

Meeting Nazionale ITACARE-P 2025

La Cardiologia Riabilitativa e Preventiva
come snodo fondamentale
della cura della persona con cardiopatia



CENTRO CONGRESSI FRENTANI
Roma, 21-22 novembre 2025



GESTIRE IL RISCHIO EMORRAGICO E TROMBOTICO NEL PAZIENTE CARDIOPATICO COMPLESSO IN RIABILITAZIONE

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ESC
European Society
of Cardiology

European Heart Journal (2025) 00, 1-102
<https://doi.org/10.1093/eurheartj/ehaf194>

ESC GUIDELINES

2025 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

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STRATIFICAZIONE DEL RISCHIO TROMBOTICO ED EMORRAGICO NEL PAZIENTE SOTTOPOSTO A CHIRURGIA/PROCEDURA VALVOLARE

TIPO DI INTERVENTO:

- Protesi meccaniche
- Protesi biologiche
- Riparazioni valvolari

TIPO DI APPROCCIO:

- Chirurgico
- Transcatetere

FATTORI AGGIUNTIVI

- Fibrillazione atriale
- Posizione della valvola
- Timing dall'intervento



STRATIFICAZIONE DEL RISCHIO TROMBOTICO ED EMORRAGICO NEL PAZIENTE SOTTOPOSTO A CHIRURGIA/PROCEDURA VALVOLARE

RISCHIO TROMBOTICO

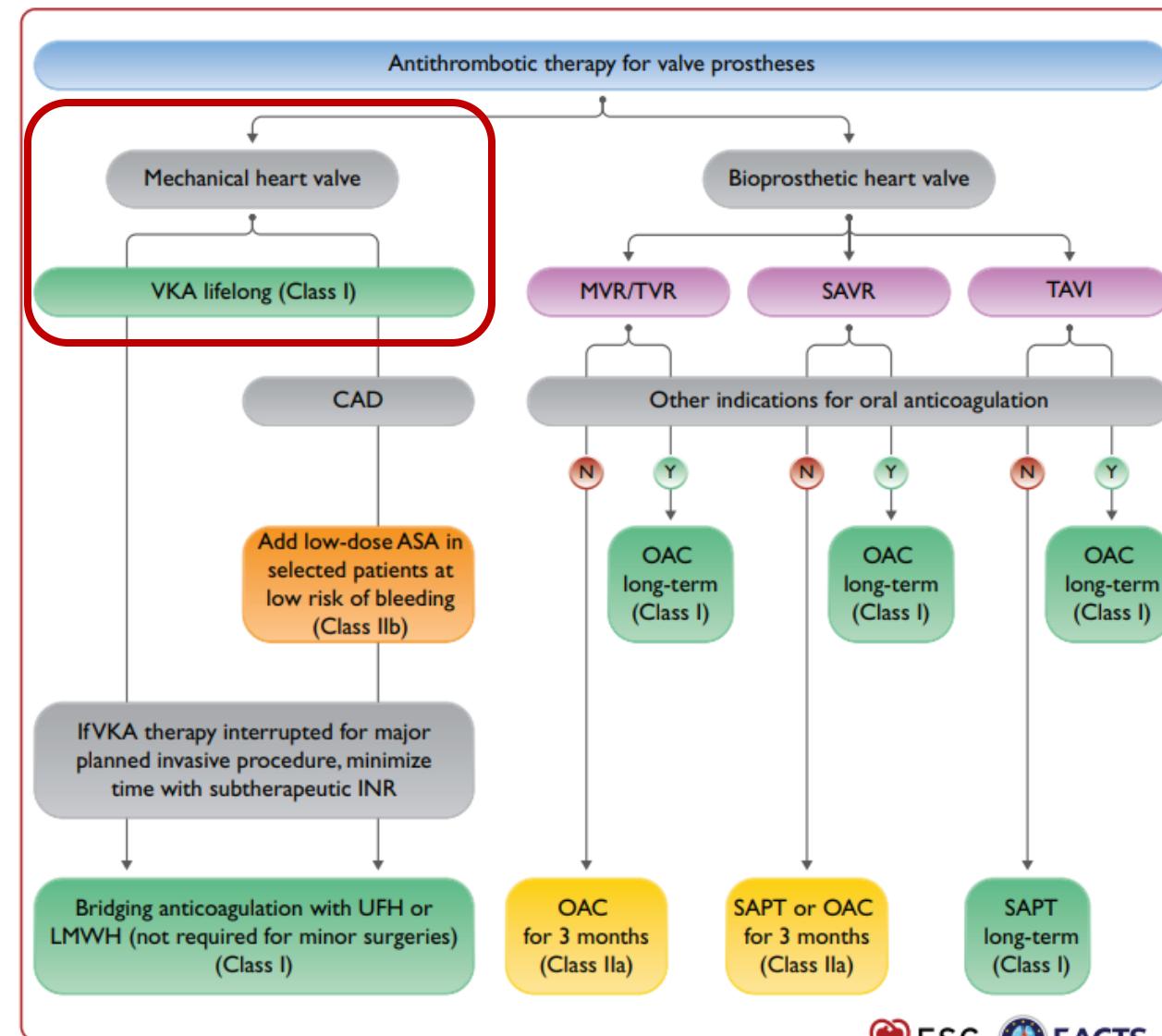
- Età > 65 anni
- Ipertensione arteriosa
- Alterata funzione renale
- Diabete mellito
- Pregresso ictus ischemico
- Malattia vascolare
- Scompenso cardiaco
- Immobilità prolungata
- Obesità
- Neoplasie
- Trombocitosi
- Terapie mediche (contraccettivi orali)
- Fattori genetici

RISCHIO EMORRAGICO

- Età > 65 anni
- Ipertensione arteriosa
- Alterata funzione renale
- Diabete mellito
- Alterata funzione epatica
- Stroke
- Pregressa emorragia
- INR labile
- Neoplasie
- Anemia, piastrinopenia
- Droghe/alcool
- Terapie mediche (antiaggreganti, FANS)
- Rischio eccessivo di caduta

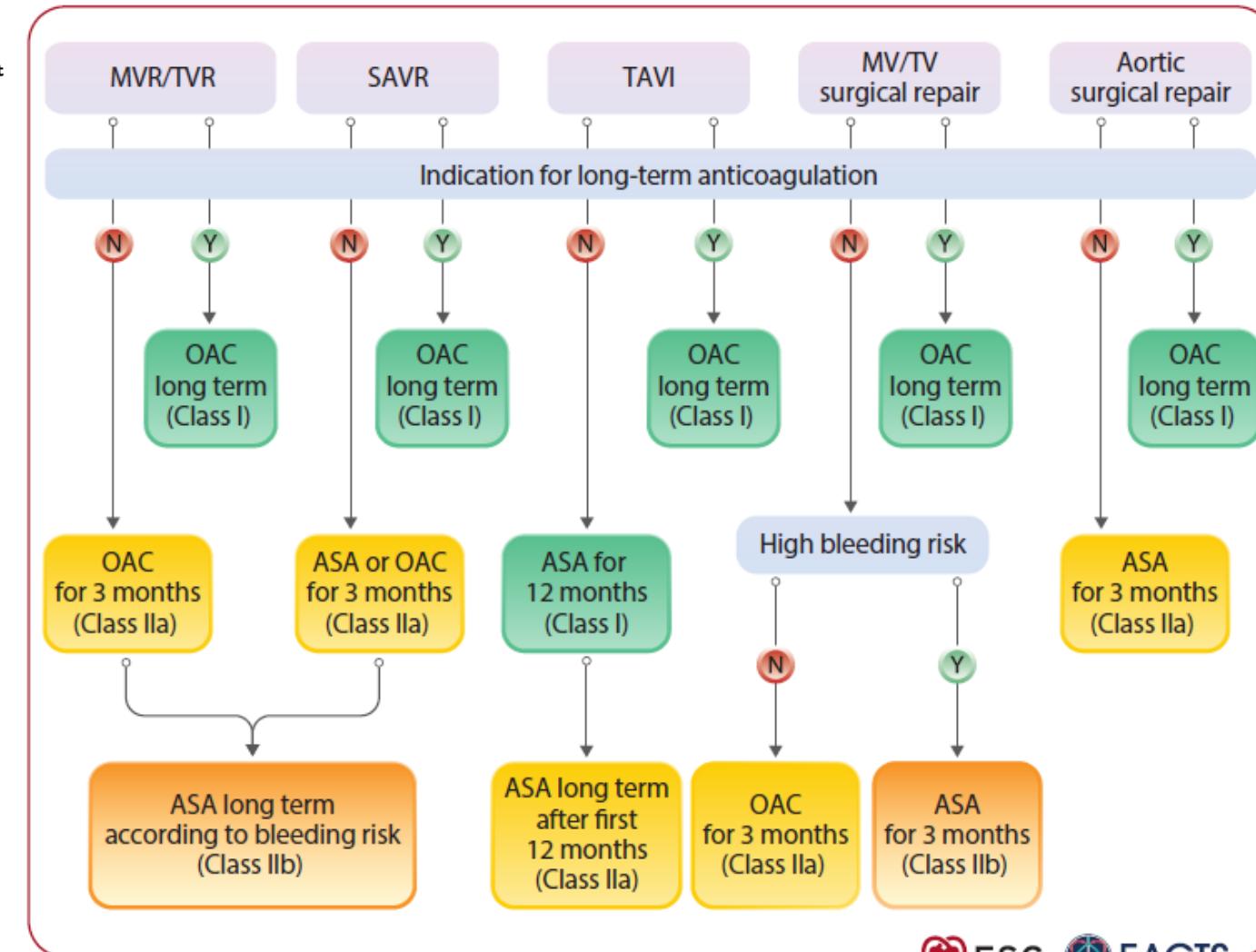
2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



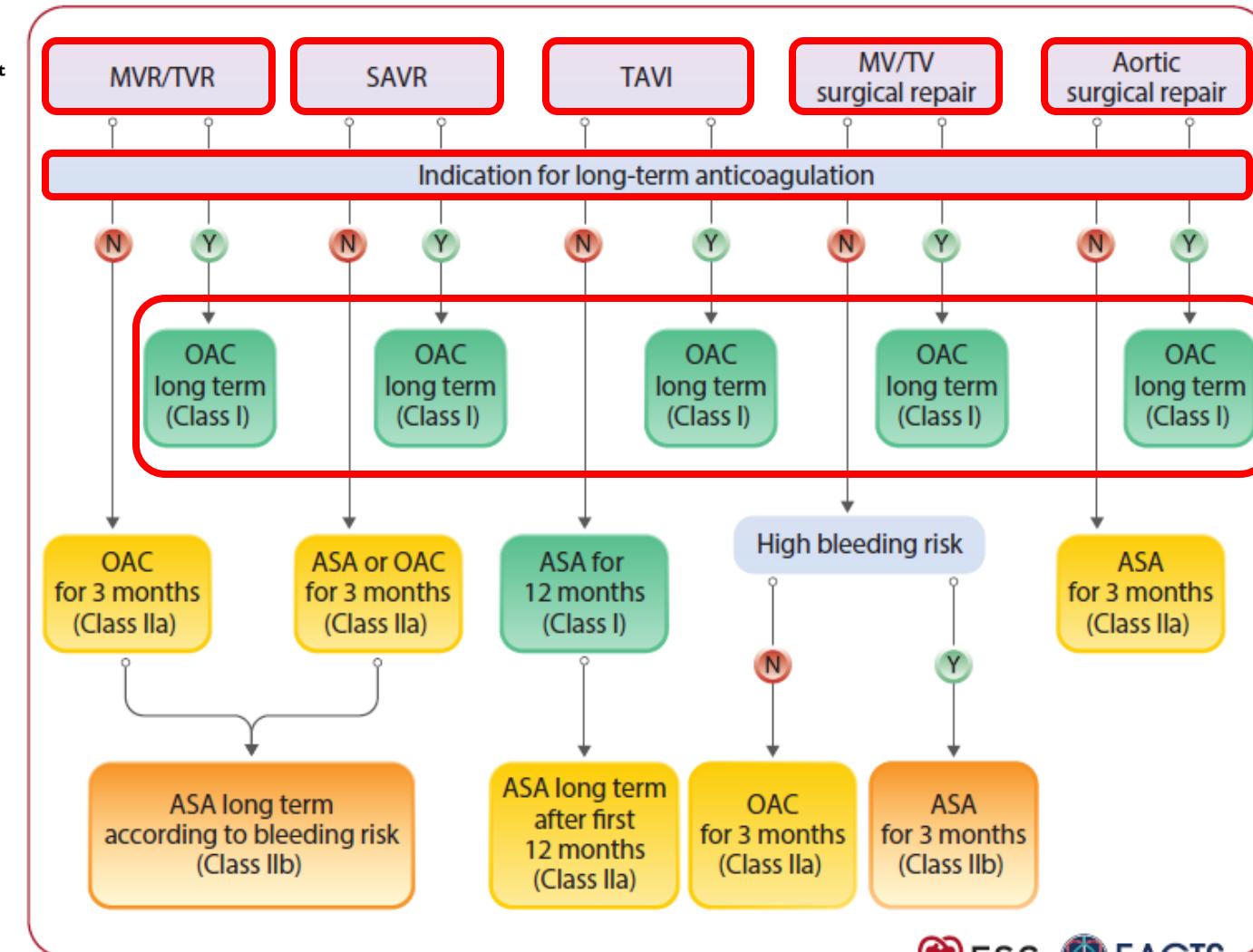
2025 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



