Deutschlandsberg – November 2023

Antikoagulations-Management im perioperativen Setting

Assoz. Prof. PD Dr. Dirk von Lewinski

Abteilung für Kardiologie

Medizinische Universität Graz

Agenda

- MINS – myocardial infarction during non-cardiac surgery
- VHF – ESC guideline
- Andere kardiologische Erkrankungen – Antikoagulation?
- Verwendung von NOAKs – EHRA statement
- Verwendung am LKH/MedUNI bei
  - PCI
  - TAVI
  - Deviceimplantation
  - Post-OP
  - Blutungen
- Antikoagulation in der ESC guideline non-cardiac surgery

MINS

myocardial injury after non-cardiac surgery

PMI

Peroperative myocardial injury

MINS – Definition/Häufigkeit

- Postoperativer Troponinanstieg* innerhalb von 30 Tagen nach OP und vermutlich ischämischer Genese**
- Symptomatik od. typische Bildgebung ist nicht notwendig
- Etwa 8 Mio. Fälle jährlich weltweit

Table 2. Peak Postoperative hsTnT Thresholds Associated With 30-Day Mortality[a]

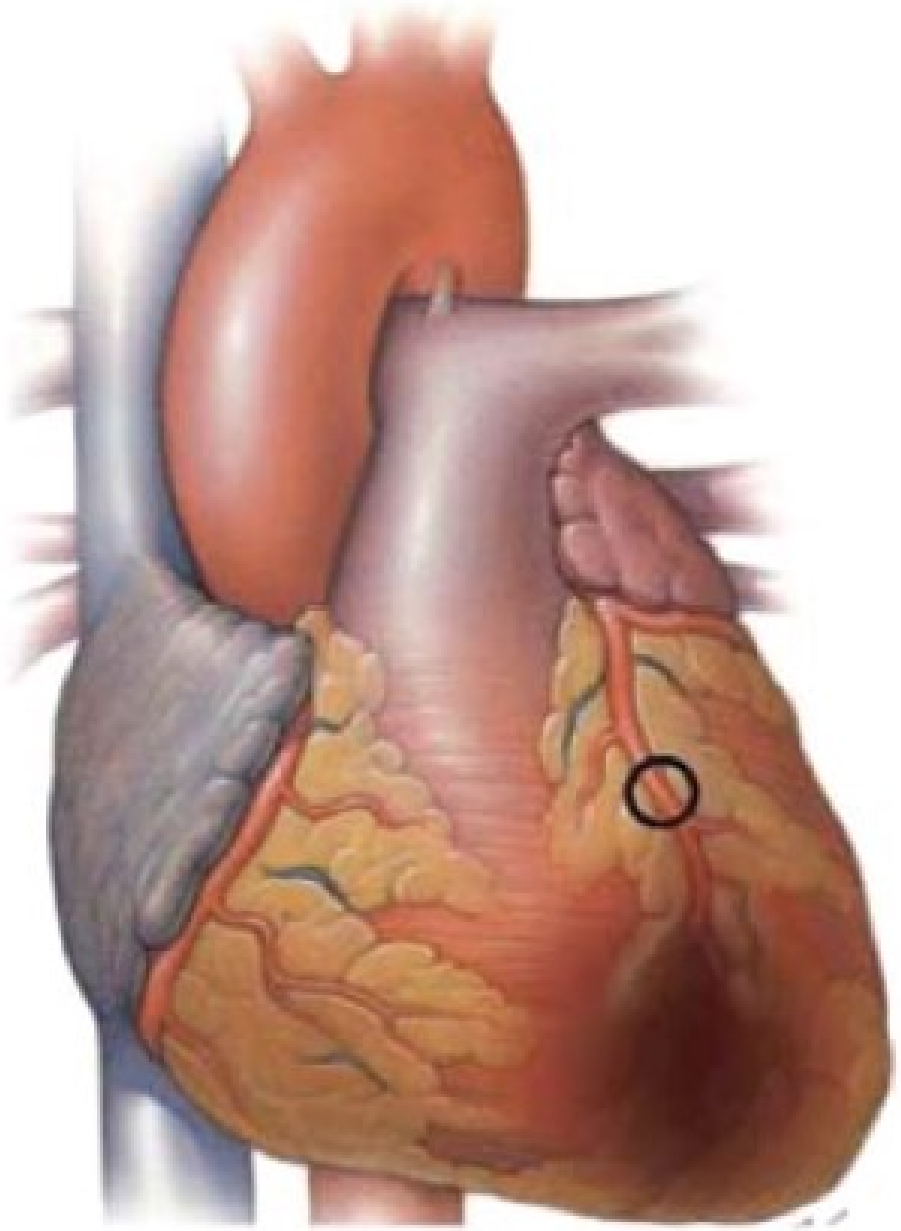
	hsTnT Thresholds, ng/L					
	<5	5 to <14	14 to <20	20 to <65	65 to <1000	≥1000
Patients, No. (%)	5318 (24.4)	8750 (40.1)	2530 (11.6)	4049 (18.6)	1118 (5.1)	54 (0.2)
Deaths, No. (%)	6 (0.1)	40 (0.5)	29 (1.1)	123 (3.0)	102 (9.1)	16 (29.6)
Adjusted hazard ratio (95% CI)	1 [Reference]	3.73 (1.58-8.82)	9.11 (3.76-22.09)	23.63 (10.32-54.09)	70.34 (30.60-161.71)	227.01 (87.35-589.92)
P Value		.003	<.001	<.001	<.001	<.001

* Troponinanstieg: hsTrop > 65ng/L oder Dynamik von 5 bei Troponin zwischen 20 und 65ng/L

** ca. 10-15% nicht-ischämisch (Sepsis, PAE, Tachykardien)

JAMA. 2017;317(16):1642-1651.

