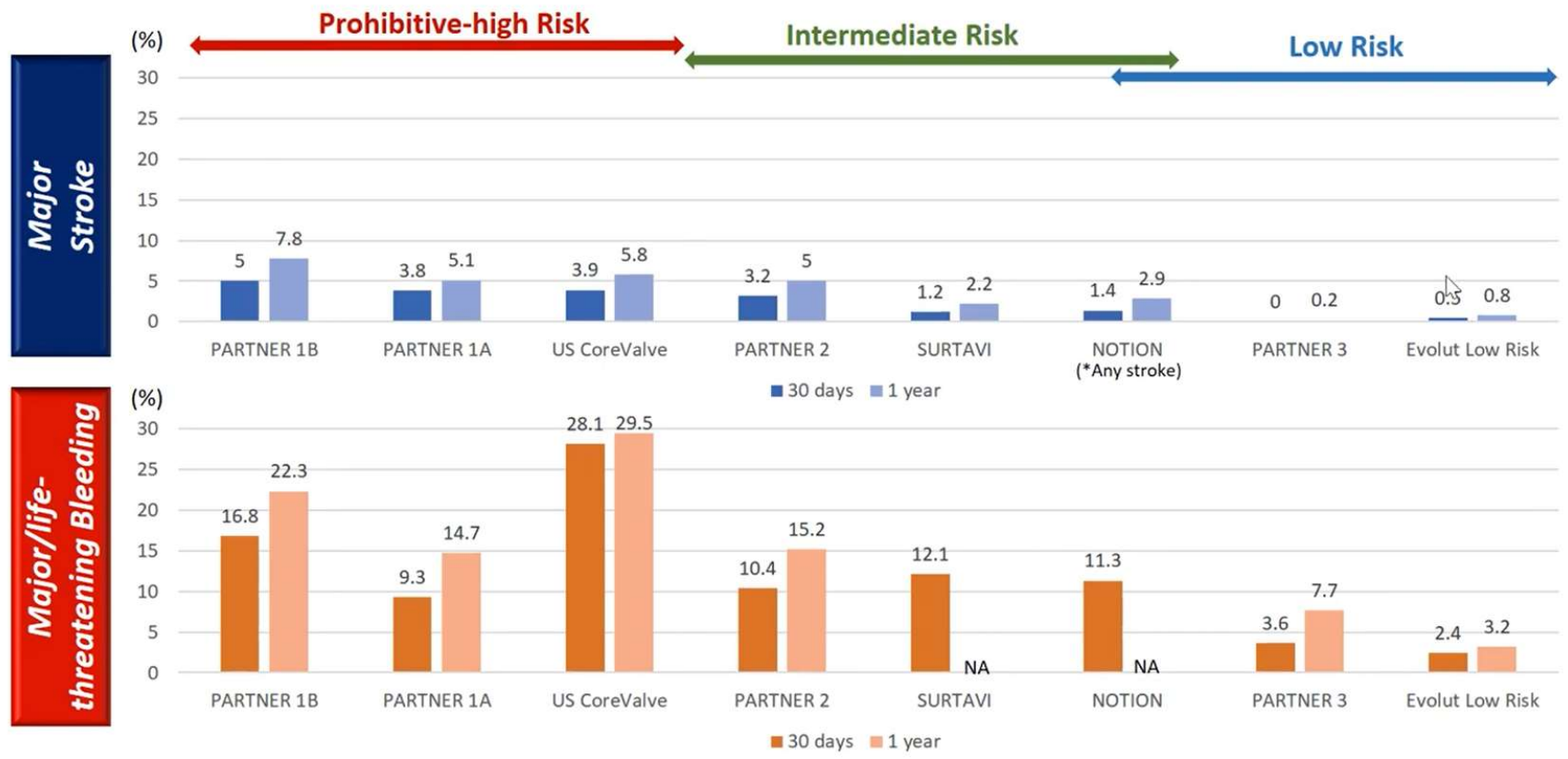
Heyde syndrome



Angiodysplasia



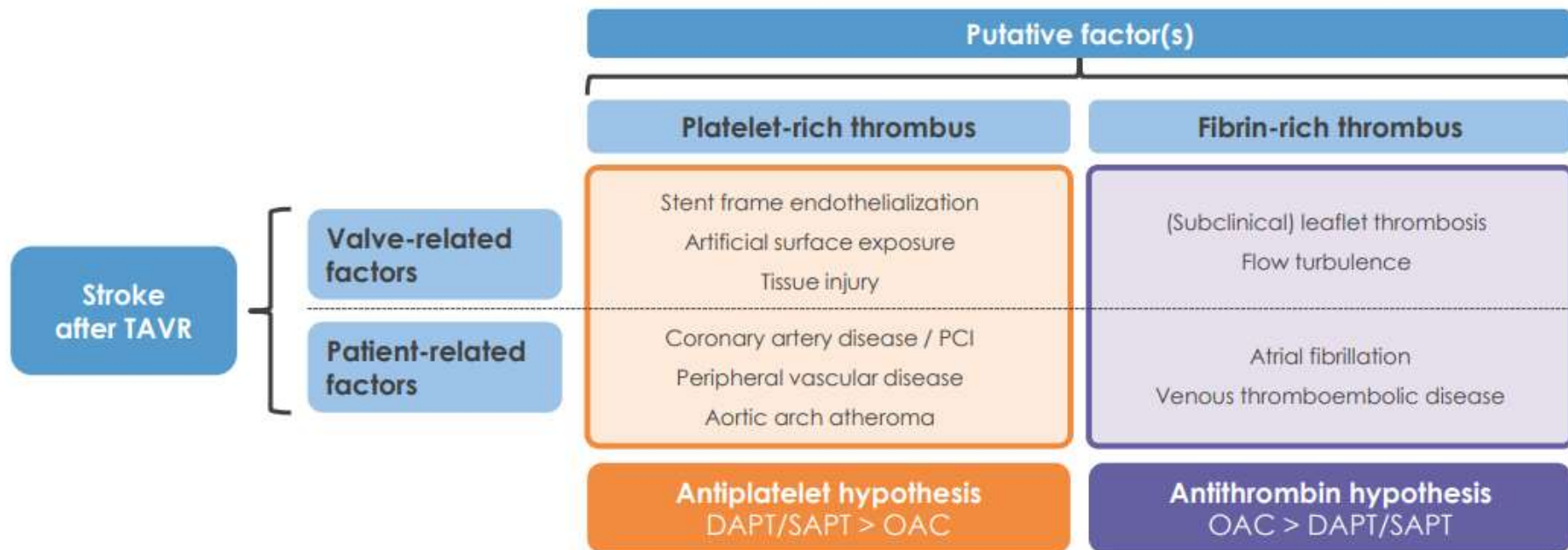
Thrombotic and Bleeding Risk in RCTs





Causes of Stroke After TAVI

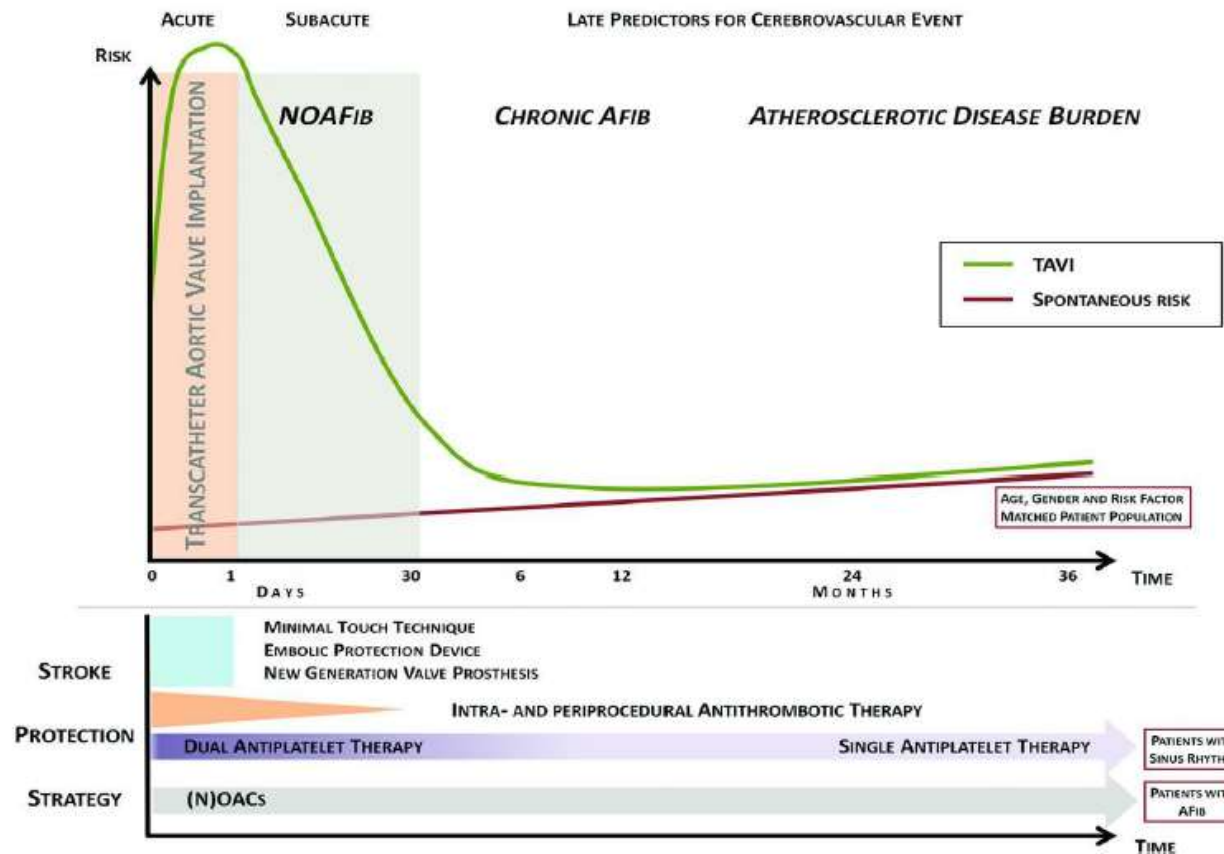
A multifactorial phenomenon