2025 ESC/EACTS Guidelines for the management of valvular heart disease

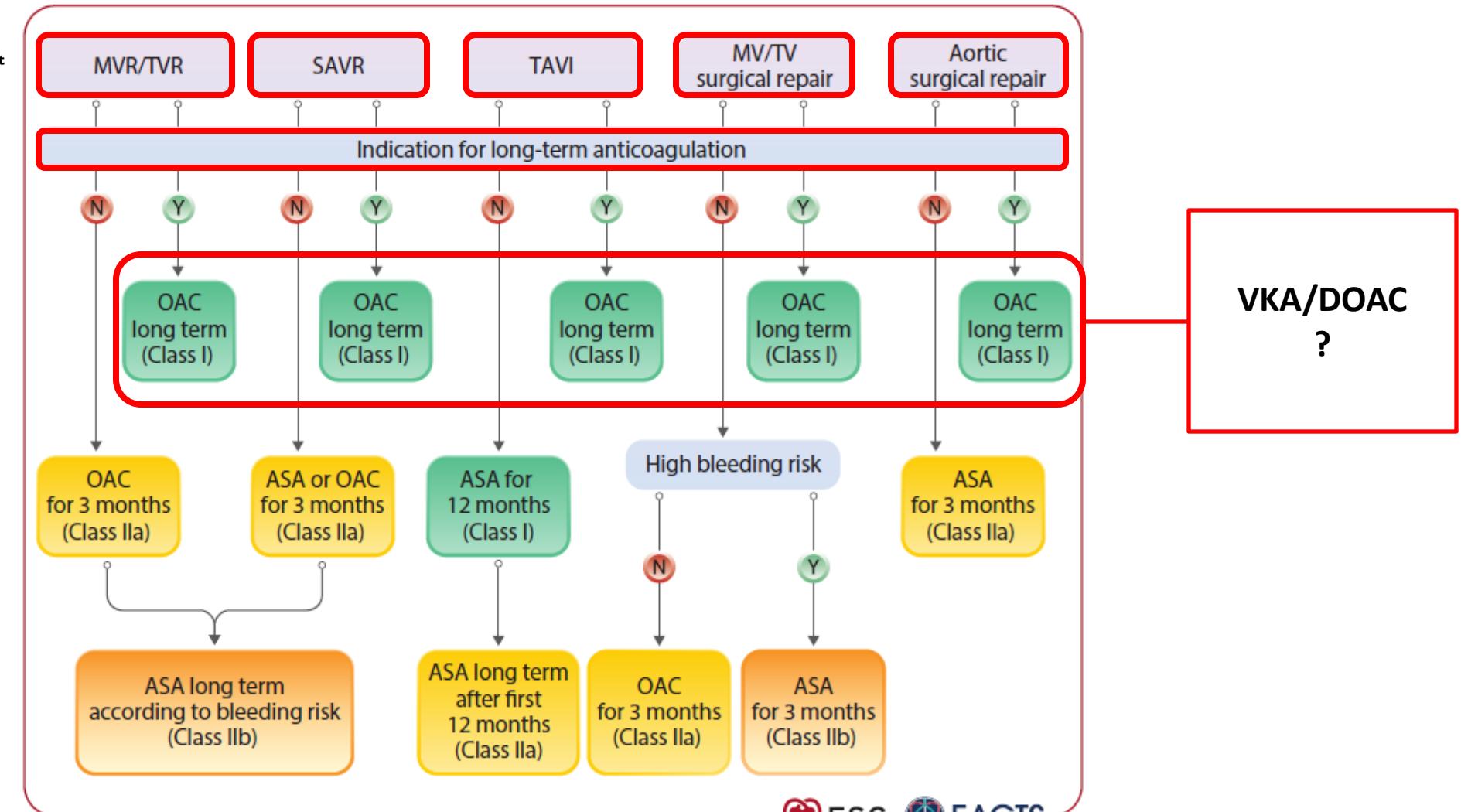
Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



In presenza di
fibrillazione
atriale...

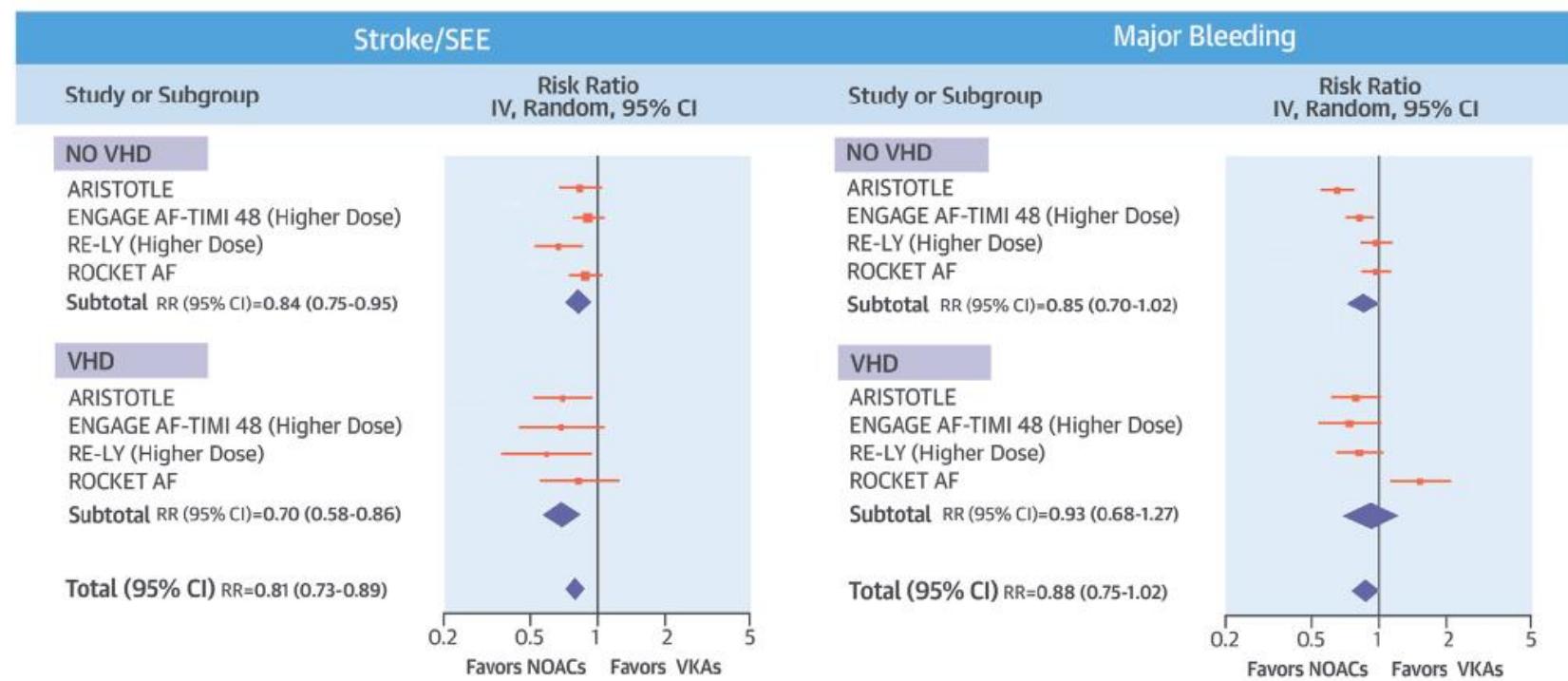
2025 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



Meta-analysis of clinical trials of DOACs versus warfarin in AF and VHD

CENTRAL ILLUSTRATION SSEE and Major Bleeding in Patients Without and With VHD, Treated With Higher-Dose NOACs or Warfarin

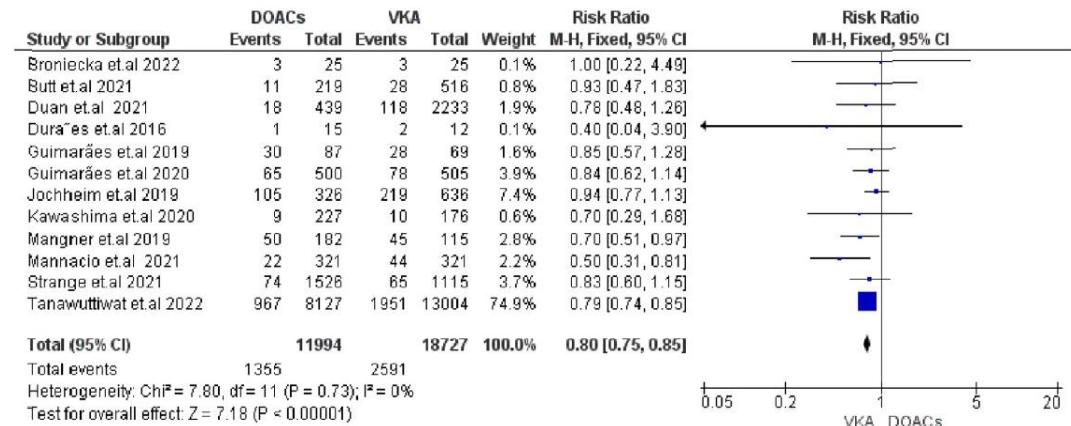


Renda, G. et al. J Am Coll Cardiol. 2017;69(11):1363-71.

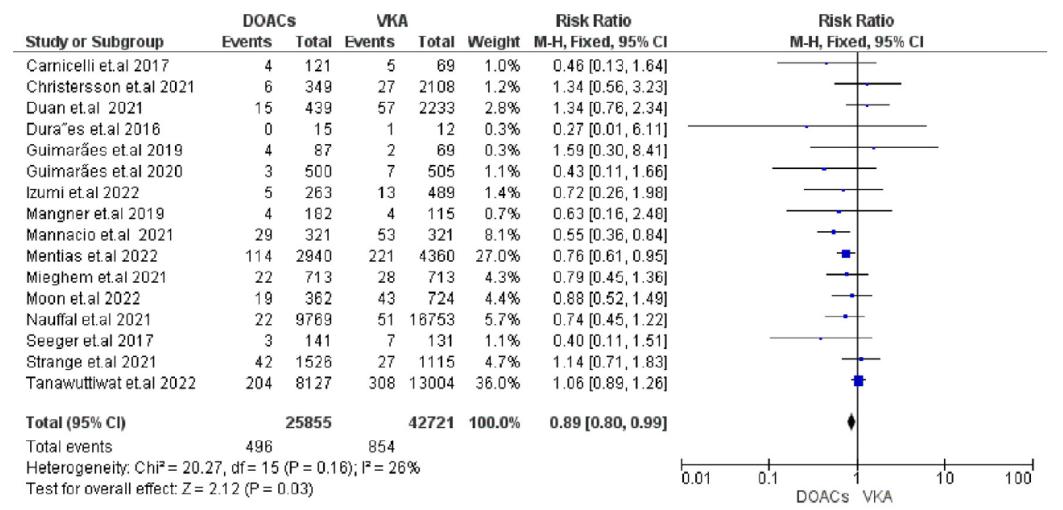


An Evidence-Based Approach to Anticoagulation Therapy Comparing Direct Oral Anticoagulants and Vitamin K Antagonists in Patients With Atrial Fibrillation and Bioprosthetic Valves: A Systematic Review, Meta-Analysis, and Network Meta-Analysis

Mustafa Suppah, MD^{a,*}, Abdallah Kamal, MD^b, Rakan Saadoun, MD^b, Ahmed M.A. Baradeiya, MD^c, Bishoy Abraham, MD^a, Said Alsidawi, MD^a, Dan Sorajja, MD^a, F. David Fortuin, MD^a, and Reza Arsanjani, MD^a