MINS - Ursache



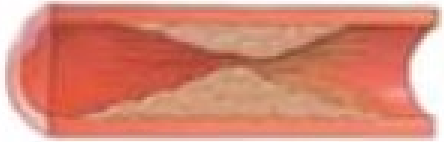
Plaque rupture with thrombus

MI Type 1

Vasospasm or endothelial dysfunction

MI Type 2

Fixed atherosclerosis and supply-demand imbalance

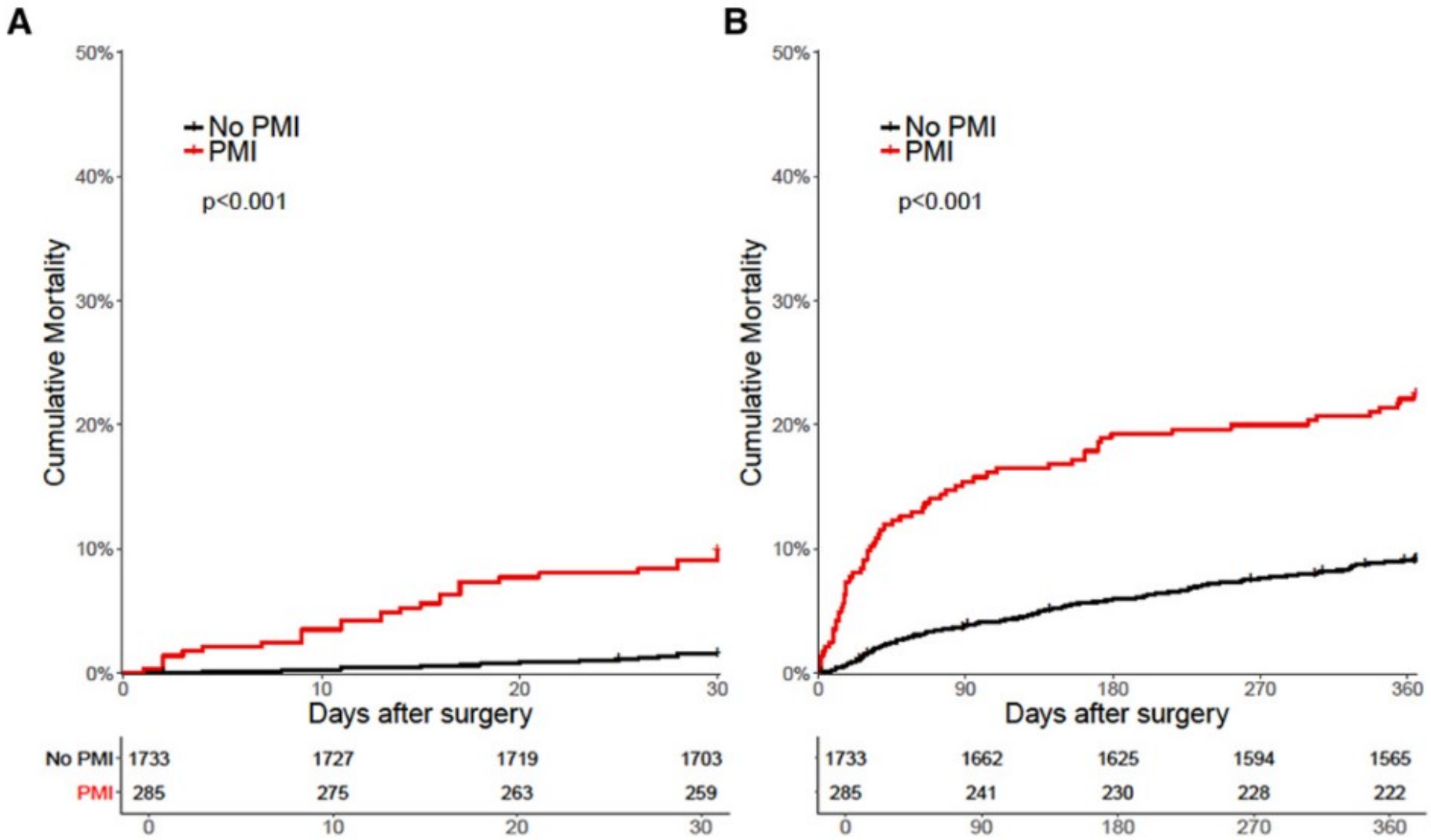


MI Type 2

Supply-demand imbalance alone

MI Type 2

Starker Einfluss auf 30-Tages und 1 Jahres-Mortalität

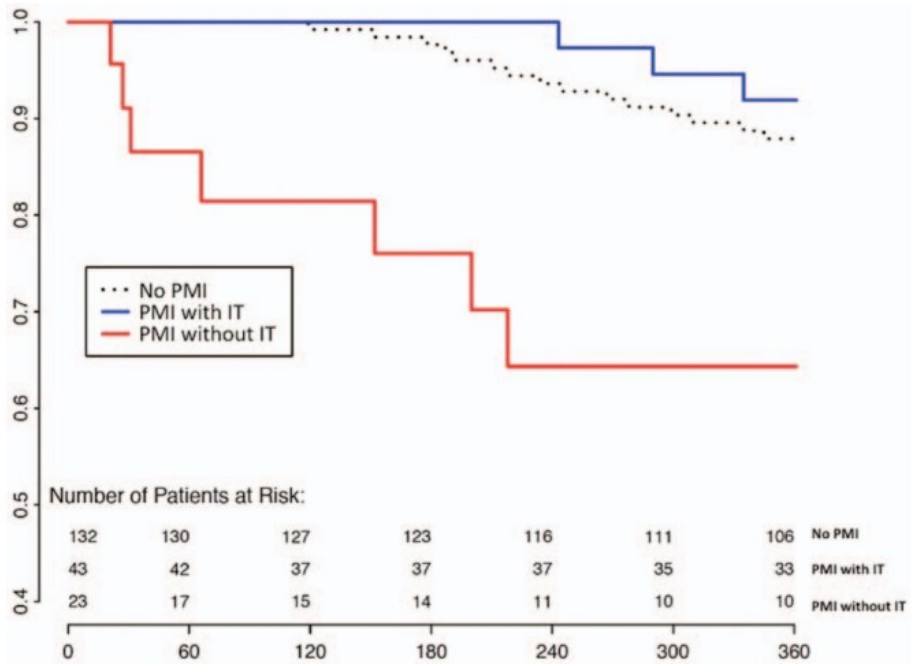


Circulation
Volume 137, Issue 12, 20 March 2018, Pages 1221-1232

Therapie bei Entlassung und 30 Tages Mortalität

- Aspirin (HR 0.54)
- Statin (HR 0.26)
- Intensivierte Therapie (TASS, Statin, Betablocker, ACE-Hemmer)

Ann Intern Med. 2011 Apr 19;154(8):523-8.

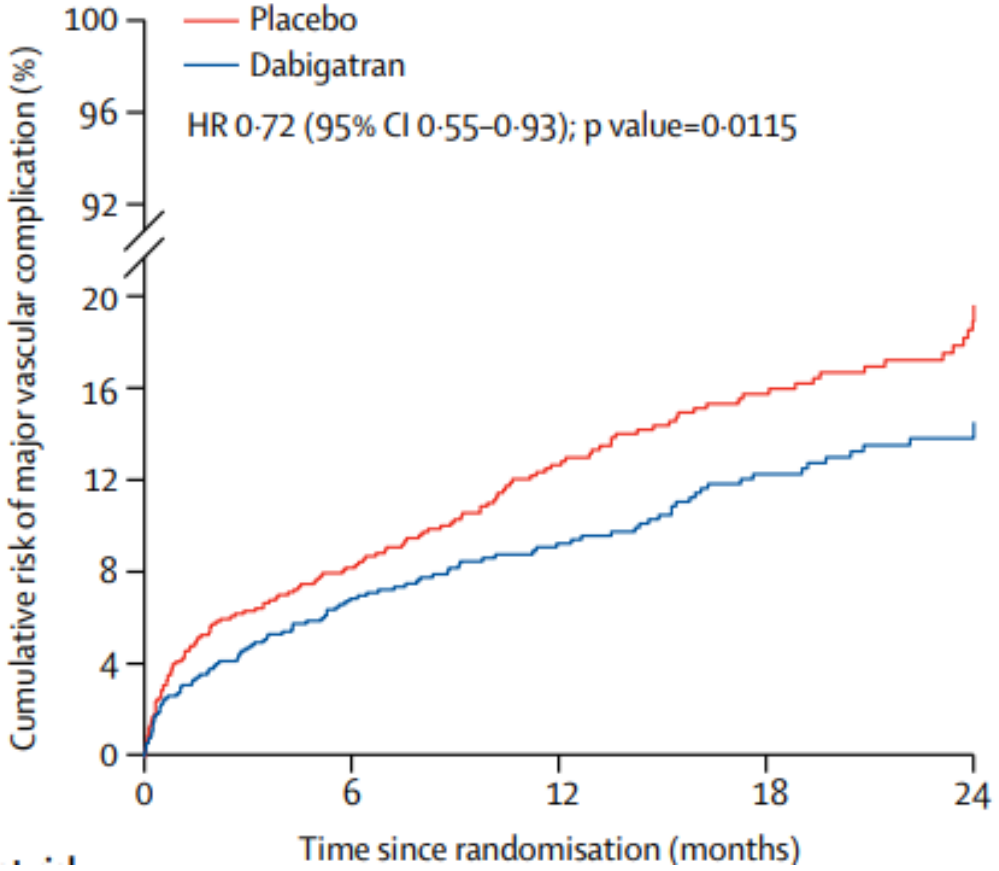


(Anesth Analg 2014;119:1053–63)

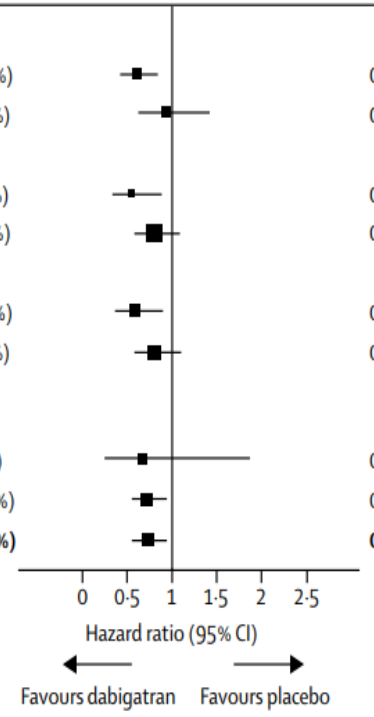
Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial

MANAGE trial

- 1754 Patienten mit MINS aus 84 Zentren, randomisiert Dabigatran 110mg 2x1 vs. Placebo für bis zu 2 Jahre
- Einschluss innerhalb von 35 Tagen nach MINS

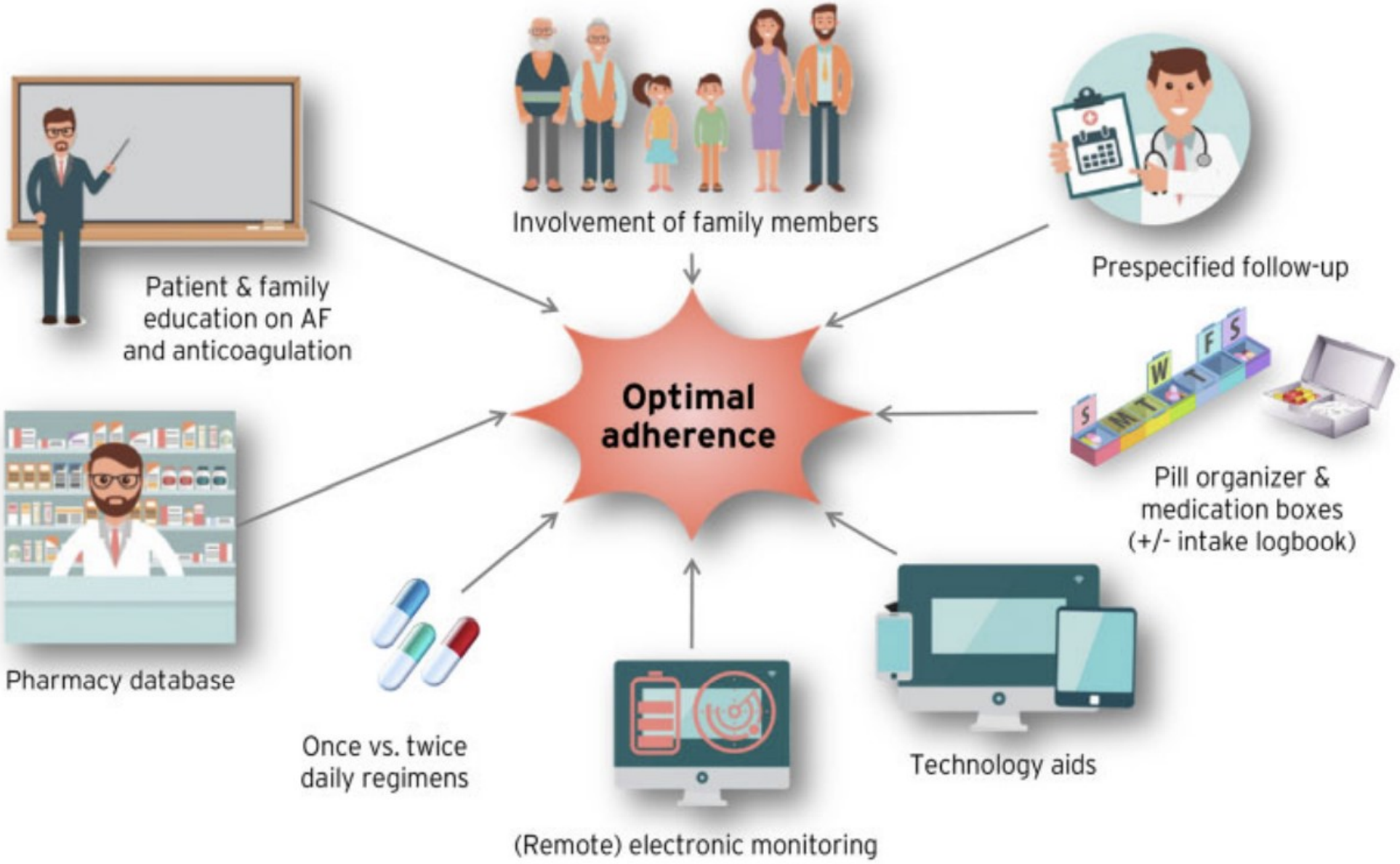


	Dabigatran	Placebo	Hazard ratio (95% CI)
	Events/patients	Events/patients	
Timing of randomisation			
≤5 days of MINS while still in hospital	52/432 (12%)	85/436 (20%)	0·60 (0·42–0·84)
>5 days after MINS or after hospital discharge	45/445 (10%)	48/441 (11%)	0·94 (0·63–1·42)
MINS diagnostic criterion			
Myocardial infarction	25/172 (15%)	44/173 (25%)	0·55 (0·33–0·89)
Isolated ischaemic troponin elevation	72/705 (10%)	89/704 (13%)	0·80 (0·58–1·09)
History of peripheral arterial disease			
Yes	30/124 (24%)	51/128 (40%)	0·58 (0·37–0·91)
No	67/753 (9%)	82/749 (11%)	0·80 (0·58–1·11)
Receiving dual antiplatelet therapy at the time of randomisation			
Yes	6/22 (27%)	11/29 (38%)	0·68 (0·25–1·87)
No	91/855 (11%)	122/848 (14%)	0·72 (0·55–0·95)
Overall	**97/877 (11%)**	**133/877 (15%)**	**0·73 (0·56–0·95)**



Lancet 2018; 391: 2325–34

VHF


Involvement of family members
Patient & family education on AF and anticoagulation
Prespecified follow-up
Optimal adherence
Pharmacy database
Pill organizer & medication boxes (+/- intake logbook)
Once vs. twice daily regimens
Technology aids
(Remote) electronic monitoring

Grundlage

ESC European Society of Cardiology

European Heart Journal (2020) **00**, 1–125
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Authors/Task Force Members: Gerhard Hindricks* (Chairperson) (Germany), Tatjana Potpara* (Chairperson) (Serbia), Nikolaos Dagres (Germany), Elena Arbelo (Spain), Jeroen J. Bax (Netherlands), Carina Blomström-Lundqvist (Sweden), Giuseppe Boriani (Italy), Manuel Castella[1] (Spain), Gheorghe-Andrei Dan (Romania), Polychronis E. Dilaveris (Greece), Laurent Fauchier (France), Gerasimos Filippatos (Greece), Jonathan M. Kalman (Australia), Mark La Meir[1]

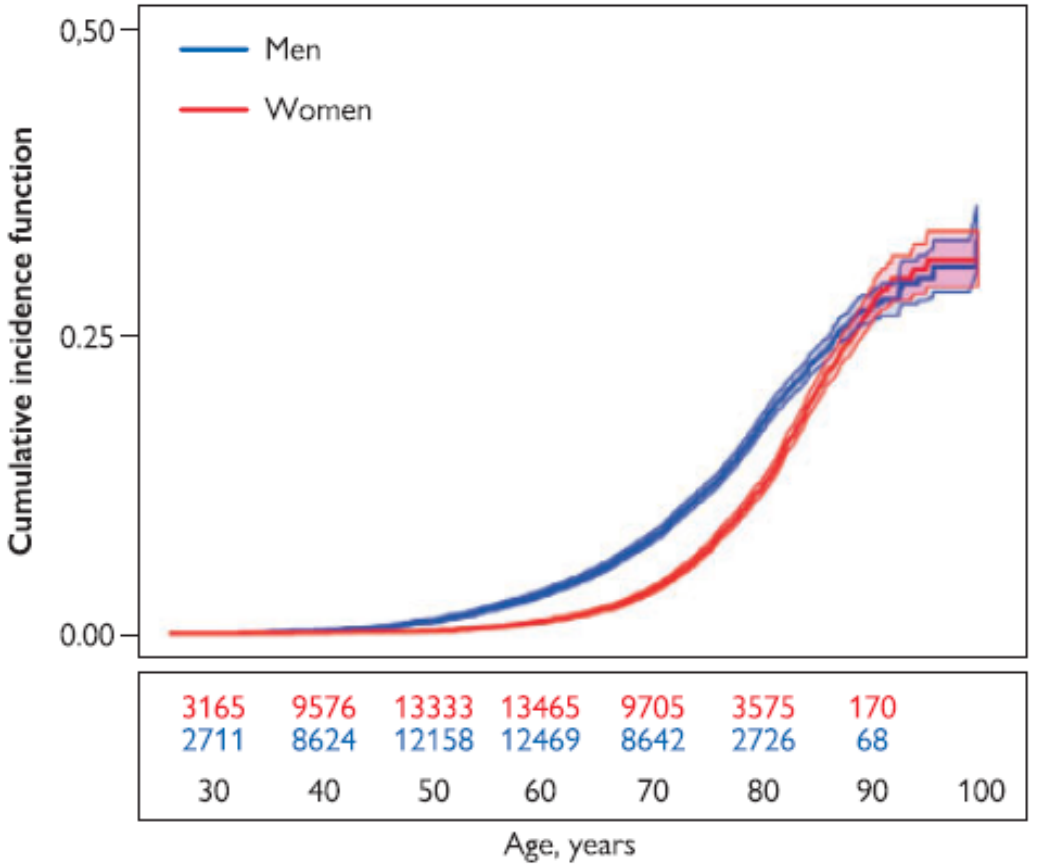
Warum eigene Guidelines für Vorhofflimmern (VHFA)?