Risk of Cerebrovascular Events after TAVI

Different Risk @ Different Timepoints



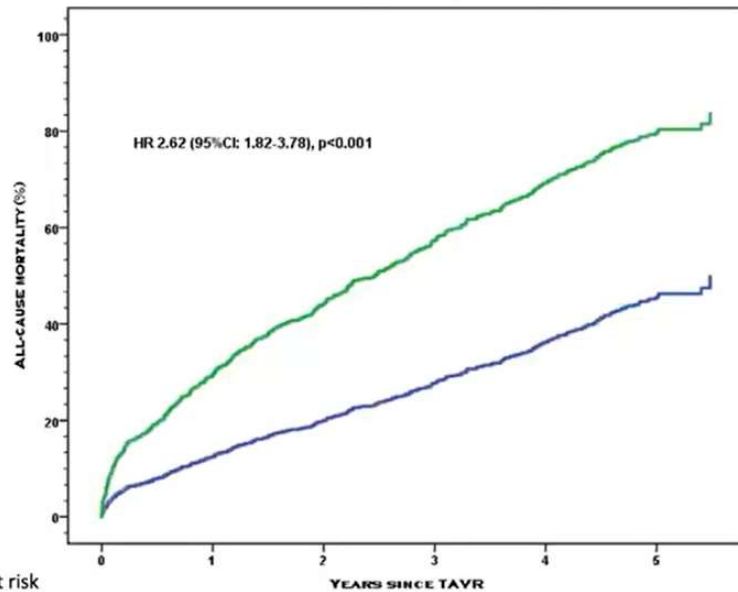
Stortecky S, Windecker S. *Circulation* 2012;126:2921-24



Impact of Stroke with Mortality

Bern TAVI Registry (N=2,279)