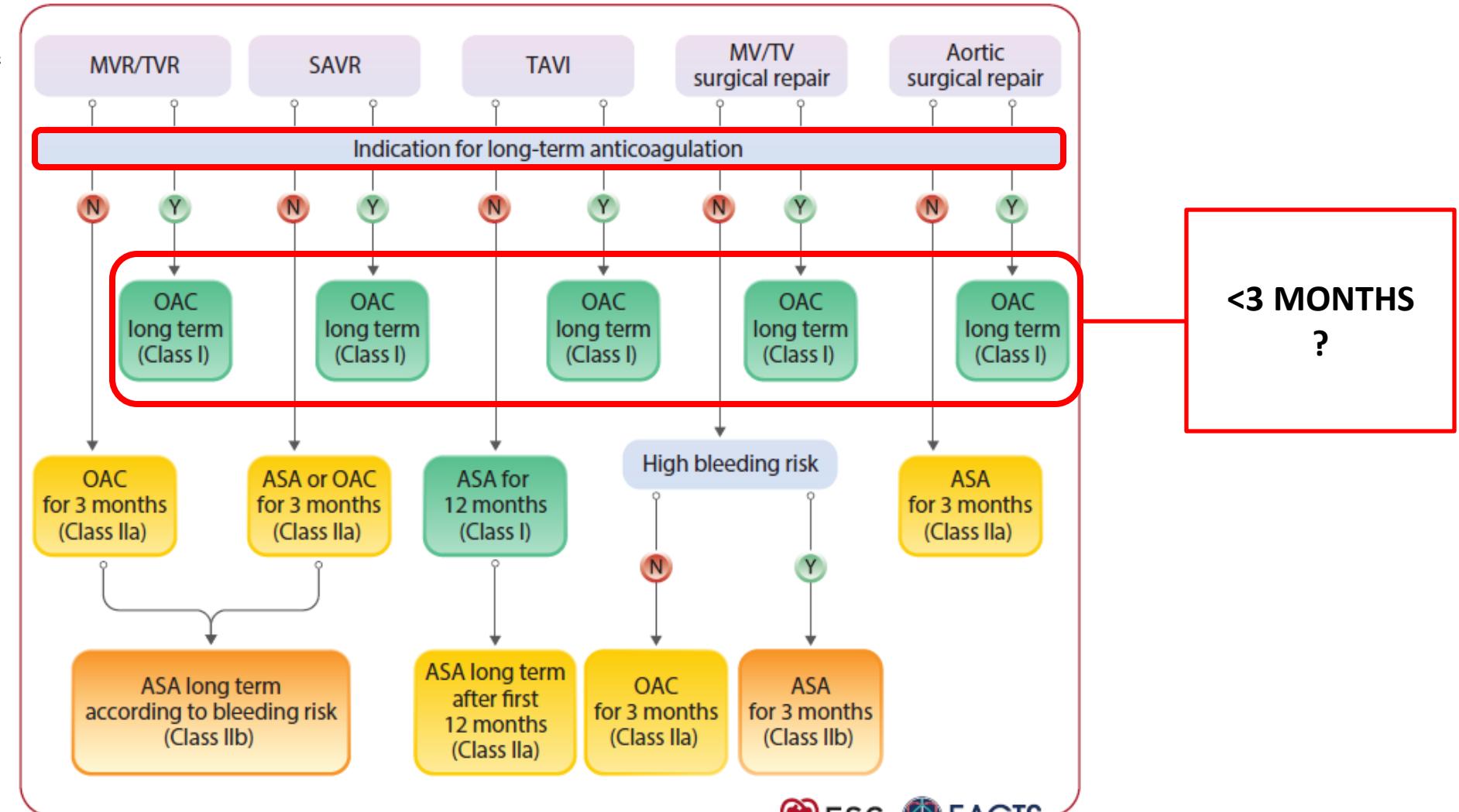
Forest plot of all-cause bleeding



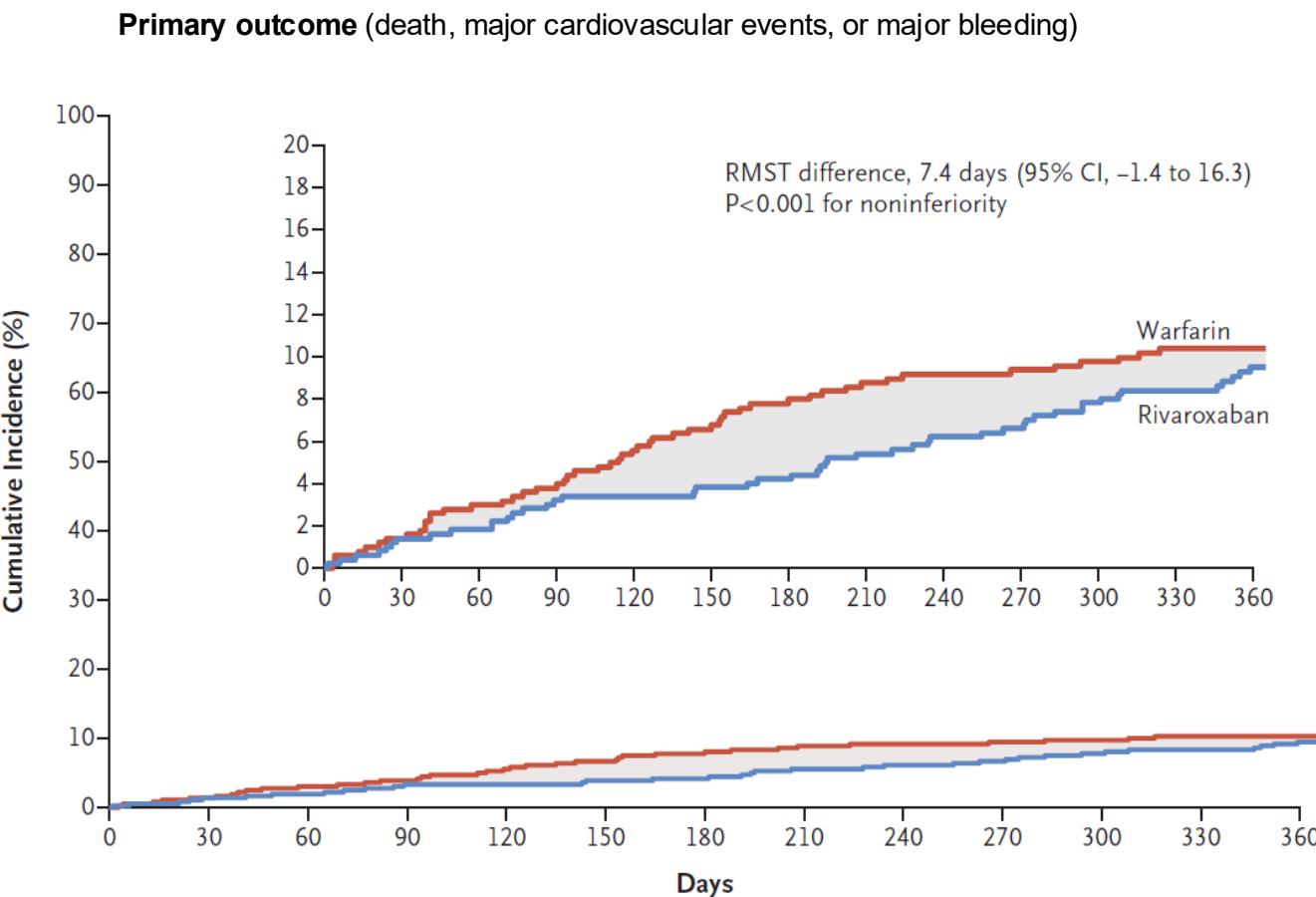
Forest plot of stroke and SE

2025 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



Rivaroxaban in patients with atrial fibrillation and a bioprosthetic mitral valve



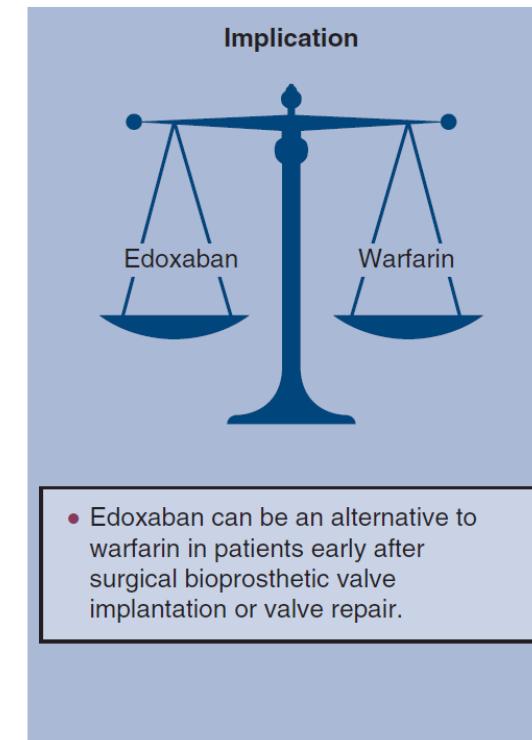
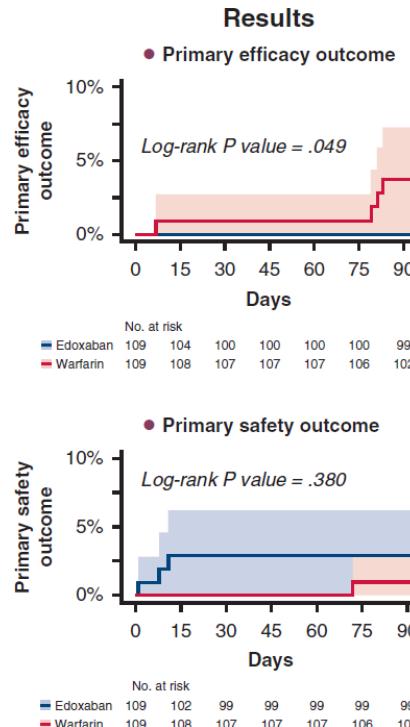
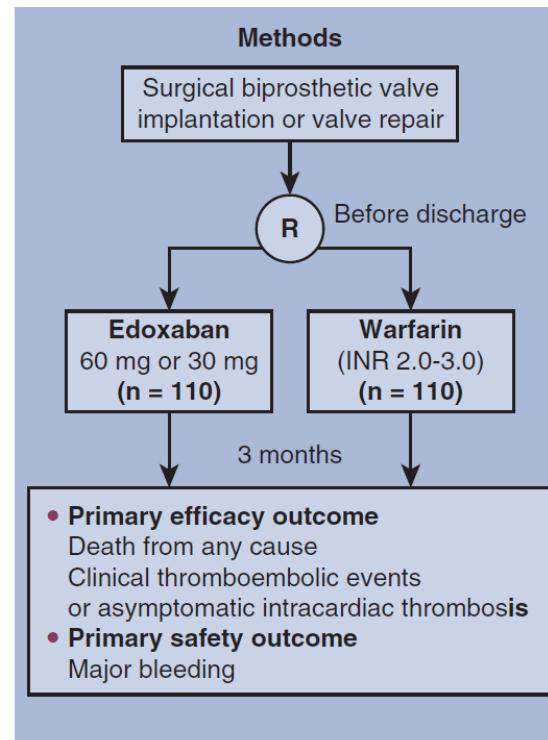
RIVER study

- 1005 pts
 - Biological mitral valve + AF
 - Eligible ≥ 48 hrs after surgery
- Note: 18.8% <3mos

Guimarães HP et al. *N Engl J Med* 2020;383:2117–26

Efficacy and safety of edoxaban in patients early after surgical bioprosthetic valve implantation or valve repair: a randomized clinical trial

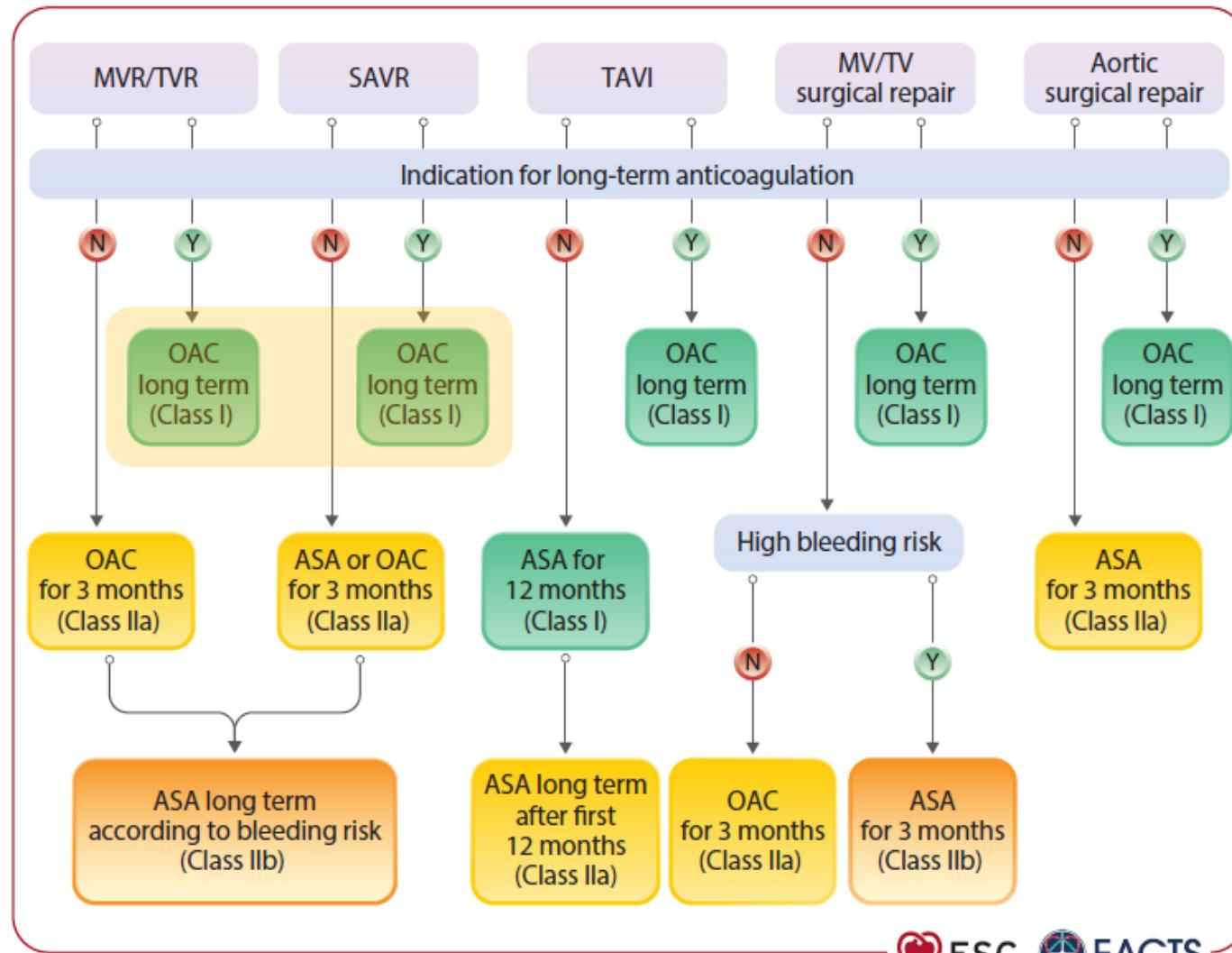
Edoxaban is Noninferior to Warfarin in the First 3 Months after Surgical Bioprosthetic Valve Implantation or Valve Repair



The ENAVLE study

- Prospective, randomized, open-label
- 218 pts randomly assigned to receive edoxaban 60/30mg OD vs warfarin for the first 3 mos after surgical bioprosthetic aortic or mitral valve implantation/mitral valve repair
- AF in 61% of cases

Shim CY et al. Efficacy and safety of edoxaban in patients early after surgical bioprosthetic valve implantation or valve repair: a randomized clinical trial. *J Thorac Cardiovasc Surg* 2023;165:58-67.e54



Surgical biological heart valve with indication for oral anticoagulation

OAC continuation is recommended in patients with a clear indication for OAC undergoing surgical BHV implantation.

| | |
|---|---|
| I | B |
|---|---|

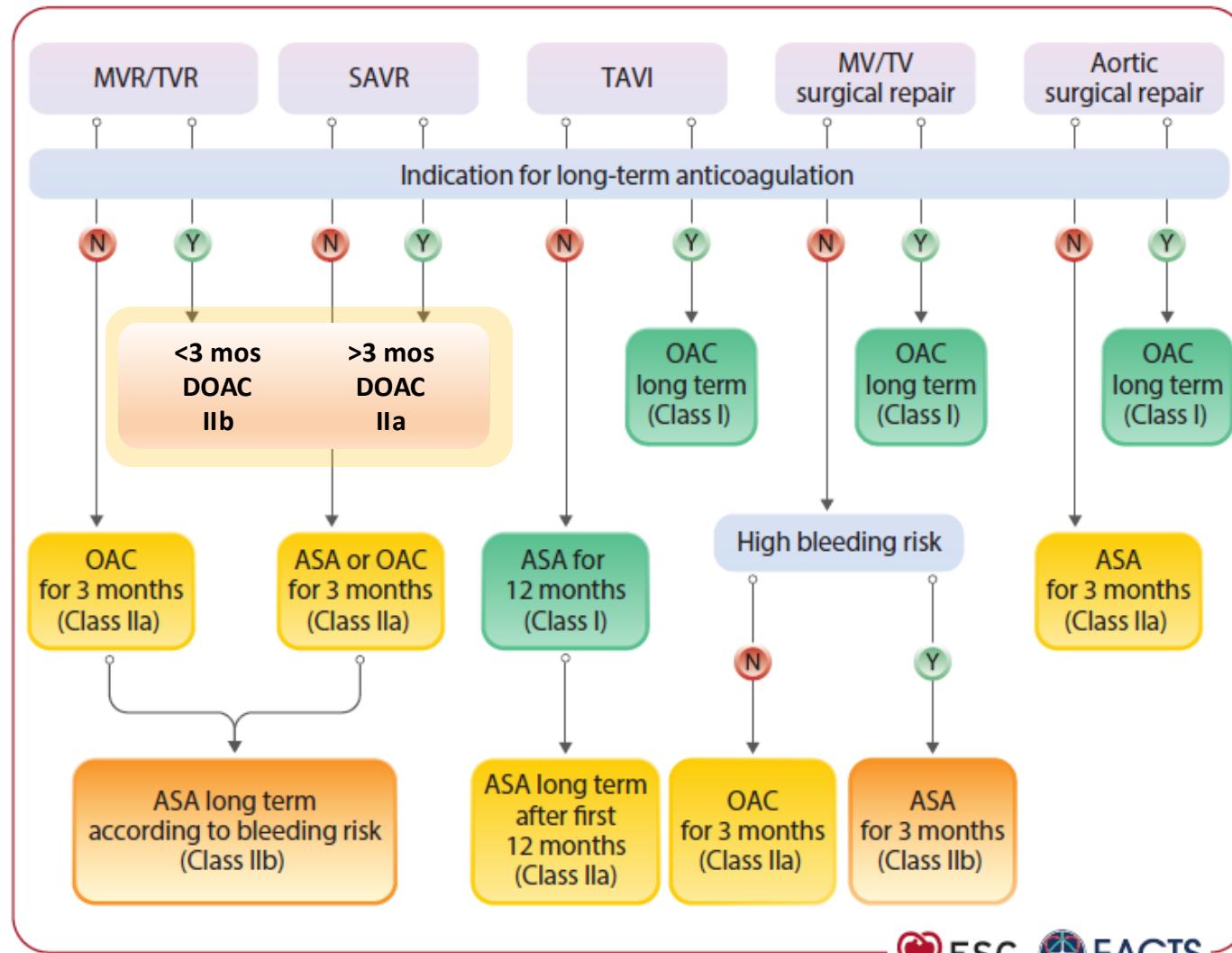
DOACs should be considered over VKAs after 3 months following surgical implantation of a BHV in patients with AF.

| | |
|-----|---|
| IIa | B |
|-----|---|

DOAC continuation may be considered after surgical BHV implantation in patients with an indication for DOAC.

| | |
|-----|---|
| IIb | B |
|-----|---|

A previously existing therapy with a DOAC may be continued after BHV implantation and should be restarted, as soon as considered surgically safe, usually within 2–3 days of surgery.