LIFETIME RISK for AF
1 in 3 individuals

of European ancestry
at index age of 55 years
37.0% (34.3% to 39.6%)

AF is more common in males

Cumulative incidence curves and 95% CIs
for AF in women and men with death as a competing risk



2-3fach erhöhte Mortalitätsrate

Ursache von 20-30% aller ischämischen Insulte

Hindricks G et al. Eur Heart J. 2021;42:373-498.

VHFA Guidelines 2020: Das „ABC“ der Therapie

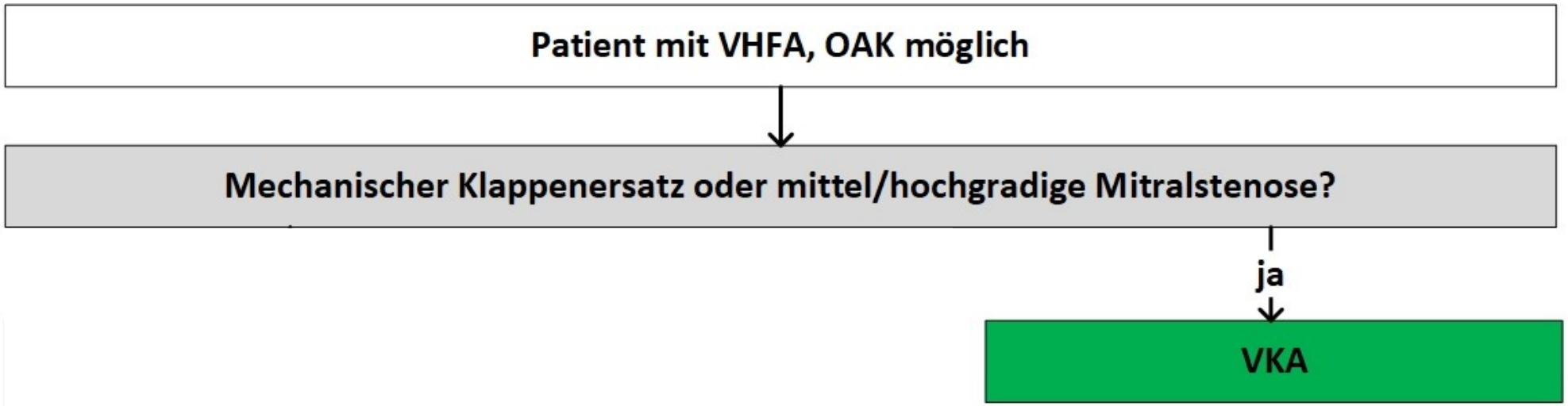
Hindricks G et al. Eur Heart J. 2021;42:373-498.

VHFA: Schlaganfallrisiko - CHADSVASc Score

CHA_2DS_2-VASc-Score (max
C (cong. heart failure)
H (hypertension)
A_2 (age)
D (diabetes)
S_2 (stroke)
V (vascular disease)
A (age)
S (sex)

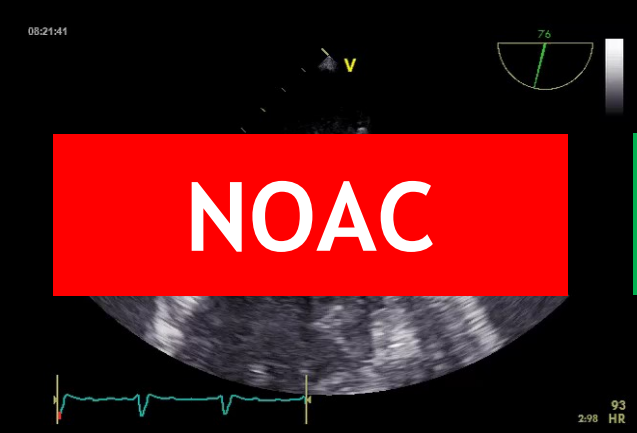
CHA2DS2-VASc Score	Adjusted stroke rate (% / year)
0	0
1	1.3
2	2.2
3	3.2
4	4
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

VHFA: Antikoagulation



Hindricks G et al. Eur Heart J. 2021;42:373-498.