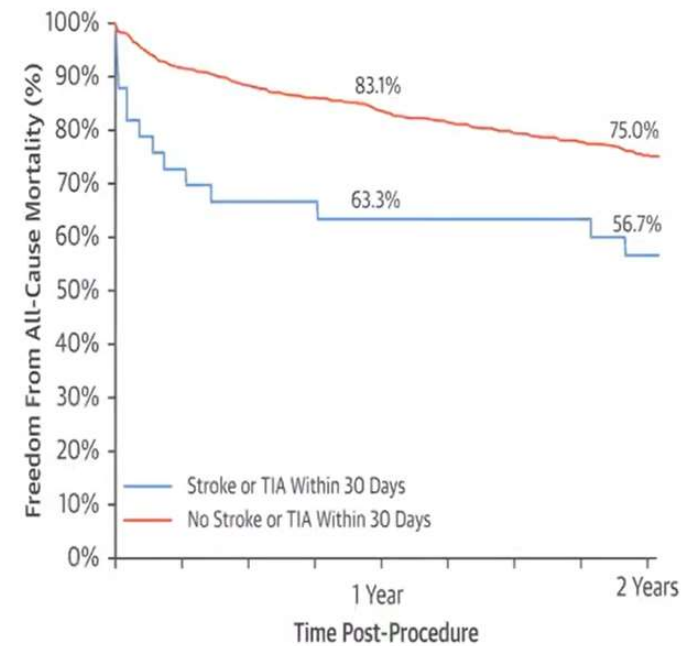
Okuno and Overtchouk et al. *Sci Rep* 2021;11:18754



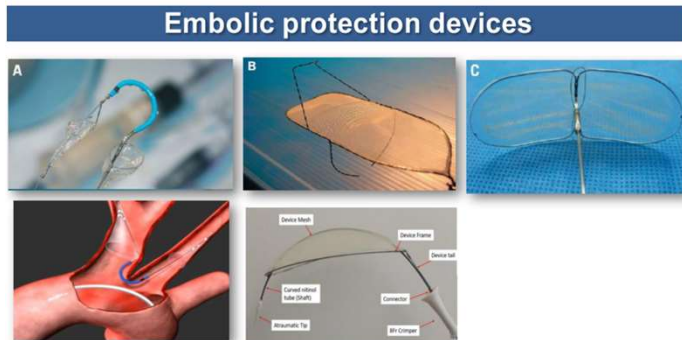
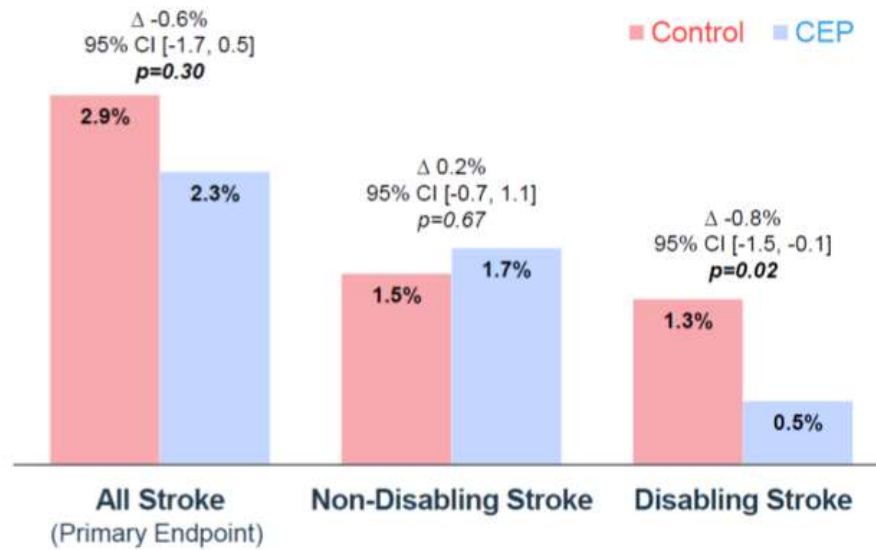
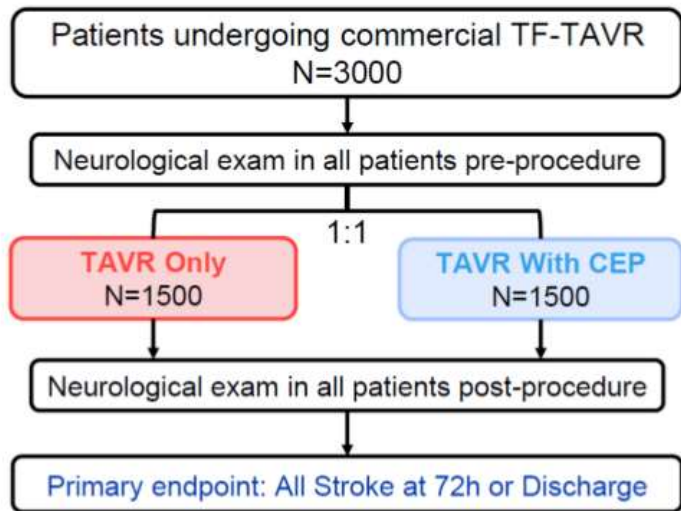
Number at risk	0	1	2	3	4	5
No CVE	1,437	1,095	957	627	390	201
CVE	55	30	22	14	6	2

ADVANCE Study (N=1,015)

Bosmans et al. *J Am Coll Cardiol* 2015; 66:209-17



Efficacy of Cerebral Protection: PROTECT TAVR



SENTINEL™
Cerebral Protection System

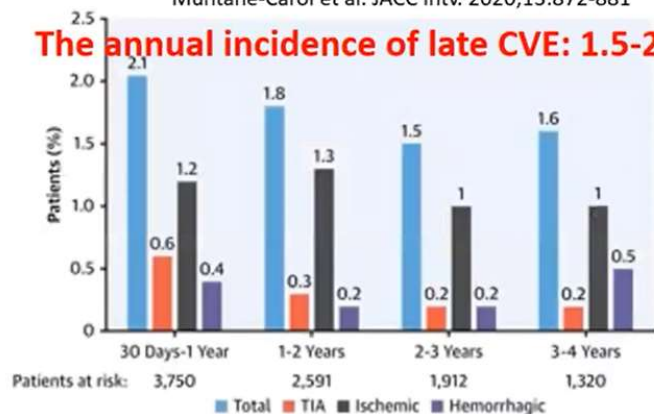
Kapadia SR et al. *N Engl J Med* 2022

Late Stroke Beyond 30 Days

Multi-center study TAVI survivors beyond 30 days (N=3,750)