Surgical biological heart valve with indication for oral anticoagulation

OAC continuation is recommended in patients with a clear indication for OAC undergoing surgical BHV implantation.

| | |
|----------|----------|
| I | B |
|----------|----------|

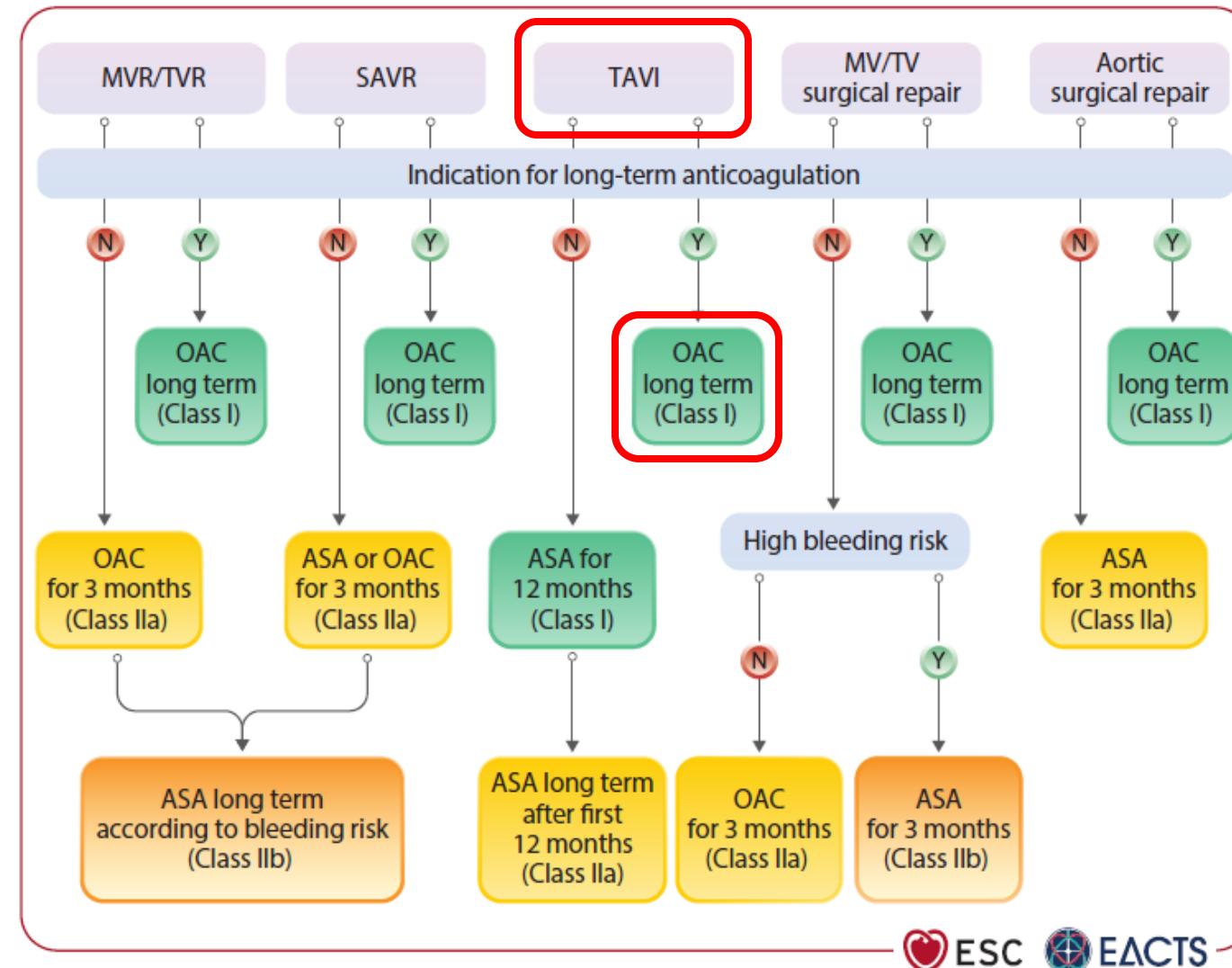
DOACs should be considered over VKAs after 3 months following surgical implantation of a BHV in patients with AF.

| | |
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| IIa | B |
|------------|----------|

DOAC continuation may be considered after surgical BHV implantation in patients with an indication for DOAC.

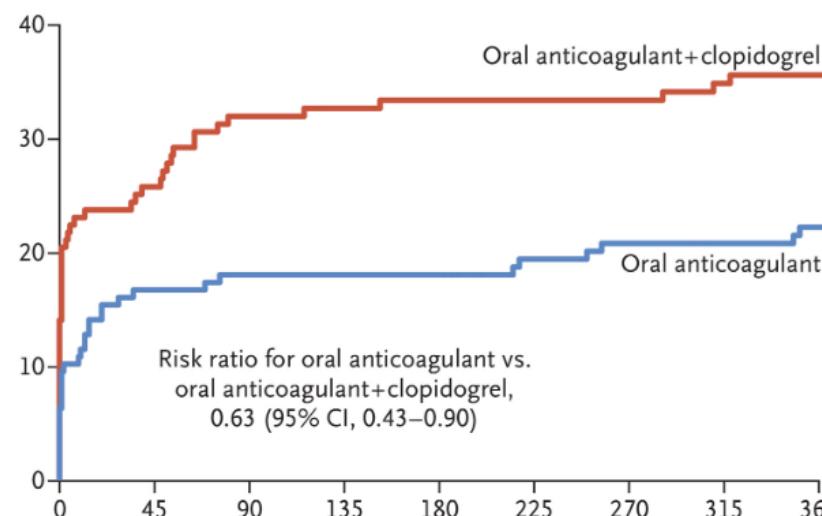
| | |
|------------|----------|
| IIb | B |
|------------|----------|

A previously existing therapy with a DOAC may be continued after BHV implantation and should be restarted, as soon as considered surgically safe, usually within 2–3 days of surgery.

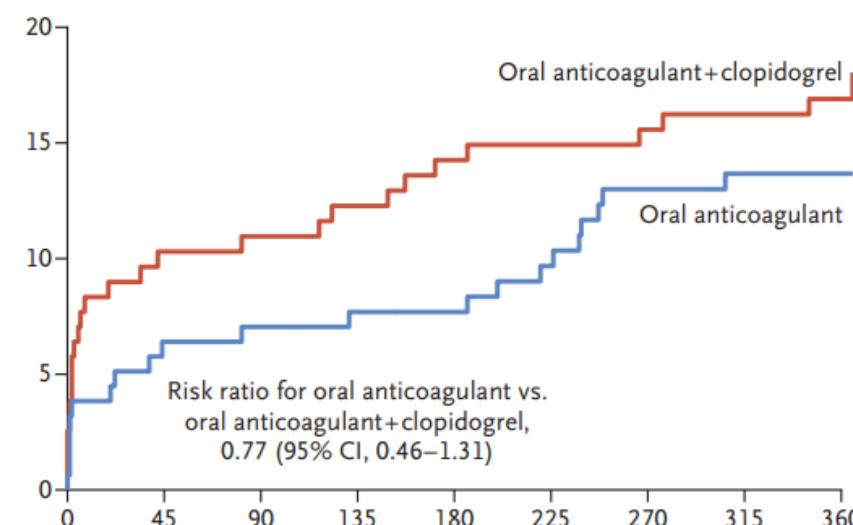


Anticoagulation with or without Clopidogrel after Transcatheter Aortic-Valve Implantation

Primary outcome of all bleeding

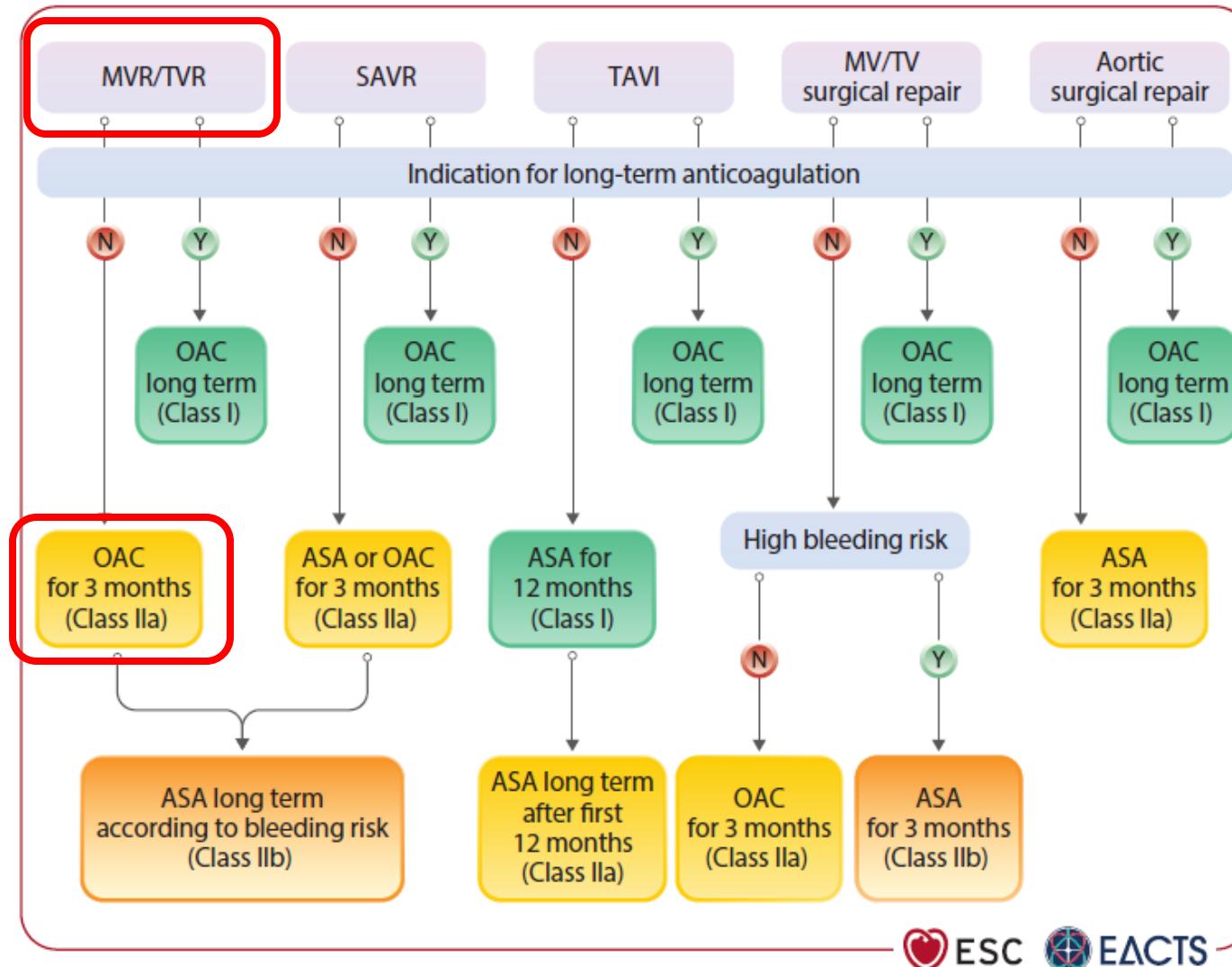


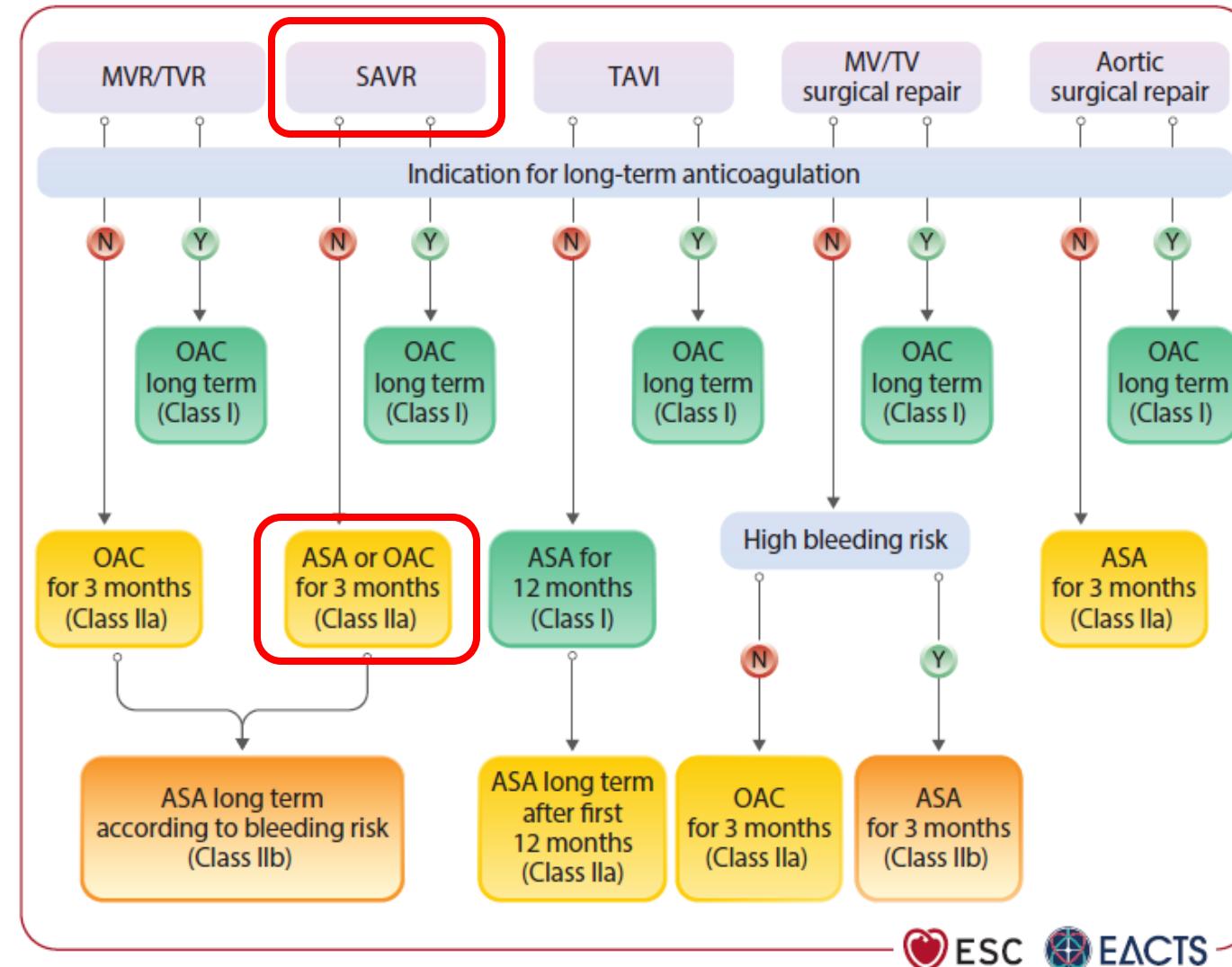
Cardiovascular death, ischemic stroke, MI