Antikoagulation bei kardialen Erkrankungen

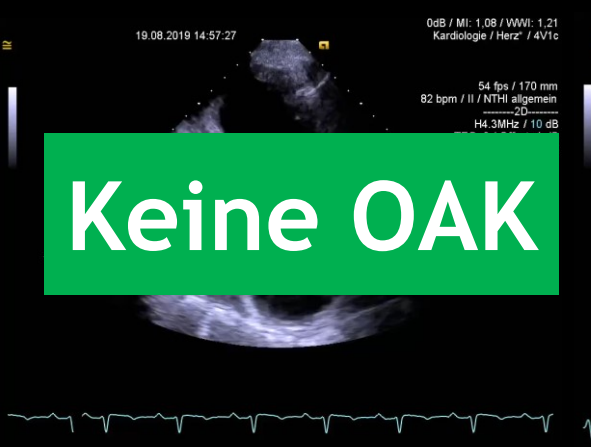


NOAC

Vorhofflimmern

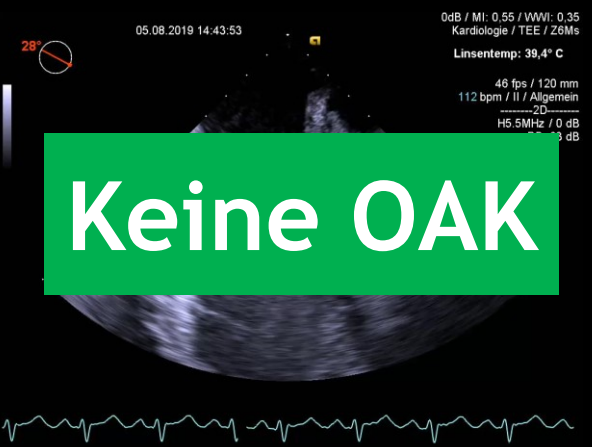
Keine OAK

Herzinsuffizienz



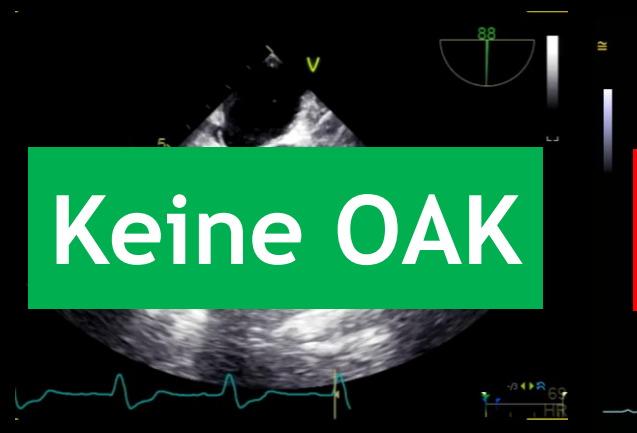
Keine OAK

Aneurysma



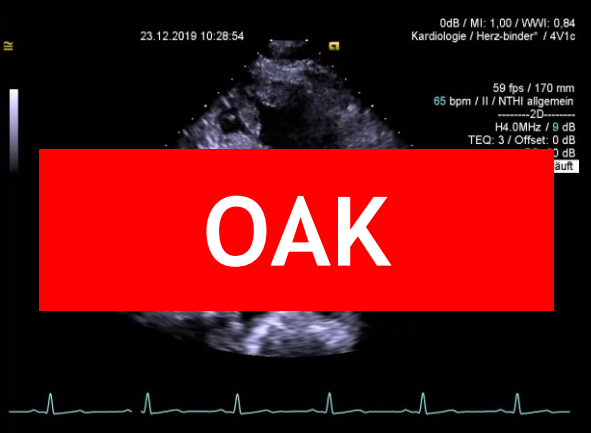
Keine OAK

Endokarditis



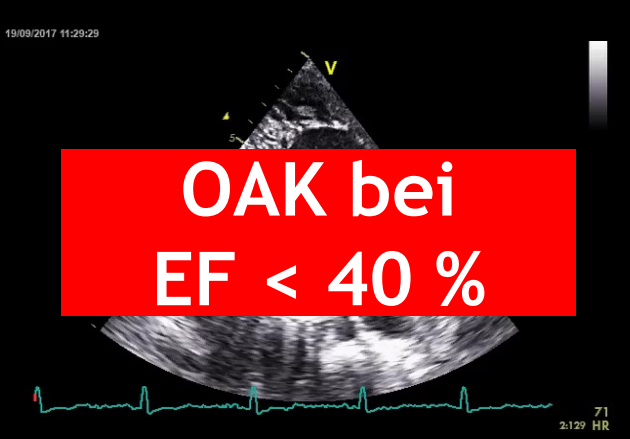
Keine OAK

PFO



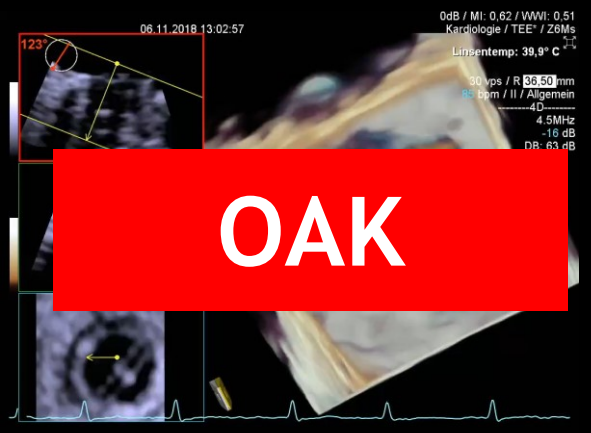
OAK

Ventrikelthrombus



OAK bei EF < 40 %

LVNC



OAK

Klappenprothesen

Grundlage

ESC European Society of Cardiology

Europace (2021) **00**, 1–65
doi:10.1093/europace/euab065

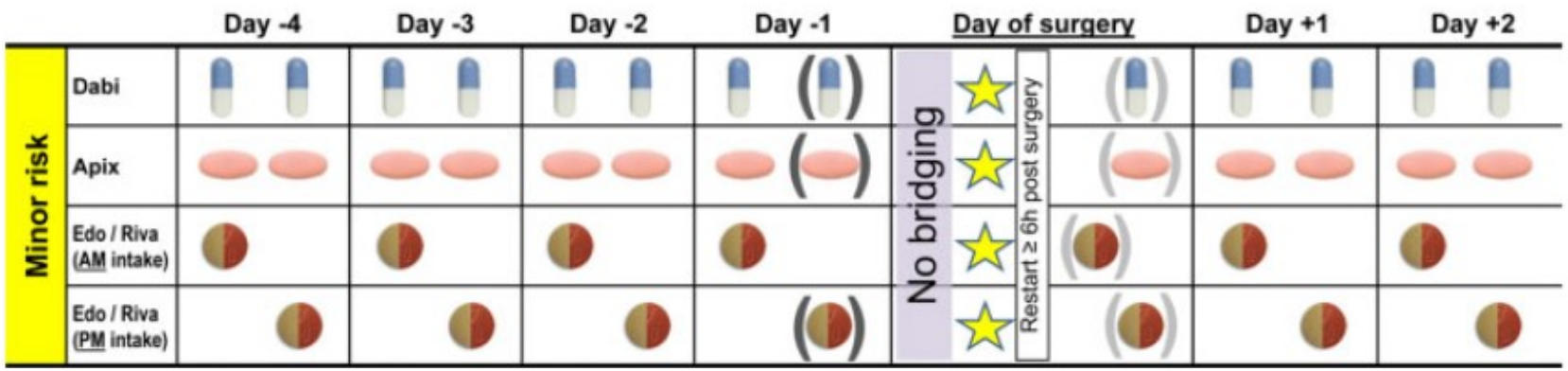
POSITION PAPER
EHRA PRACTICAL GUIDE

2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation

Jan Steffel[1]*, Ronan Collins[2], Matthias Antz[3], Pieter Cornu[4], Lien Desteghe[5,6], Karl Georg Haeusler[7], Jonas Oldgren[8], Holger Reinecke[9], Vanessa Roldan-Schilling[10], Nigel Rowell[11], Peter Sinnaeve[12], Thomas Vanassche[12], Tatjana Potpara[13], A. John Camm[14], and Hein Heidbüchel[5,6]

External reviewers: Gregory Y.H. Lip (review coordinator)[15,16,17] Thomas Deneke[18], Nikolaos Dagres[19], Giuseppe Boriani[20], Tze-Fan Chao[21], Eue-Keun Choi[22], Mellanie True Hills[23], Itamar de Souza Santos[24,25], Deirdre A. Lane[15,16,17], Dan Atar[26,27], Boyoung Joung[28], Oana Maria Cole[15,16], and Mark Field[15,16]