Muntané-Carol et al. JACC Intv. 2020;13:872-881

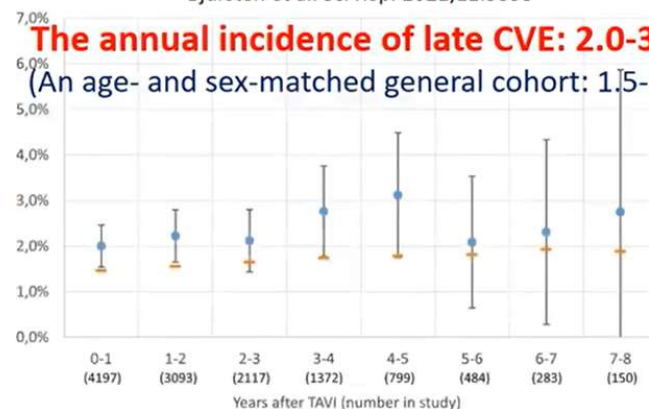
The annual incidence of late CVE: 1.5-2.1%



Sweden national registry TAVI survivors beyond 30 days (N=4,205)

Bjursten et al. Sci Rep. 2021;11:9593

The annual incidence of late CVE: 2.0-3.1%
(An age- and sex-matched general cohort: 1.5-1.9%)



Potential Causes

✓ **Atherosclerotic Burden**

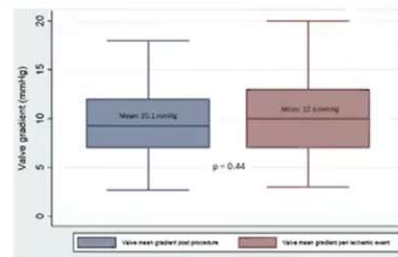


✓ **Atrial Fibrillation**

Fanning, Circulation. 2014;129:504-515



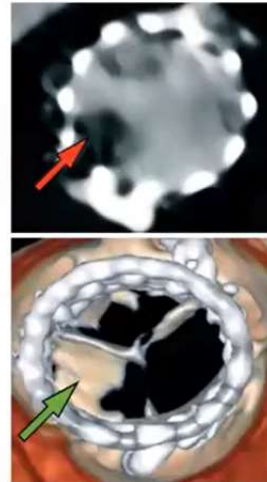
✓ **Bioprosthetic valve thrombosis**





Clinical Spectrum of Prosthetic Valve Thrombosis

Clinically Apparent	Subclinical	Silent
Valve dysfunction	Hypoattenuating opacities	Silent Brain Infarction
Stroke/TIA	Reduced leaflet motion	
Systemic embolism		





Subclinical Leaflet Thrombosis

Lessons from the PARTNER 3 CT substudy

1

Incidence

10% at 30 days and 24% at 1 year

2

Natural history

Spontaneously resolved in 50%. New in 20%

3

TAVI vs SAVR

Significantly higher with TAVR at 30 days

4

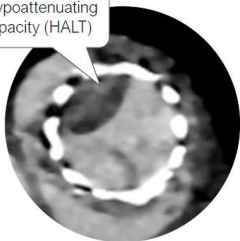
Hemodynamics

Minimal increase in valve gradients



There were no deaths or MIs in patients with HALT. The pooled rates of death/stroke/TIA/thromboembolic events were numerically higher in patients with HALT

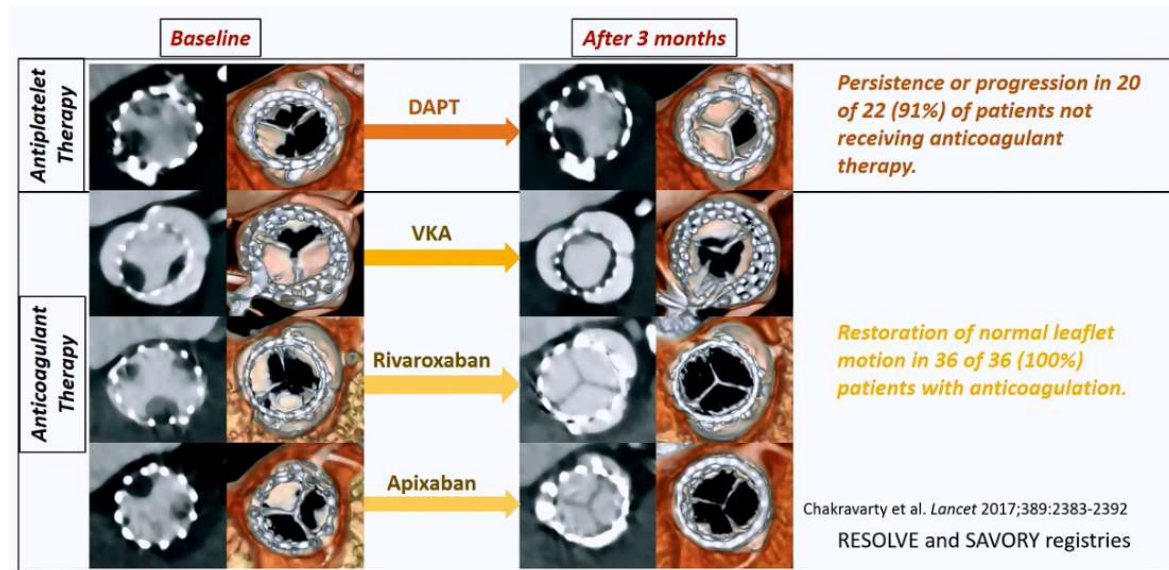
Hypoattenuating opacity (HALT)



Makkar RR et al. JACC 2020



Restoration of Leaflet Motion with Anticoagulant



Restoration/appearance of reduced leaflet motion occurs also spontaneously, irrespective of anticoagulation therapy at 1 yrs.