POPular TAVI trial cohort B

331 pts VKA/DOAC (AF 95%)
Randomization to
OAC vs OAC+clopidogrel







Antithrombotic therapy after bioprosthetic aortic valve implantation: Warfarin versus aspirin, a randomized controlled trial

Sulman Rafiq ¹, Daniel Andreas Steinbrüchel ², Nikolaj Bang Lilleør ³, Christian Holdflod Møller ⁴,
Jens Teglgaard Lund ⁵, Jens Juel Thiis ⁶, Lars Køber ⁷, Peter Skov Olsen ⁸

Abstract

Background: The optimal medical strategy for prevention of thromboembolic events after surgical bioprosthetic aortic valve replacement (BAVR) is still debated. The objective of this study was to compare warfarin therapy (target INR of 2.0 to 3.0) with aspirin 150mg daily as antithrombotic therapy for the first three months after BAVR with or without concomitant coronary artery bypass grafting (CABG). The aim was to evaluate thromboembolic complications, major bleeding complications and death.

Materials and methods: Prospective, single-centre, open-label, randomized controlled trial. 370 patients were enrolled, 328 were available for data analysis.

Results: At baseline the warfarin and aspirin groups were comparable. Thromboembolic events were comparable between groups 11 (6.6%) vs. 12 (7.5%), $p=0.83$. Major bleeding events occurred numerically more often in warfarin patients 9 (5.4%) vs. 3 (1.9%), $p=0.14$. Warfarin was in multivariate analysis significantly associated with major bleeding OR 5.18 (CI 1.06-25.43), $p=0.043$. 90-day mortality was comparable between groups 8 (4.7%) vs. 6 (3.7%), $p=0.79$.

Conclusions: Our results suggest that aspirin might be equally effective as warfarin in preventing thromboembolic events after BAVR, but with less major bleedings. Although this is numerically the largest trial testing this hypothesis in a prospective randomized trial, further adequately powered studies are warranted.



Antithrombotic Treatment After Surgical and Transcatheter Heart Valve Repair and Replacement

Andreas Verstraete^{1*}, Marie Christine Herregods¹, Peter Verbrugge², Marie Lamberigts², Thomas Vanassche¹, Bart Meyns², Wouter Oosterlinck², Filip Rega², Tom Adriaenssens¹, Lucas Van Hoof², Siegmund Keuleers¹, Christophe Vandenbriele¹, Peter Sirnæve¹, Stefan Janssens¹, Christophe Dubois¹, Bart Meuris² and Peter Verhamme¹

¹ Department of Cardiovascular Diseases, University Hospitals Leuven, Leuven, Belgium, ² Department of Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium

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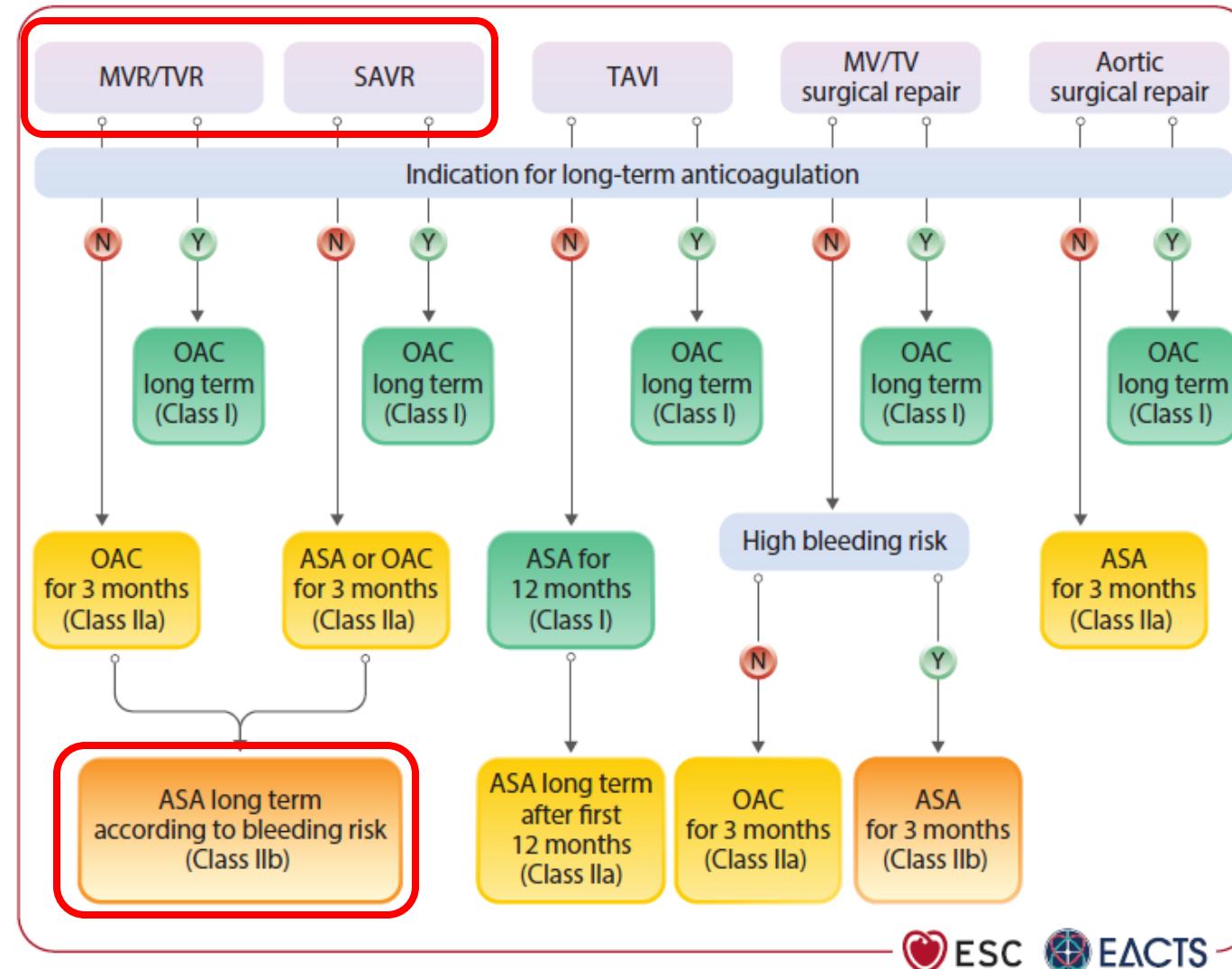
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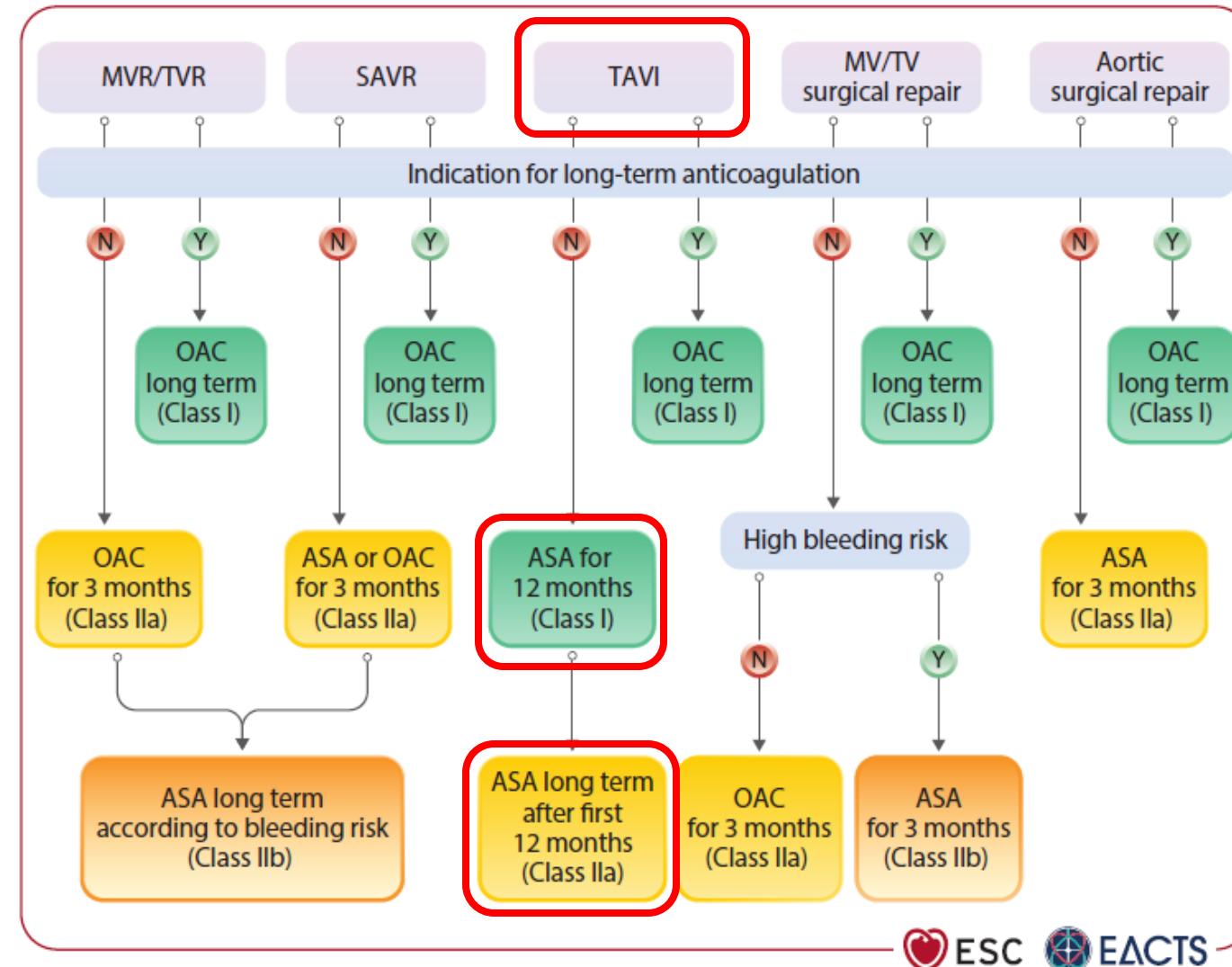
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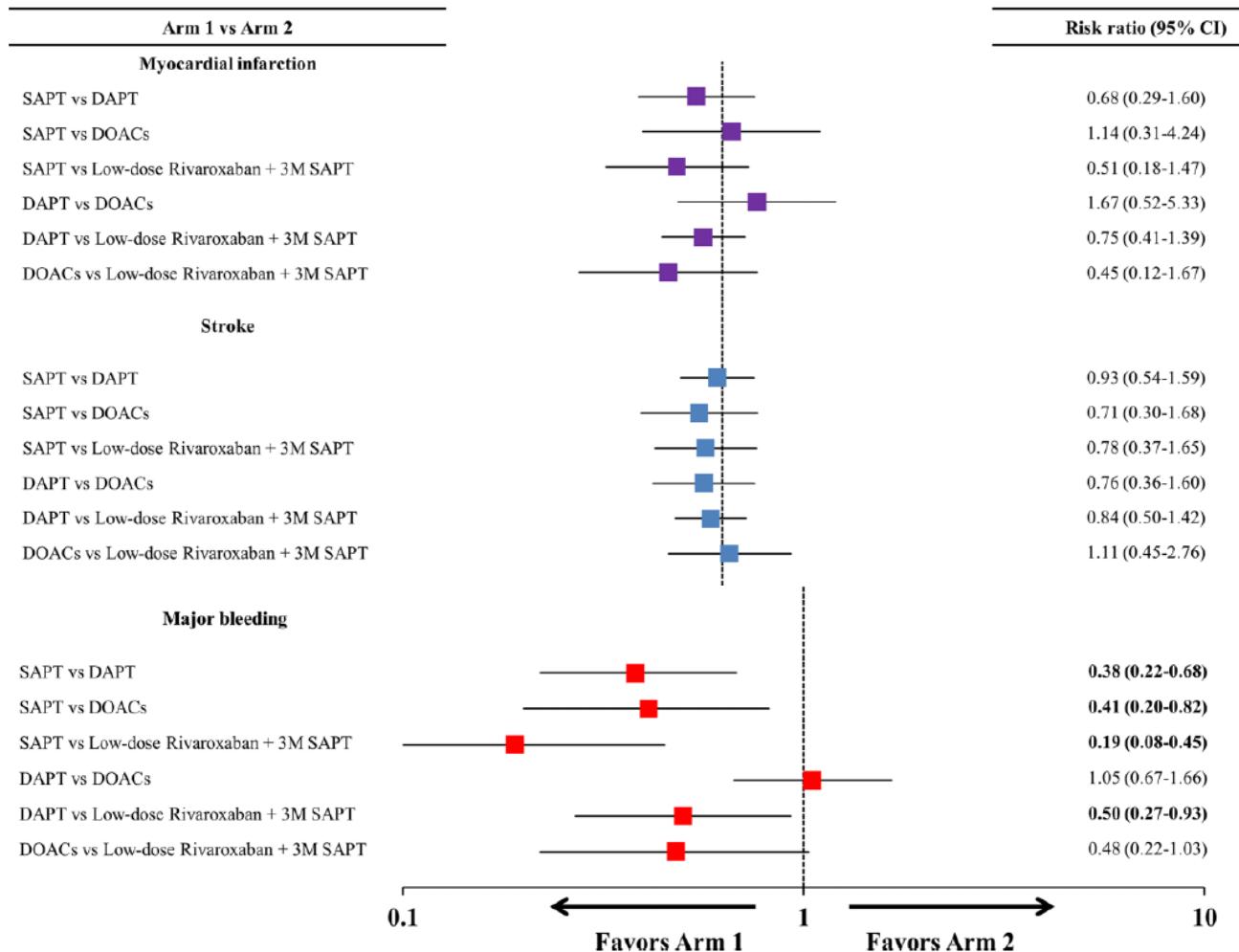
New antithrombotic drugs have been developed, new valve types have been designed and minimally invasive transcatheter techniques have emerged, making the choice of antithrombotic therapy after surgical or transcatheter heart valve repair and replacement increasingly complex. Moreover, due to a lack of large randomized controlled trials many recommendations for antithrombotic therapy are based on expert opinion, reflected by divergent recommendations in current guidelines. Therefore, decision-making in clinical practice regarding antithrombotic therapy for prosthetic heart valves is difficult, potentially resulting in sub-optimal patient treatment. This article compares the 2017 ESC/EACTS and 2020 ACC/AHA guidelines on the management of valvular heart disease and summarizes the available evidence. Finally, we established a convenient consensus on antithrombotic therapy after valve interventions based on over 800 annual cases of surgical and transcatheter heart valve repair and replacement and a multidisciplinary team discussion between the department of cardiovascular diseases and cardiac surgery of the University Hospitals Leuven, Belgium.