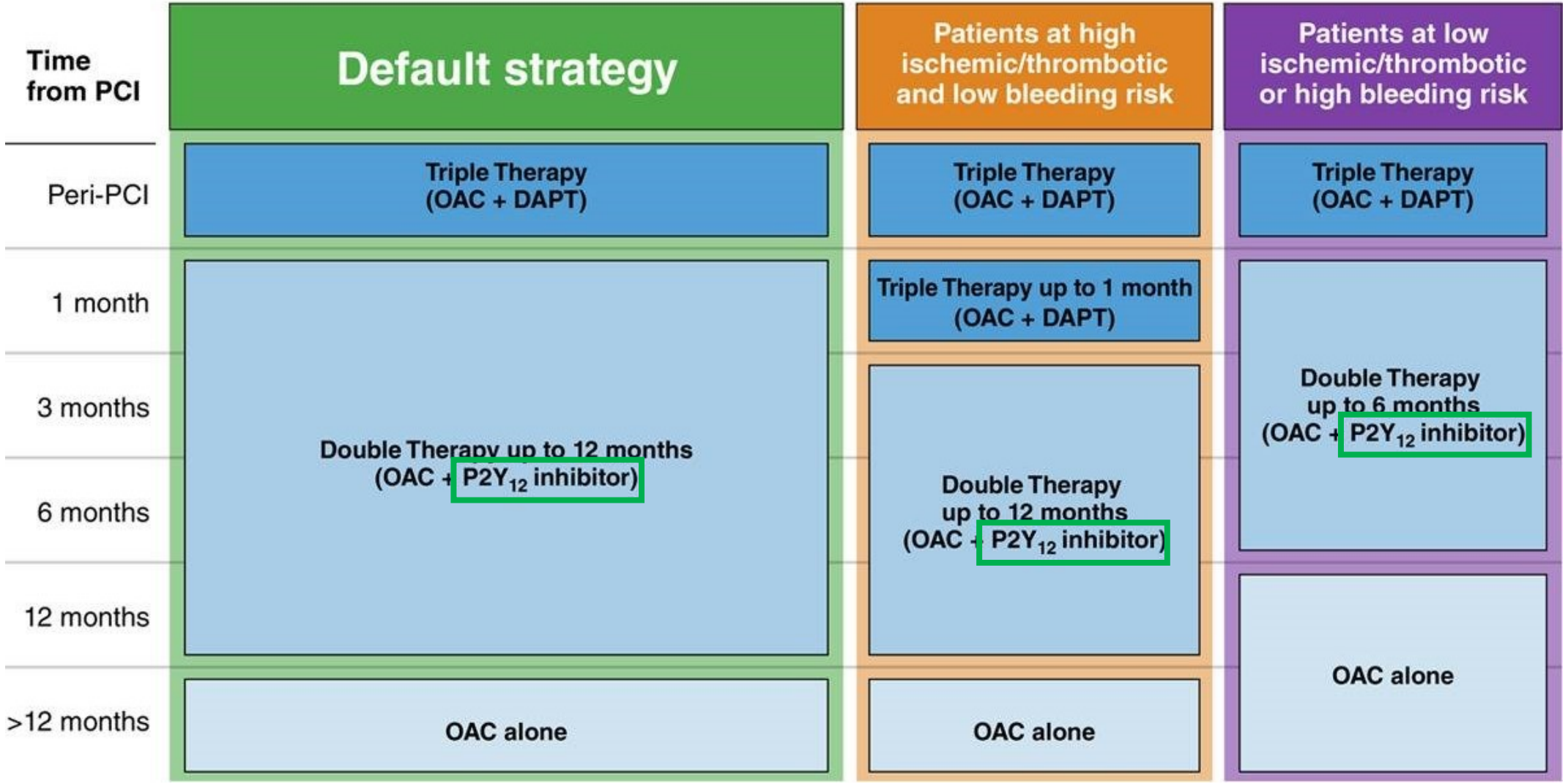
EHRA NOAC Practical Guide: Bridging



Zahnextraktionen, Augen, Endoskopie ohne Biopsie, oberfl. Chirurgie, SM/ICDs, EPU, CA

Steffel J et al. Eur Heart J. 2021;39:1330-93.

Antikoagulation bei PCI + VHF



OAK: bei GFR<15 | metallische Herzklappe!

NOAC: Rivaroxaban 15 oder 20 / Dabigatran2x110 oder 150 / Apixaban 5 2x1 / Edoxaban 60

Antikoagulation nach TAVI - SOP UHZ Graz

Indikation zur OAC (ca. 20-30%)

Keine Indikation zur OAC (ca. 70-80%)

KHK*

TAVI

12 Monate

TAPT 1 Woche

O + A und C

DAPT 6-12 Monate

O + A oder C

OAC Monotherapie

O

(DAPT)

A und C

oder

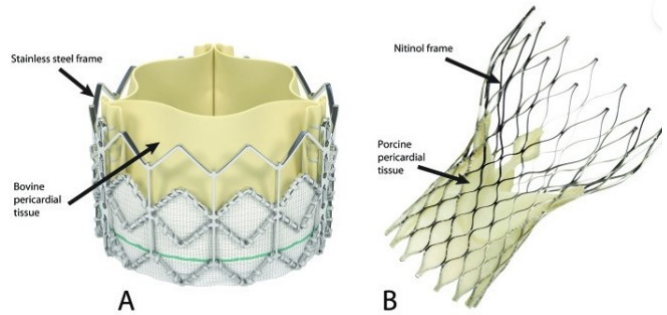
SAPT

A oder C

O OAC (präferentiell NOAKs, alternativ VKAs)

A Aspirin 75-100mg täglich

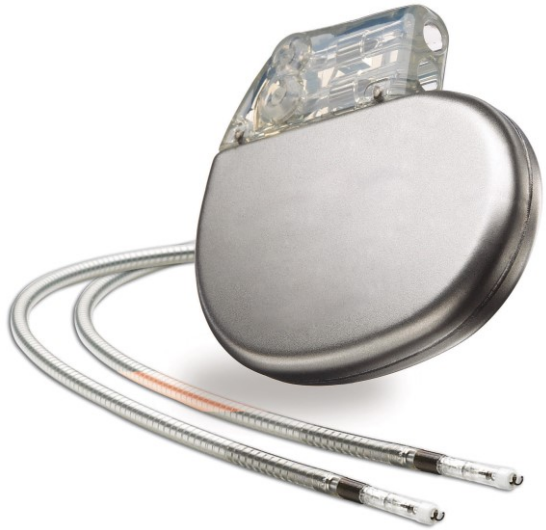
C Clopidogrel 75mg täglich



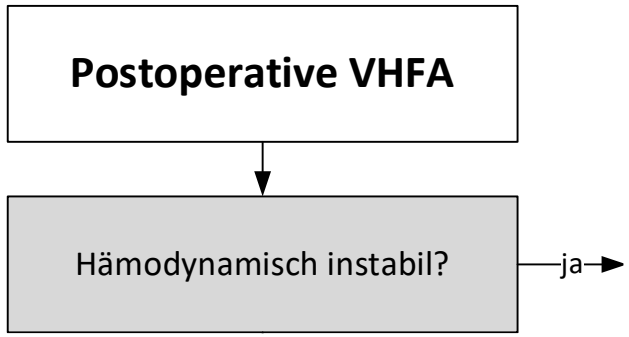
NOAKs und Deviceimplantation - SOP UHZ Graz

- Unter laufender SAPT, DAPT
- Unter NOAK bzw. OAK INR 2,0-2,5
- Nicht während Triple Therapie
- Unter NOAK + [Plavix oder ASS]
- NOAK Pause It Schema EHRA Practical NOAK Guide 2021

	Dabigatran		Apixaban - Edoxaban - Rivaroxaban	
No perioperative bridging with LMWH / UFH				
Minor risk procedures: - Perform procedure at NOAC trough level (i.e., 12 h / 24 h after last intake). - Resume same day or latest next day.				
	Low risk	**High risk**	**Low risk**	**High risk**
CrCl ≥80 ml/min	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h
CrCl 50-79 ml/min	**≥ 36 h**	**≥ 72 h**		
CrCl 30-49 ml/min	**≥ 48 h**	**≥ 96 h**		
CrCl 15-29 ml/min	Not indicated	Not indicated	**≥ 36 h**	
CrCl <15 ml/min	No official indication for use			