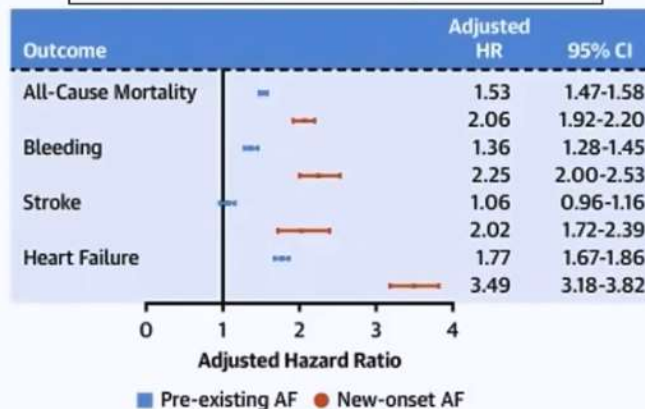
[PARTNER 3 Trial and Evolut Low Risk Trial. Makkar RR et al. JACC 2020; Blanke P et al JACC 2020.]



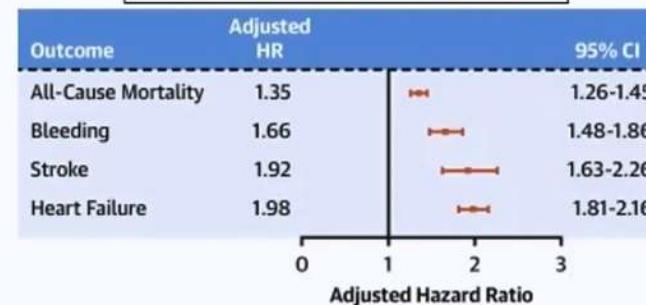
New Onset of Atrial Fibrillation and Outcome



New-onset AF/Pre-existing AF vs. No AF



New-onset AF vs. Pre-existing AF



- ✓ Among 72,660 Medicare patients, 2,948 (6.8%) experienced new-onset AF after TAVI.
- ✓ New-onset AF was associated with increased risk of mortality, bleeding, stroke, and HF hospitalization compared with pre-existing AF or no AF

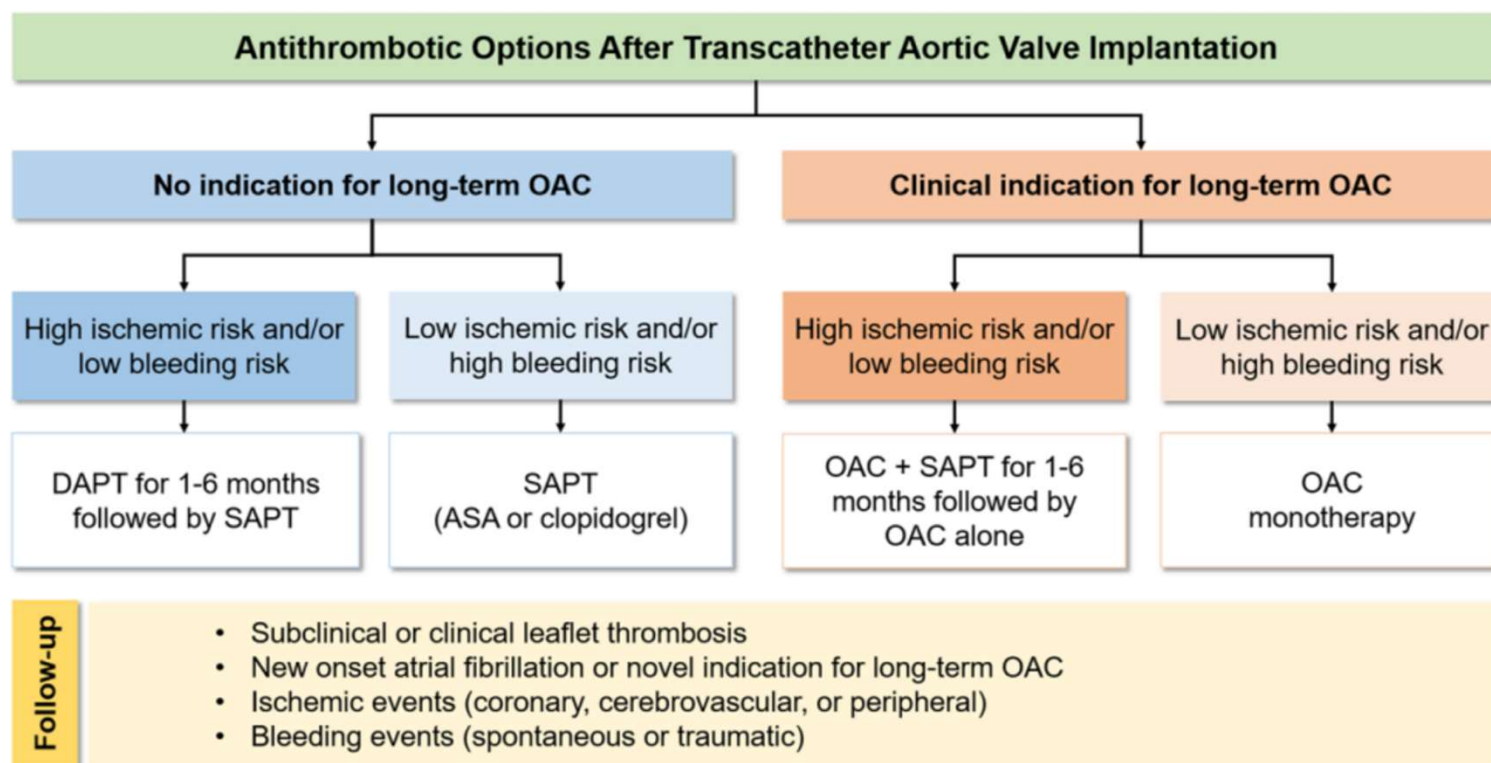
A red heart icon with a white fleur-de-lis symbol inside.