... in the late phase, from 3 to 6 months after surgery, there is controversy about the need for lifelong low-dose aspirin...

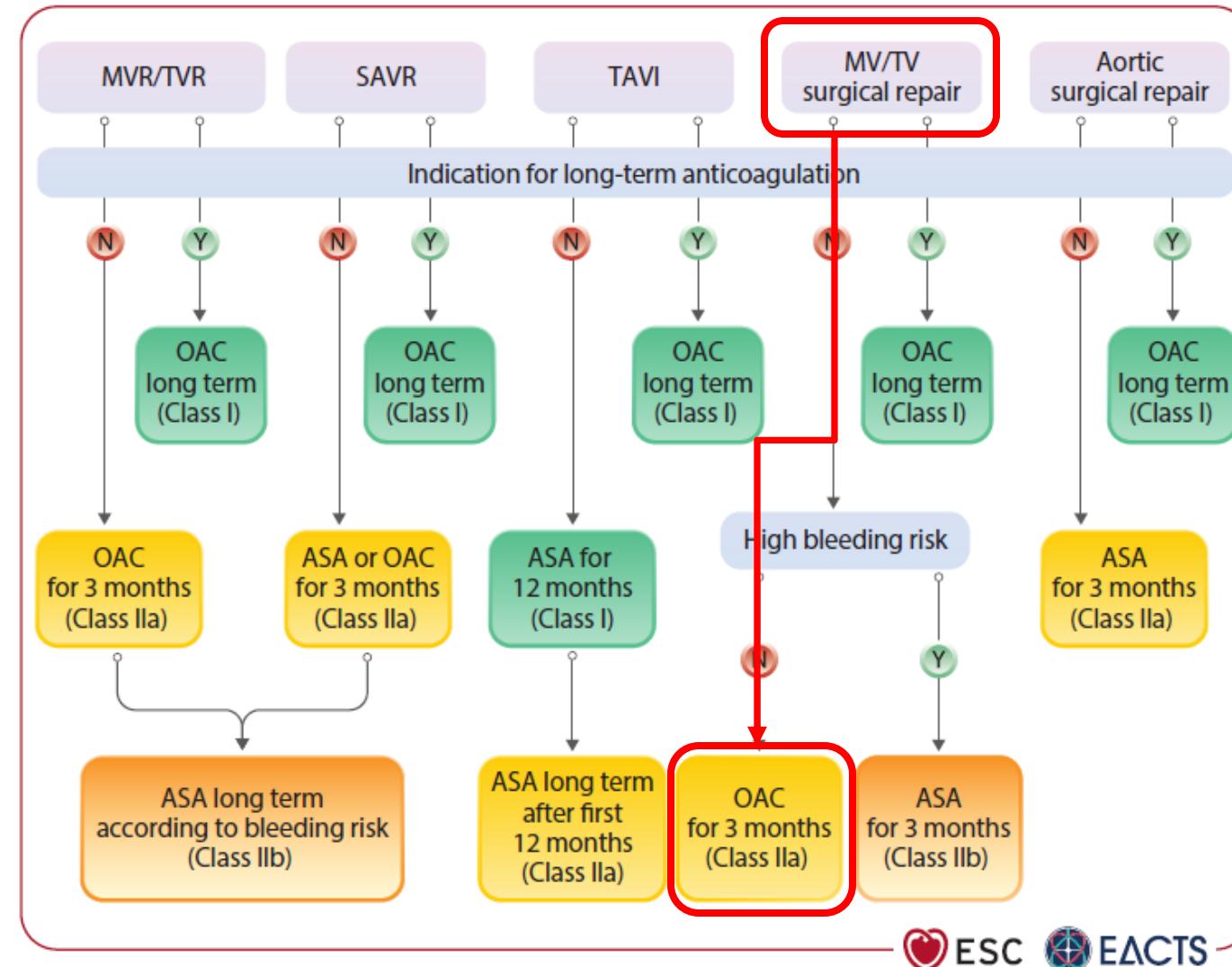




Antithrombotic therapy and cardiovascular outcomes after TAVI in patients without indications for chronic oral anticoagulation: a systematic review and network meta-analysis of randomized controlled trials



Following TAVI in patients without an indication for chronic oral anticoagulant, SAPT more than halved the risk of bleeding compared with DAPT and direct oral anticoagulant-based regimens without significant ischaemic offset.



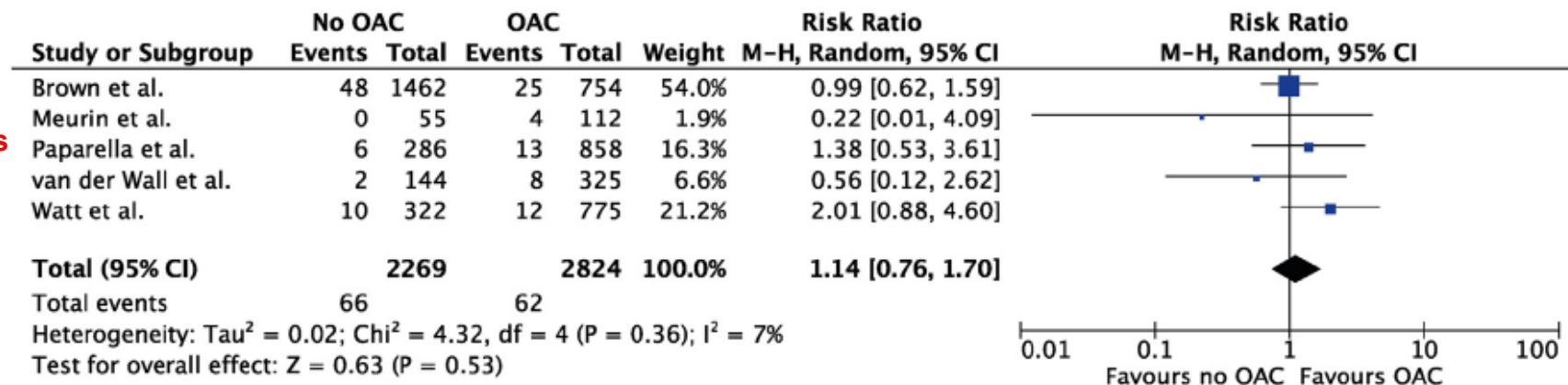
Oral Anticoagulation Versus Antiplatelet Treatment After Mitral Valve Repair: A Systematic Review and Meta-Analysis

Metanalisi 5 studi (5093 pts)

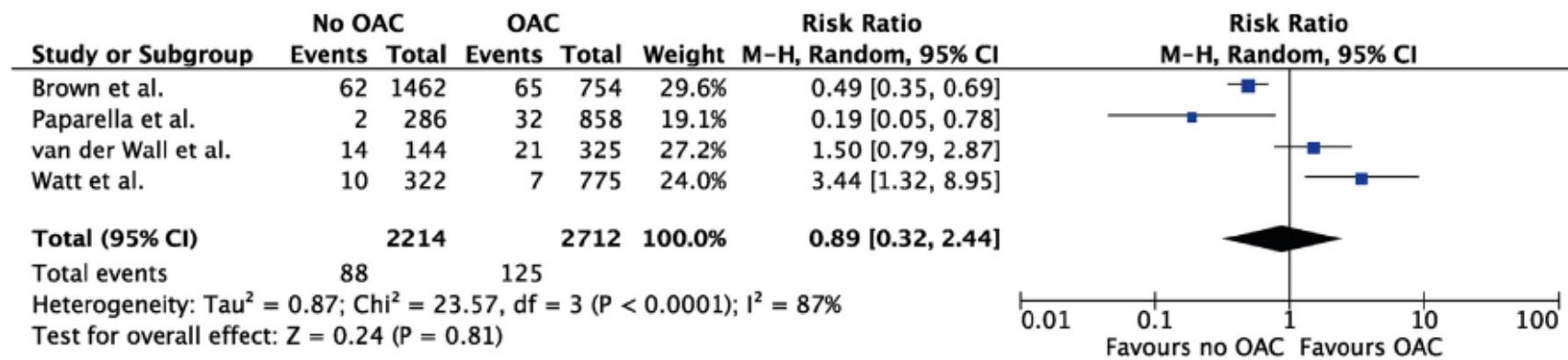
Anton Tomšič, MD, PhD^{a,*}, Chengji Zhao, BSc^a, Jan W. Schoones, MA^b,

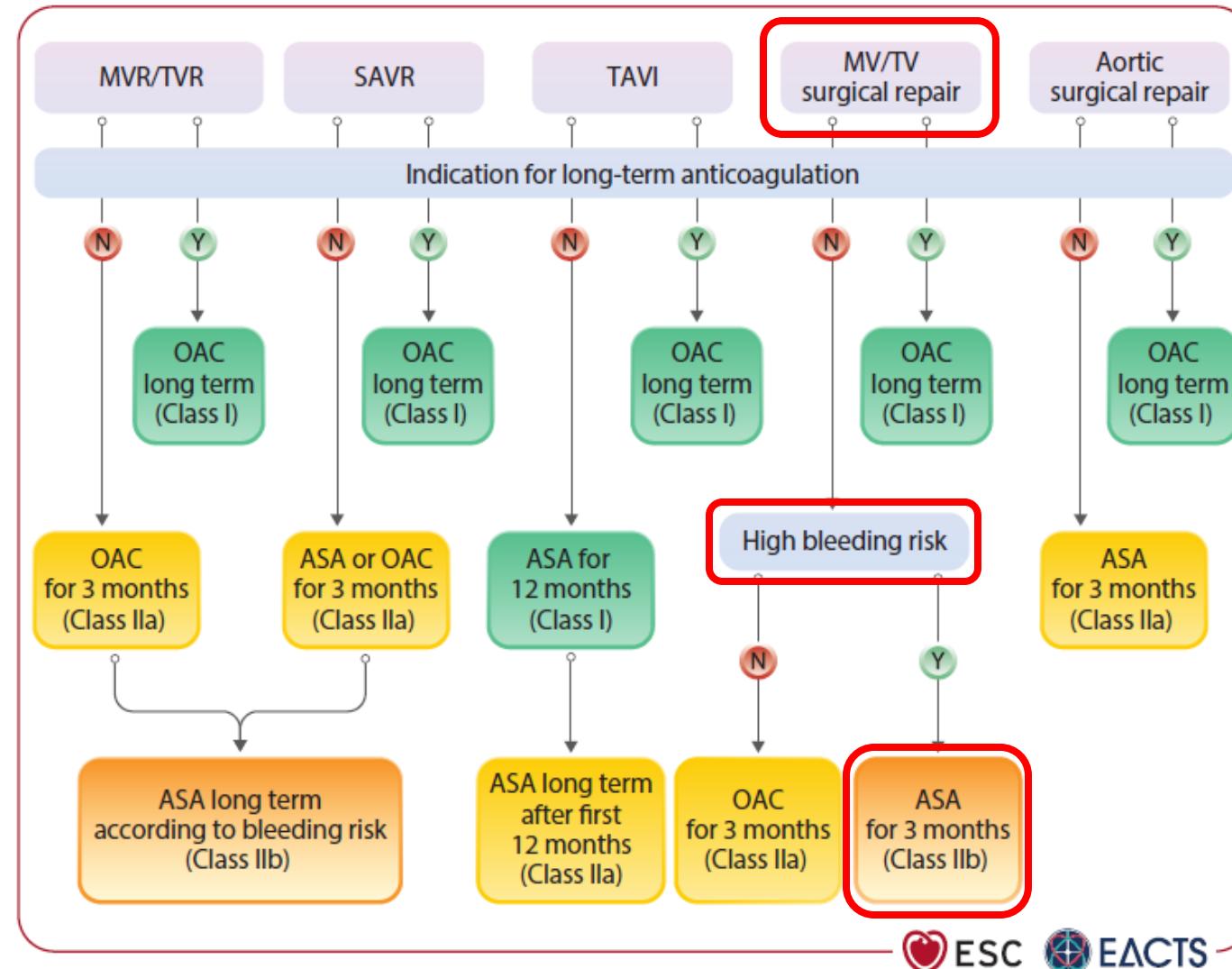
Robert J.M. Klautz, MD, PhD^a, and Meindert Palmen, MD, PhD^a

Thromboembolic complications



Bleeding complications







Clinical Therapeutics 46 (2024) 122–133



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journal homepage: www.elsevier.com/locate/clinthera