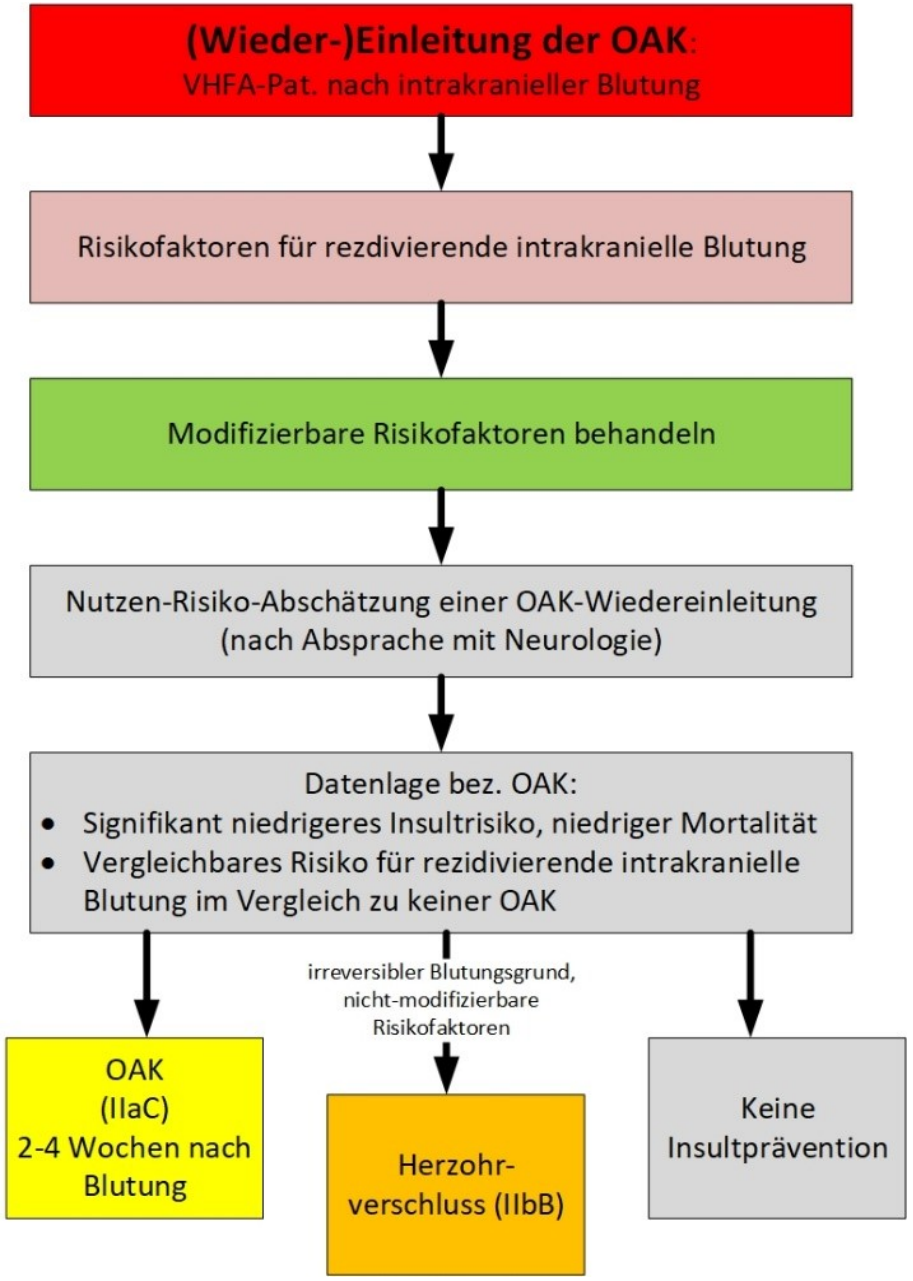


Post-OP VHF: Langzeit-OAK



Hindricks G et al. Eur Heart J. 2020.

OAK nach intrakranieller Blutung



PCI+NOAKs: Risikofaktoren und Strategien

THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

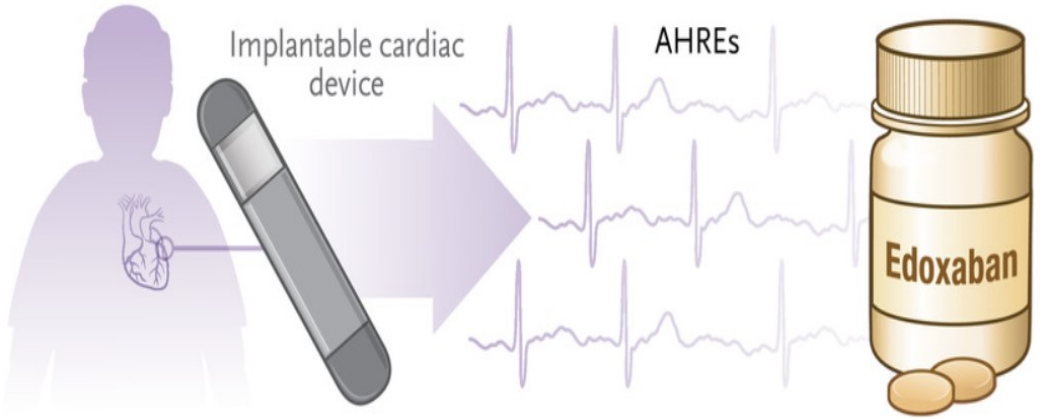
STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

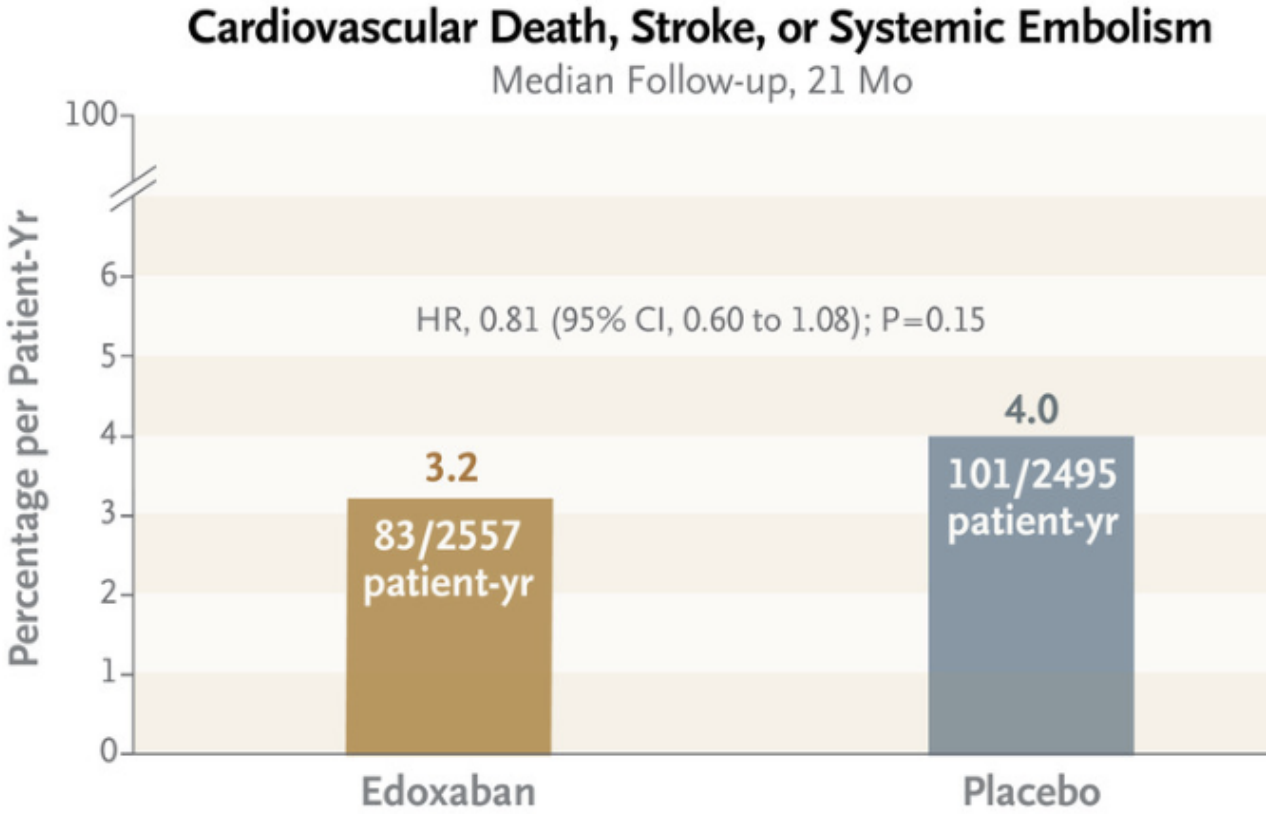
- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non–administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a $P2Y_{12}$ inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy

Hindricks G et al. Eur Heart J. 2020.