Key Points in Antithrombotic Therapy Management After TAVI

1. Single antiplatelet therapy (SAPT) or dual-antiplatelet therapy (DAPT) in patients **without an indication for oral anticoagulation.**
2. VKA/NOAC oral anticoagulation or SAPT/DAPT in patients **without an indication for oral anticoagulation.**
3. VKA or NOAC oral anticoagulation in patients **with an indication for oral anticoagulation.**
4. SAPT added to OAC in patients **with an indication for oral anticoagulation.**
5. Antithrombotic therapy in **TAVI patients undergoing PCI.**

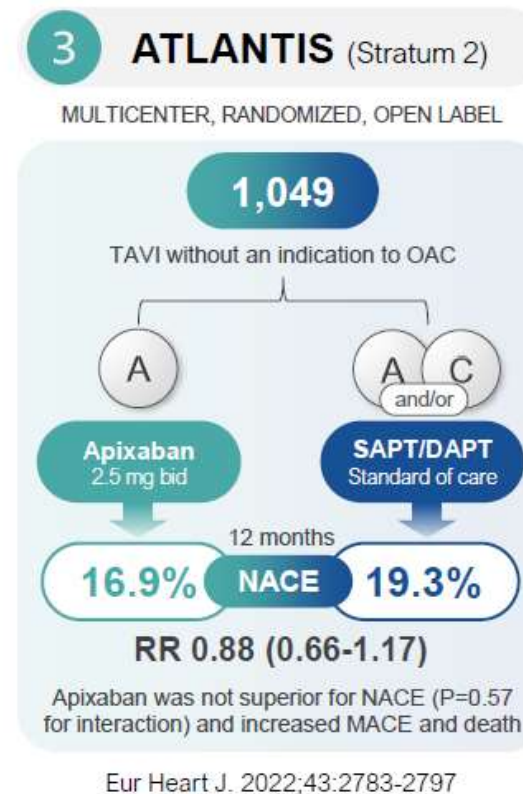
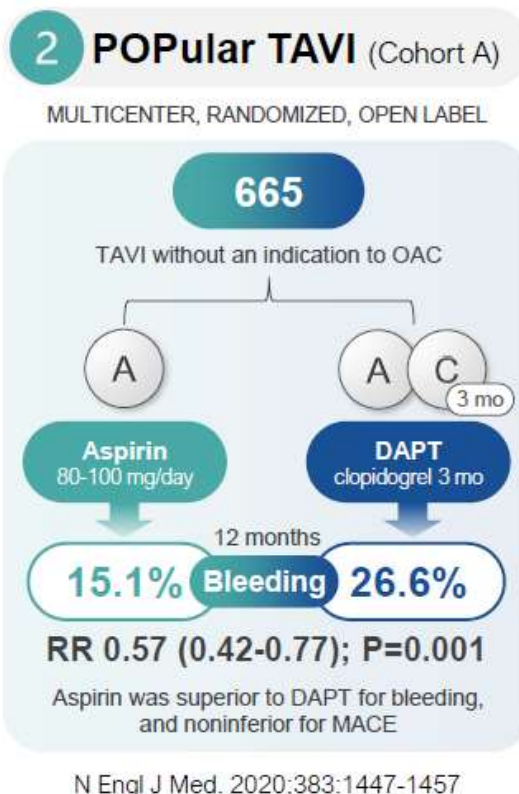
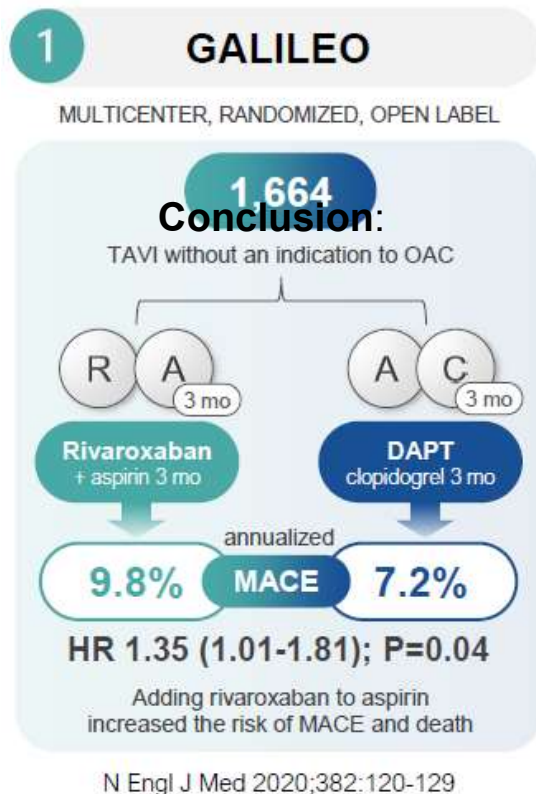


Thrombotic and Bleeding Risk Assessment and Antithrombotic Management of Patients Undergoing TAVI





Trials in Patients with **NO NEED** for OAC



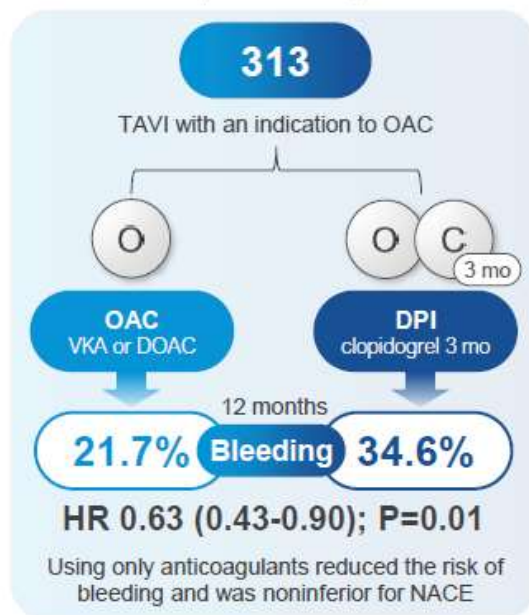
- ✓ Rivaroxaban was found to be harmful in both bleeding and thrombotic protection.
- ✓ SAPT was associated with bleedings reduction without increase of MACE.
- ✓ Apixaban was not superior to standard of care (DAPT).