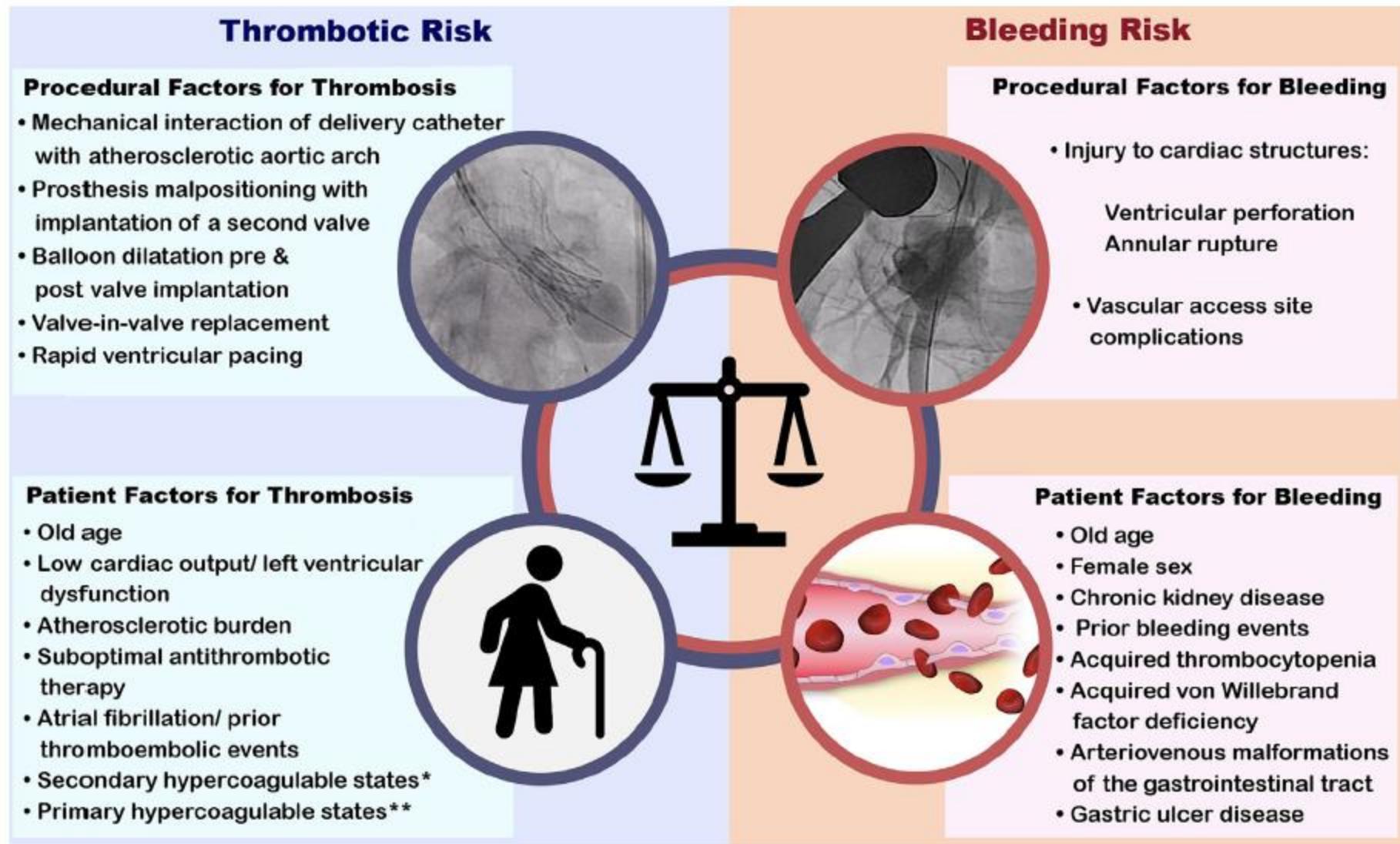
Review

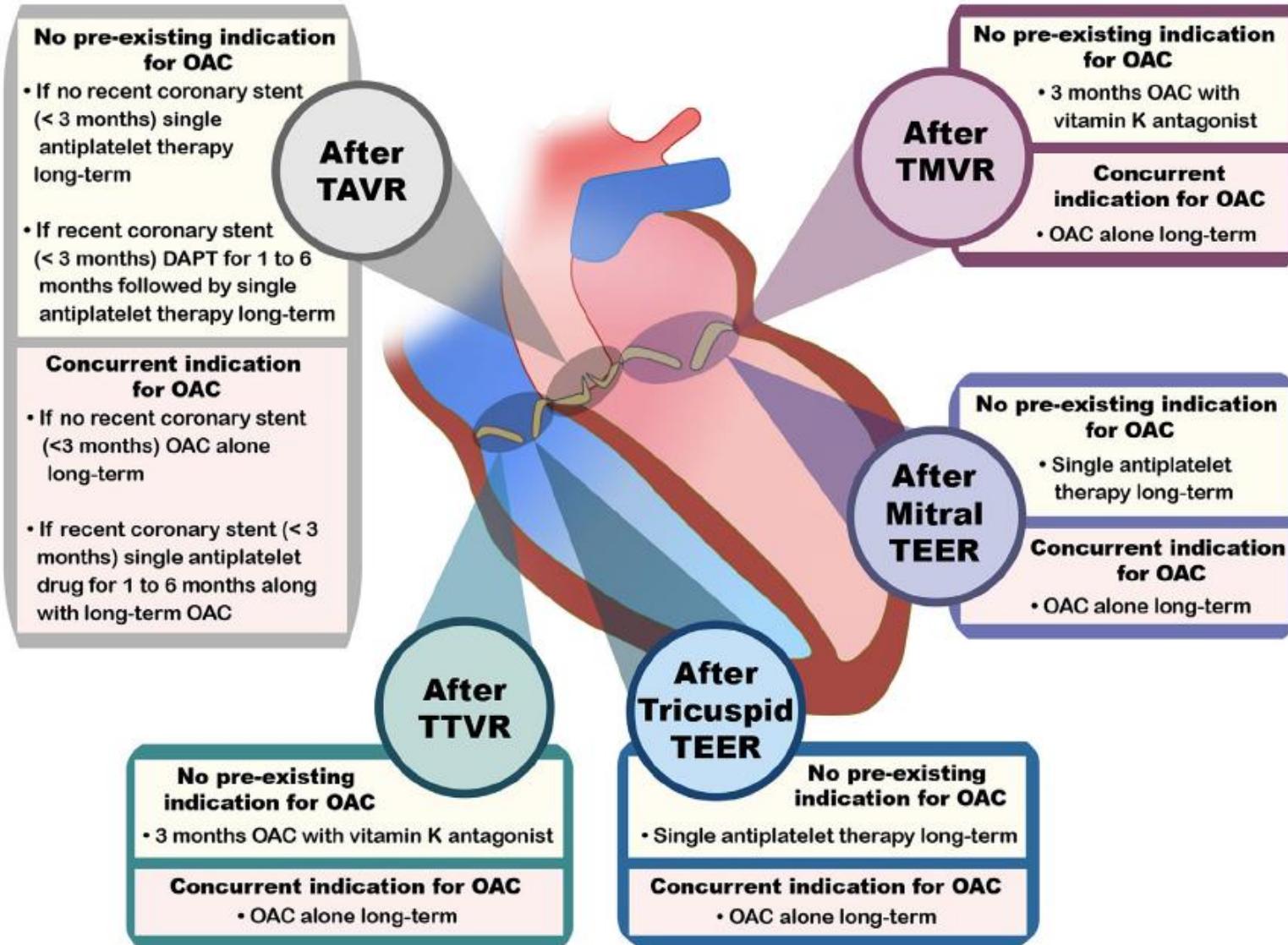
Antithrombotic Treatment After Transcatheter Valve Interventions: Current Status and Future Directions

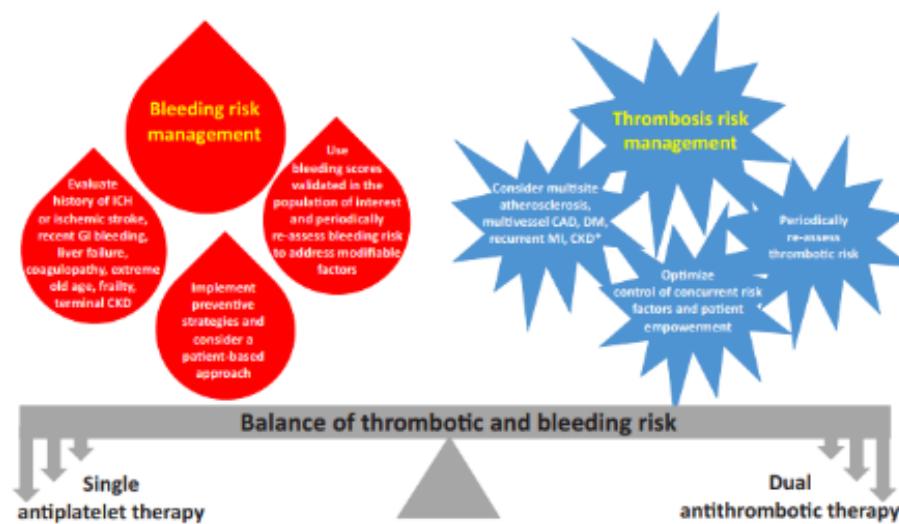
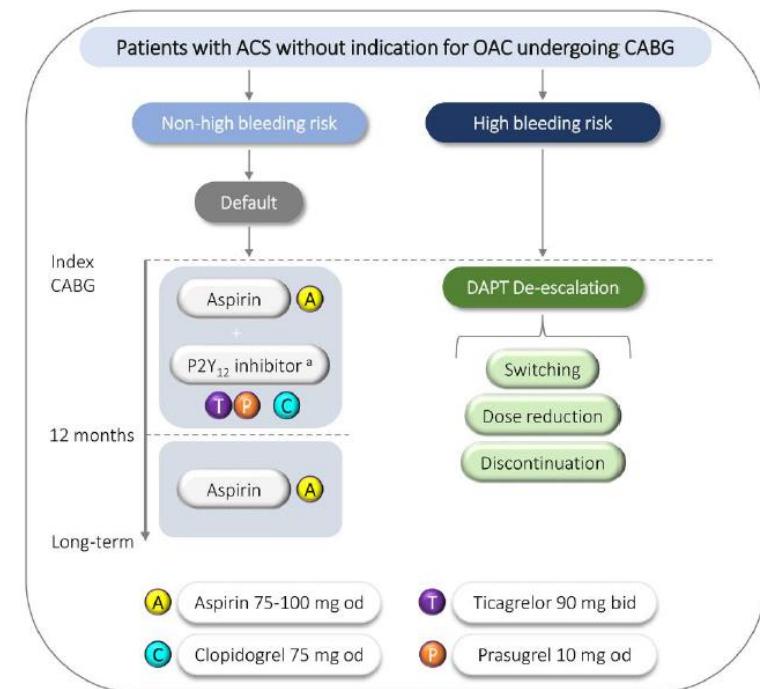
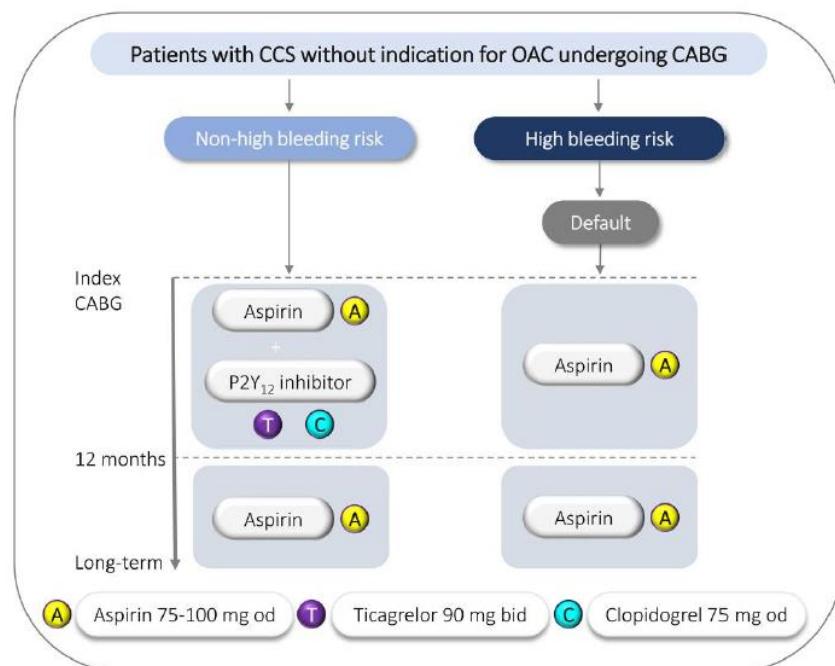


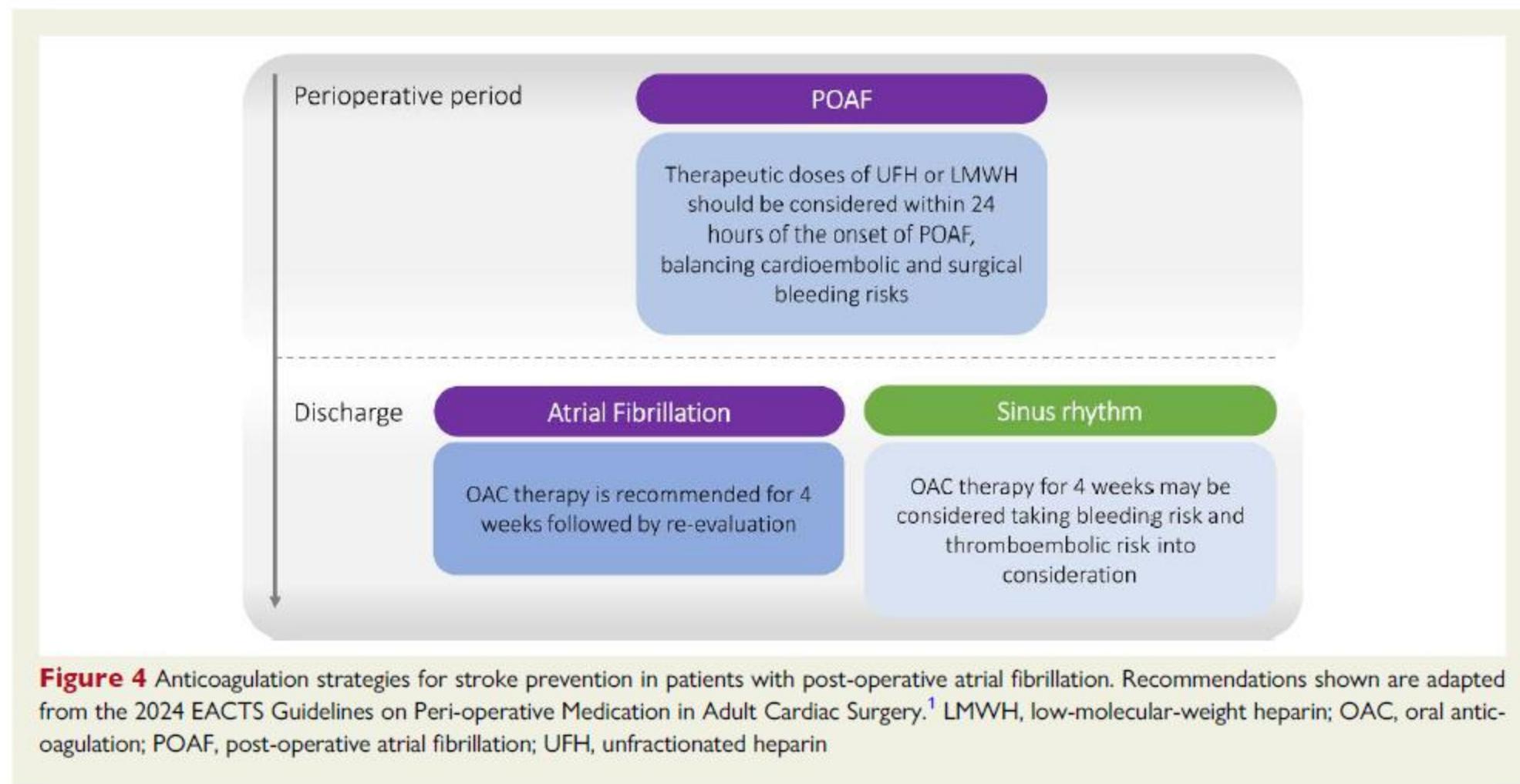
Annette Maznyczka, MBChB(Hons), PhD, MSc, BSc(Hons), MRCP, Thomas Pilgrim, MD, MSc*

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I'insufficienza renale cronica è un fattore di rischio trombotico o emorragico?

L'insufficienza renale cronica (IRC) è un fattore di rischio sia per gli eventi trombotici che per quelli emorragici, creando una situazione paradossale e complessa nella gestione clinica. La coesistenza di questi due rischi contrapposti è dovuta a molteplici alterazioni a carico dei sistemi di coagulazione e delle piastrine.

Rischio trombotico

L'insufficienza renale cronica aumenta il rischio di eventi trombotici, in particolare la tromboembolia venosa (TEV). Questo aumento è graduale: più la funzionalità renale si riduce (cioè, minore è il filtrato glomerulare stimato o eGFR), maggiore è il rischio di trombosi. Le ragioni principali includono:

- **Aumento dei fattori della coagulazione:** L'IRC porta a un aumento di alcuni fattori pro-coagulanti e a una diminuzione dei fattori anticoagulanti.
- **Disfunzione endoteliale:** Il danno ai vasi sanguigni (endotelio) è comune nell'IRC e favorisce l'attivazione della coagulazione.
- **Attivazione piastrinica:** Le piastrine diventano più attive e propense ad aggregarsi, anche se la loro funzione è paradosalmente compromessa (vedi rischio emorragico).
- **Altre comorbidità:** I pazienti con IRC spesso presentano altre patologie che aumentano ulteriormente il rischio di trombosi, come la fibrillazione atriale, l'obesità e il diabete.

Rischio emorragico

Contemporaneamente, l'IRC è un noto fattore di rischio per gli eventi emorragici, che possono essere gravi. Questo rischio è legato principalmente alla **disfunzione piastrinica indotta dall'uremia**.

- **Anomalia delle piastrine:** Nelle fasi avanzate dell'IRC (uremia), le piastrine non funzionano correttamente: pur essendo in numero sufficiente, non sono in grado di aderire e aggregarsi in modo efficace per fermare il sanguinamento.
- **Anemia e uremia:** L'anemia, comune nei pazienti con IRC, e l'accumulo di sostanze ureemiche contribuiscono ad aggravare la disfunzione piastrinica.
- **Trattamenti anticoagulanti:** La necessità di anticoagulanti, ad esempio per fibrillazione atriale o dopo l'impianto di protesi valvolari, aumenta ulteriormente il rischio emorragico, specialmente considerando il rallentato metabolismo e l'eliminazione renale di molti di questi farmaci.

3.3. Assessment of bleeding risk due to anticoagulation

Table S5 Published bleeding risk scores

| Score | Criteria | Point | Low risk | Intermediate risk (if applicable) | High risk |
|---------------------------|---|-------|----------|-----------------------------------|-----------|
| HEMORRHAGES ²⁴ | Hepatic or renal disease | +1 | 0 or 1 | 2 or 3 | ≥4 |
| | Ethanol (alcohol) abuse | +1 | | | |
| | Malignancy history | +1 | | | |
| | Older (age >75 years) | +1 | | | |
| | Reduced platelet count or function (includes aspirin use, any thrombocytopenia or blood dyscrasia, such as haemophilia) | +1 | | | |
| | Rebleeding risk (history of past bleeding) | +2 | | | |
| | Hypertension (uncontrolled) | +1 | | | |
| | Anaemia (Hb <13 g/dL for men; Hb <12 g/dL for women) | +1 | | | |
| | Genetic factors (CYP 2C9 single-nucleotide polymorphisms) | +1 | | | |
| | | | | | |
| ORBIT ²⁵ | Age >74 years | +1 | 0-2 | 3 | ≥4 |
| | Bleeding history (any history of GI bleeding, intracranial bleeding, or haemorrhagic stroke) | +2 | | | |
| | GFR <60 mL/min/1.73 m ² | +1 | | | |
| | Treatment with antiplatelet agents | +1 | | | |
| | | | | | |



Dopo un intervento chirurgico valvolare, la stratificazione del rischio trombotico ed emorragico è fondamentale per guidare la terapia antitrombotica, bilanciando la prevenzione degli eventi ischemici (ictus, tromboembolismo) con il rischio di complicanze emorragiche. La valutazione si basa su diversi fattori, tra cui il tipo e la posizione della protesi valvolare, la presenza di altre patologie e le caratteristiche individuali del paziente.

Stratificazione del rischio trombotico

Il rischio trombotico dipende principalmente dal tipo di protesi e dalla sua posizione:

- **Protesi meccaniche:** Richiedono una terapia anticoagulante a lungo termine (spesso a vita) a base di antagonisti della vitamina K (AVK), come il warfarin. Il rischio di trombosi valvolare ostruttiva è di circa 0,3-1,3% per paziente all'anno, mentre il rischio di eventi tromboembolici sistemicì è più alto (0,7-6% per paziente all'anno).
- **Bioprotesi (valvole biologiche):** Comportano un rischio trombotico inferiore rispetto alle protesi meccaniche. Generalmente, richiedono una terapia anticoagulante (con AVK) per un periodo limitato di 3-6 mesi dopo l'intervento, per poi passare a una terapia antiaggregante (aspirina).
- **Valvole riparate:** In seguito a una riparazione valvolare, non esiste un consenso unanime sulla terapia antitrombotica. La decisione dipende da fattori come il successo dell'intervento e la presenza di fibrillazione atriale. Alcuni studi suggeriscono che un breve periodo di anticoagulazione (come 3 mesi) possa essere benefico, mentre altri non hanno riscontrato differenze significative tra l'uso di AVK e antiaggreganti.
- **Protesi transcatetere (TAVI):** Per l'impianto valvolare aortico transcatetere (TAVI), la gestione antitrombotica è un'area di ricerca attiva. La terapia può prevedere l'uso di anticoagulanti orali diretti (DOAC) o una combinazione di antiaggreganti piastrinici, specialmente in pazienti con fibrillazione atriale preesistente.

Fattori aggiuntivi per il rischio trombotico

- **Fibrillazione atriale:** La presenza di fibrillazione atriale è un fattore di rischio significativo per l'ictus tromboembolico, e spesso si utilizzano score come il CHA₂DS₂-VASc per valutare questo rischio anche nei pazienti con patologia valvolare.
- **Posizione della valvola:** Le protesi mitraliche hanno un rischio trombotico più elevato rispetto a quelle aortiche, a causa delle maggiori sollecitazioni meccaniche e del flusso sanguigno più turbolento.

Stratificazione del rischio emorragico

Il rischio emorragico è legato alla terapia anticoagulante, ma anche alle caratteristiche del paziente. Per valutarlo, si possono utilizzare score specifici, benché la loro applicabilità specifica nella chirurgia valvolare sia ancora in fase di studio.

- **Score HAS-BLED:** Sebbene sviluppato per la fibrillazione atriale non valvolare, il punteggio HAS-BLED può essere utilizzato come riferimento per stimare il rischio emorragico. Un punteggio elevato identifica i pazienti che necessitano di un monitoraggio più attento durante la terapia anticoagulante.

Altri fattori di rischio emorragico:

- **Età avanzata:** Un'età avanzata aumenta il rischio di complicanze emorragiche.
- **Comorbidità:** Patologie come l'insufficienza renale ed epatica, l'ipertensione arteriosa non controllata, e l'anemia aumentano il rischio di sanguinamento.
- **Sanguinamento pregresso:** Un'anamnesi di sanguinamenti importanti aumenta il rischio di recidiva.
- **Terapia farmacologica:** L'uso concomitante di altri farmaci (antiaggreganti, farmaci antinfiammatori) può aumentare il rischio di sanguinamento.
- **Complicanze procedurali:** Eventi come sanguinamenti intra-operatori o la necessità di revisione chirurgica per emorragia possono aumentare il rischio postoperatorio.

Considerazioni per la gestione clinica

- **Valutazione individuale:** La scelta della terapia deve essere personalizzata in base alla combinazione dei fattori di rischio trombotico ed emorragico di ciascun paziente.
- **Bilancio rischio/beneficio:** Per i pazienti con alto rischio emorragico, si deve considerare un regime antitrombotico meno aggressivo o l'utilizzo di dosaggi più bassi, se compatibile con il rischio trombotico. Ad esempio, è necessario valutare con attenzione l'uso dei DOAC rispetto agli AVK, poiché i DOAC possono essere associati a un rischio maggiore di sanguinamento gastrointestinale in alcuni casi.
- **Monitoraggio:** È cruciale un monitoraggio regolare della terapia anticoagulante (tramite l'INR per gli AVK) e una stretta sorveglianza delle condizioni del paziente per identificare e gestire tempestivamente eventuali complicanze emorragiche o tromboemboliche.



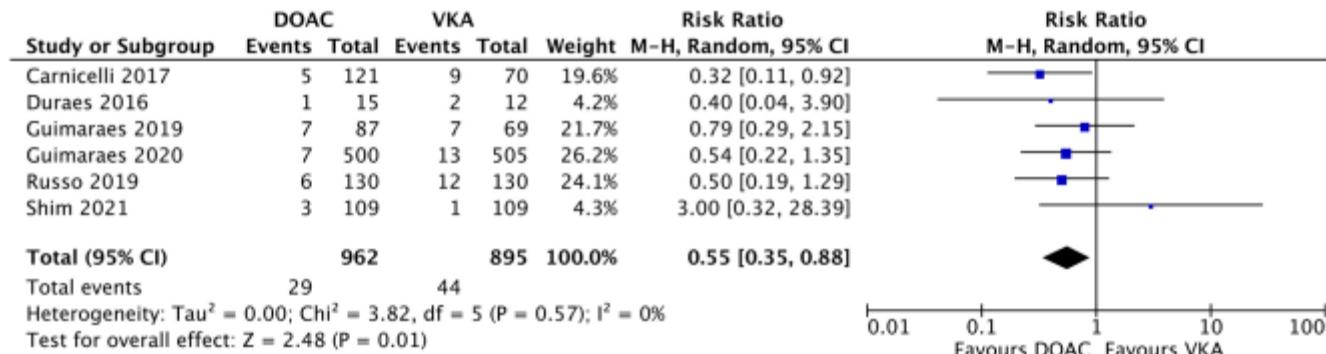
Recommendation Table 6 — Recommendations to assess and manage thromboembolic risk in AF (see also Evidence Table 6)

| Recommendations | Class ^a | Level ^b |
|--|--------------------|--------------------|
| Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. ^{239,240} | I | A |
| A CHA ₂ DS ₂ -VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | I | C |

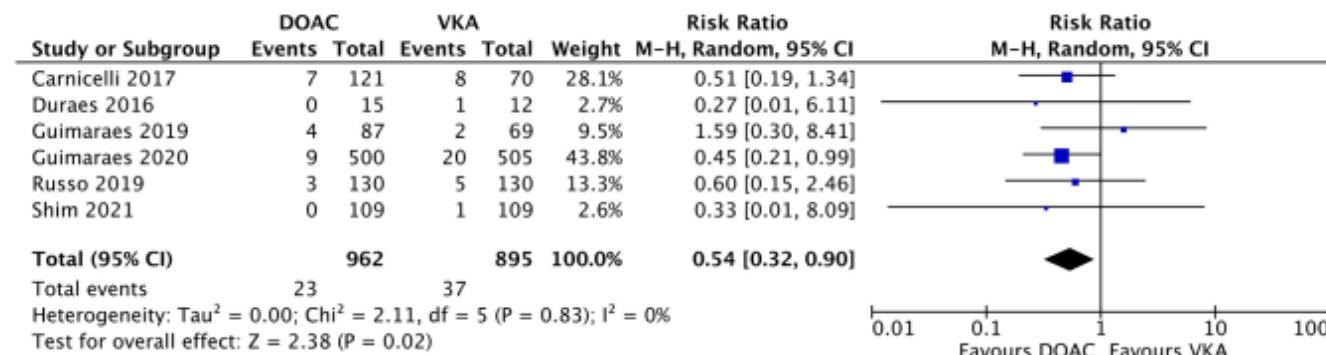
| CHA ₂ DS ₂ -VA component | | Points awarded ^a |
|--|--|-----------------------------|
| C | Chronic heart failure | 1 |
| H | Hypertension | 1 |
| A | Age 75 years or above | 2 |
| D | Diabetes mellitus | 1 |
| S | Prior stroke, TIA, or arterial thromboembolism | 2 |
| V | Vascular disease | 1 |
| A | Age 65–74 years | 1 |

DOAC vs. VKA in AF + mitral/aortic bioprosthetic implant or mitral repair

6 clinical trials with a total of 1,857 pts.



Major bleeding



TE stroke/SE

Gerfer S et al. Ther Adv Cardiovasc Dis 2022 Jan-Dec;16:17539447221093963