Trials in Patients with **NEED** for OAC

1 POpular TAVI (Cohort B)

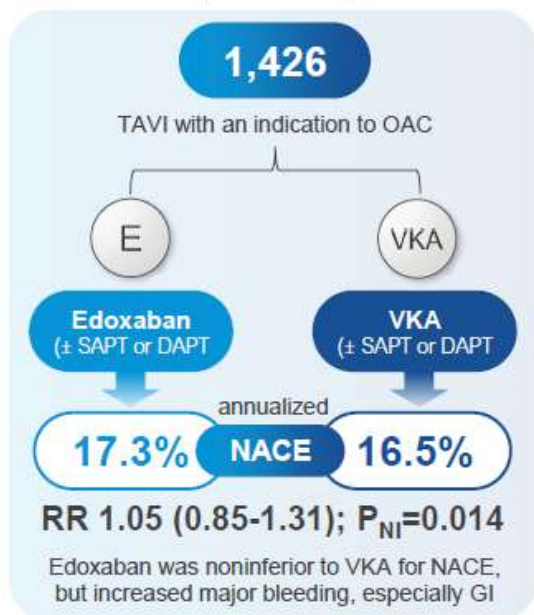
MULTICENTER, RANDOMIZED, OPEN LABEL



N Engl J Med. 2020;382:1696-1707

2 ENVISAGE TAVI AF

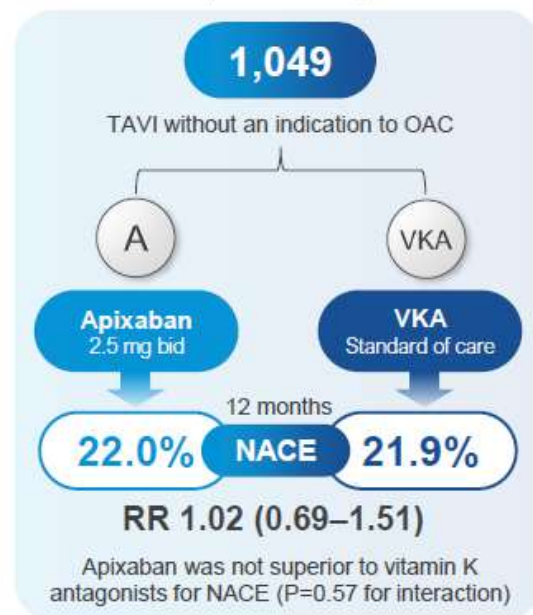
MULTICENTER, RANDOMIZED, OPEN LABEL



N Engl J Med. 2021;385:2150-2160

3 ATLANTIS (Stratum 1)

MULTICENTER, RANDOMIZED, OPEN LABEL



Eur Heart J. 2022;43:2783-2797

- ✓ OAC alone was associated with lower incidence of serious bleeding vs. OAC + Clopidogrel and was noninferior in terms of adverse ischemic outcomes.
- ✓ NOACs were similar to VKA for NACE. Edoxaban vs. VKA increased major bleeding (GI).



ORIGINAL RESEARCH ARTICLE

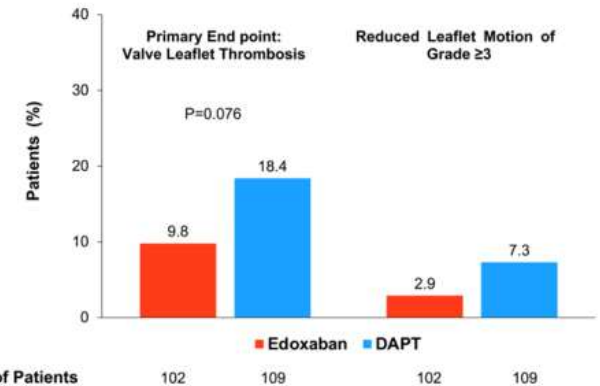
Edoxaban Versus Dual Antiplatelet Therapy for Leaflet Thrombosis and Cerebral Thromboembolism After TAVR: The ADAPT-TAVR Randomized Clinical Trial

Duk-Woo Park, MD; Jung-Min Ahn, MD; Do-Yoon Kang, MD; Kyung Won Kim, MD; Hyun Jung Koo, MD; Dong Hyun Yang, MD; Seung Chai Jung, MD; Byungjun Kim, MD; Yiu Tung Anthony Wong, MD; Cheung Chi Simon Lam, MD; Wei-Hsian Yin, MD; Jeng Wei, MD; Yung-Tsai Lee, MD; Hsien-Li Kao, MD; Mao-Shin Lin, MD; Tsung-Yu Ko, MD; Won-Jang Kim, MD; Se Hun Kang, MD; Sung-Cheol Yun, PhD; Seung-Ah Lee, MD; Euihong Ko, MD; Hanbit Park, MD; Dae-Hee Kim, MD; Joon-Won Kang, MD; Jae-Hong Lee, MD; Seung-Jung Park, MD; for the ADAPT-TAVR Investigators

Circulation. 2022;146:466–479. DOI: 10.1161/CIRCULATIONAHA.122



CT End Points, Intention-to-Treat Analysis



No. of Patients

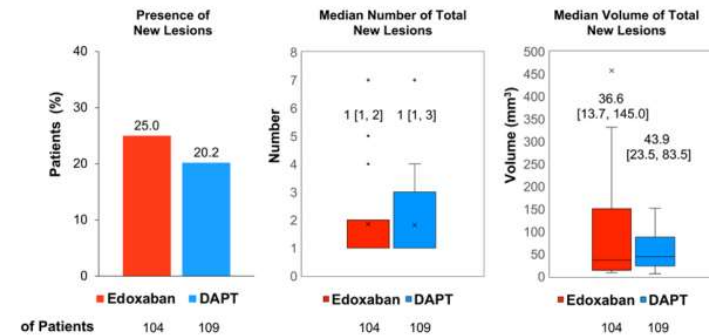
102

109

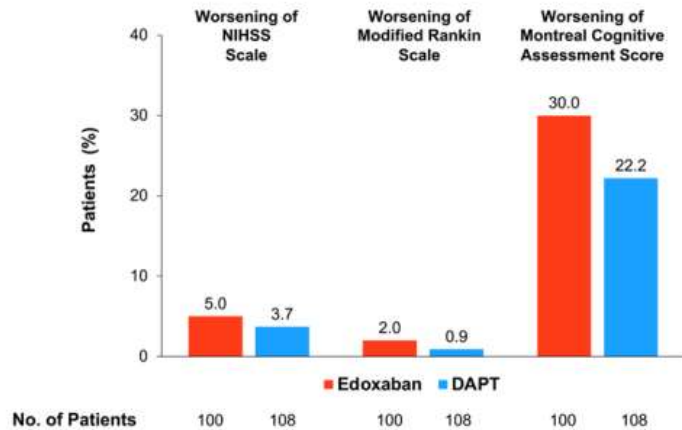
102

109

MRI End Points, Intention-to-Treat Analysis



Neurological or Neurocognitive Function End Points, Intention-to-Treat Analysis



In pts without an established indication for long-term anticoagulation after TAVR, there was a trend in favor of the edoxaban group compared with the DAPT group in the incidence of subclinical leaflet thrombosis on CT scans.

The effect on the reduction of leaflet thrombosis was not associated with a reduction of new cerebral lesions and a new development of neurological or neurocognitive dysfunction.



ESC

European Society
of Cardiology

European Heart Journal (2022) 43, 561–632

<https://doi.org/10.1093/eurheartj/ehab395>

ESC/EACTS GUIDELINES

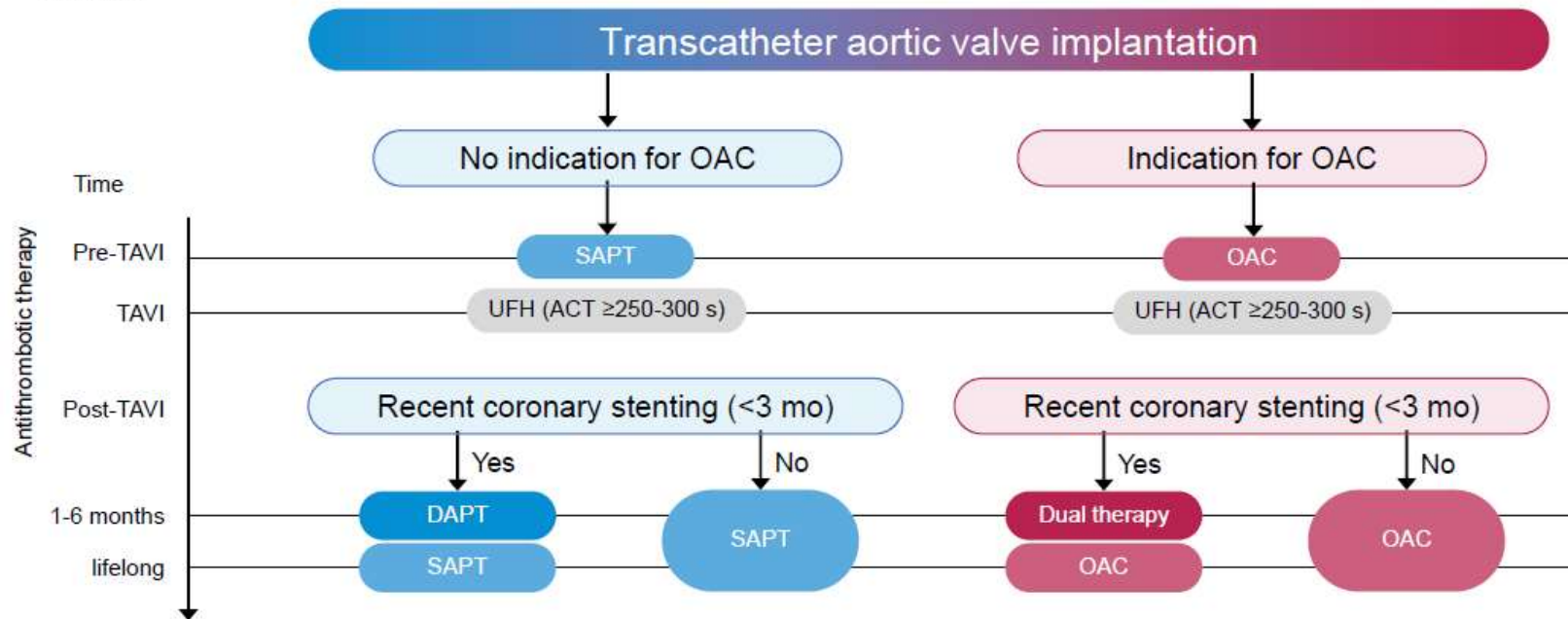


2021 ESC/EACTS Guidelines for the management of valvular heart disease

Recommendations	Class	Level
OAC is recommended lifelong for TAVI patients who have other indications for OAC	I	B
Lifelong SAPT is recommended after TAVI in patients with no baseline indication for OAC	I	A
Anticoagulation should be considered in patients with leaflet thickening and reduced leaflet motion leading to elevated gradients, at least until resolution	IIa	B
Routine use OAC is not recommended after TAVI in patients with no baseline indication for OAC	III	B



TAVI and PCI



Ten Berg J et al. Eur Heart J. 2021



Closing Remarks



- Even in low-risk patients, TAVI carries some risk of stroke and major or life-threatening bleeding, challenging the selection of antithrombotic therapy.
- In patients with no indication to OAC, current evidence supports that a SAPT is a safer strategy.
- In patients with baseline indication to OAC, the addition of SAPT/DAPT increase the risk of bleeding, with uncertain effects on efficacy.
- Despite some benefits in improving RLM and HALT, trial results raise the concerns over OAC approach in this setting of patients. Anyway, consider NOAC adjusted dose or VKA when there is evidence of subclinical prosthetic valve thrombosis and in Valve-in-Valve high risk procedure/small anatomy.
- An individualized strategy, balancing the expected benefits and harms is the key for the right management. We must integrate data from studies, trials, guidelines, recommendations and clinical judgment, to navigate the best strategy in the management of “each” patient undergoing TAVI.

A “tailored” approach in an individualized medicine era is the key for the management of patients undergoing TAVI.



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Thanks for the attention!