Atriale Hochfrequenzepisoden

NOAH-AFNET6: 2608 Patienten ohne VHF & mit AHRE (> 6 min.) und ≥ 1 RF, Edoxaban 60mg vs Placebo

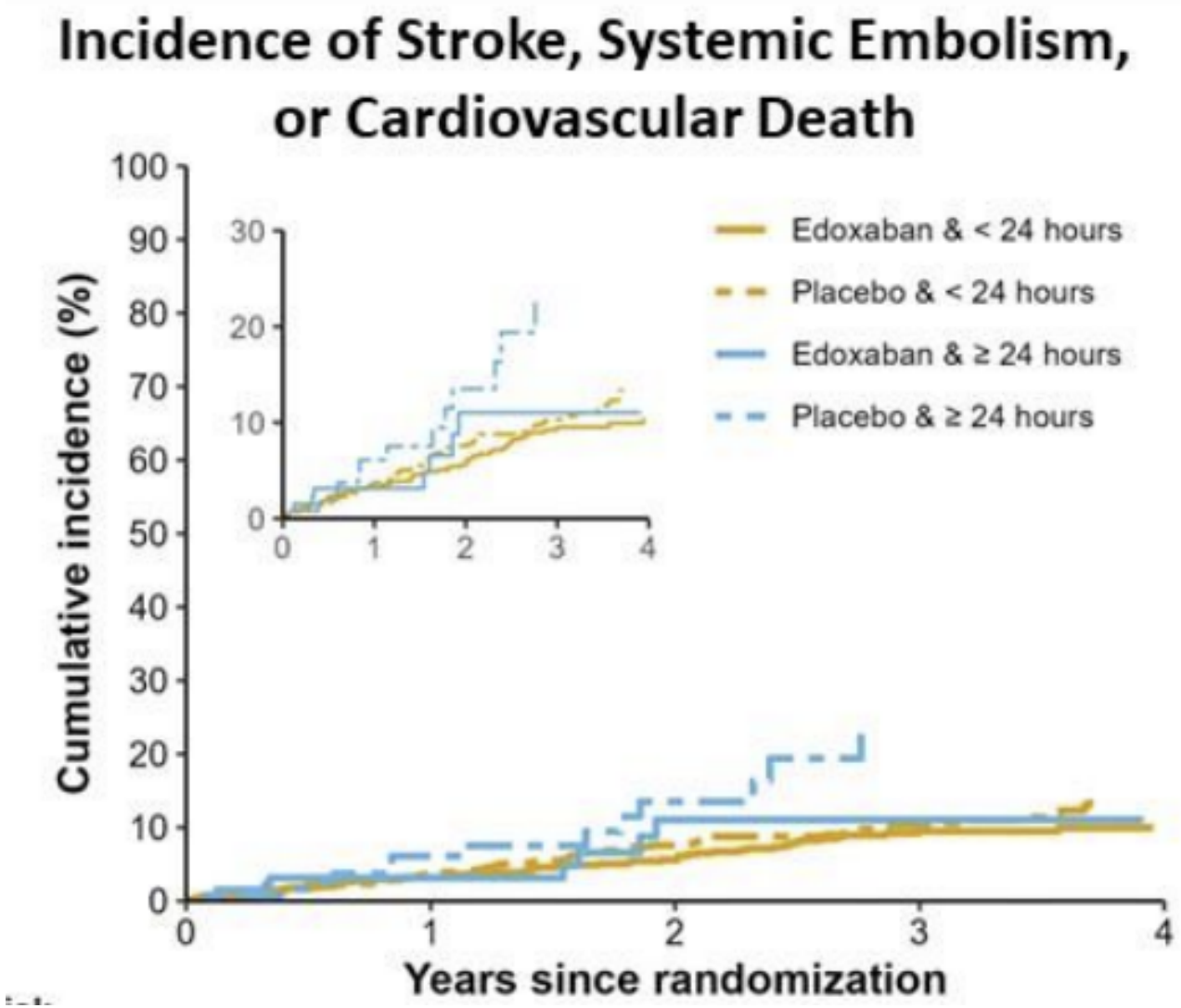


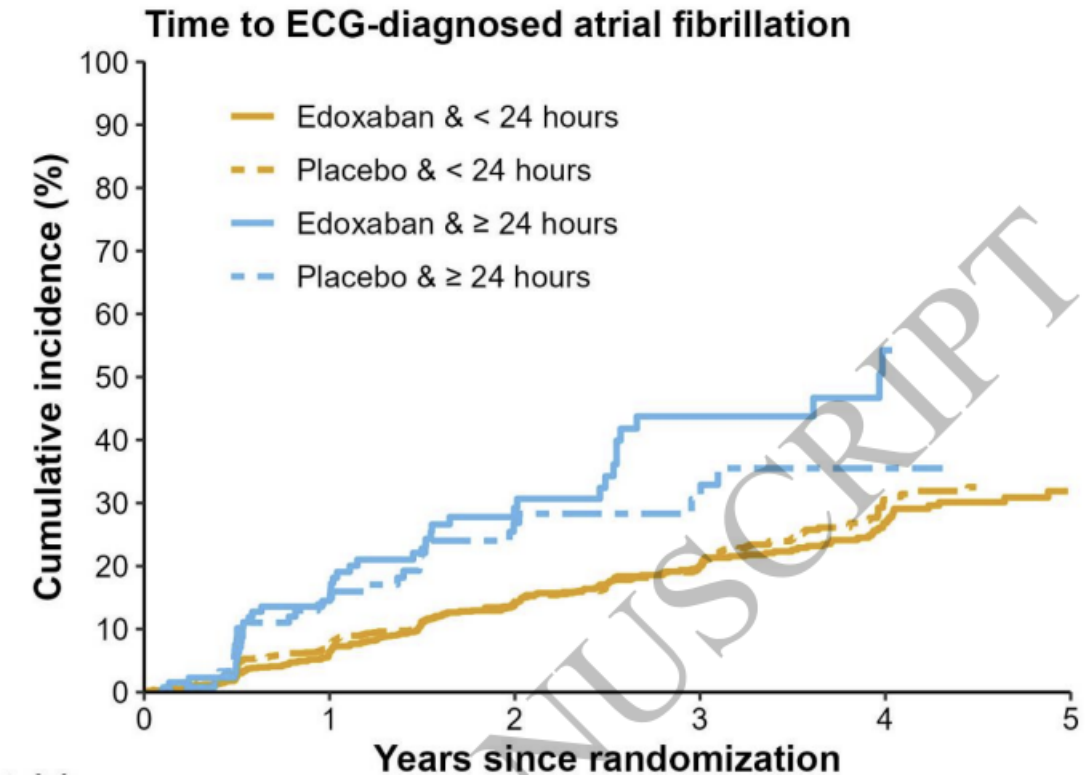


N Engl J Med. 2023 Sep 28;389(13):1167-1179.

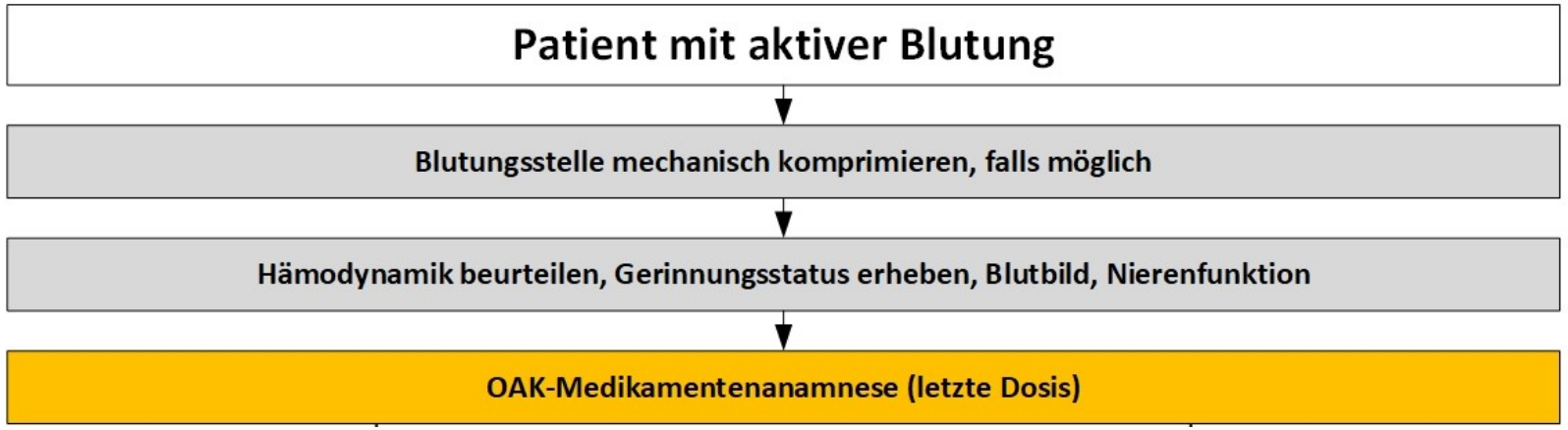
Atriale Hochfrequenzepisoden

NOAH-AFNET6 – subanalyse (AHRE > 24h bei baseline)

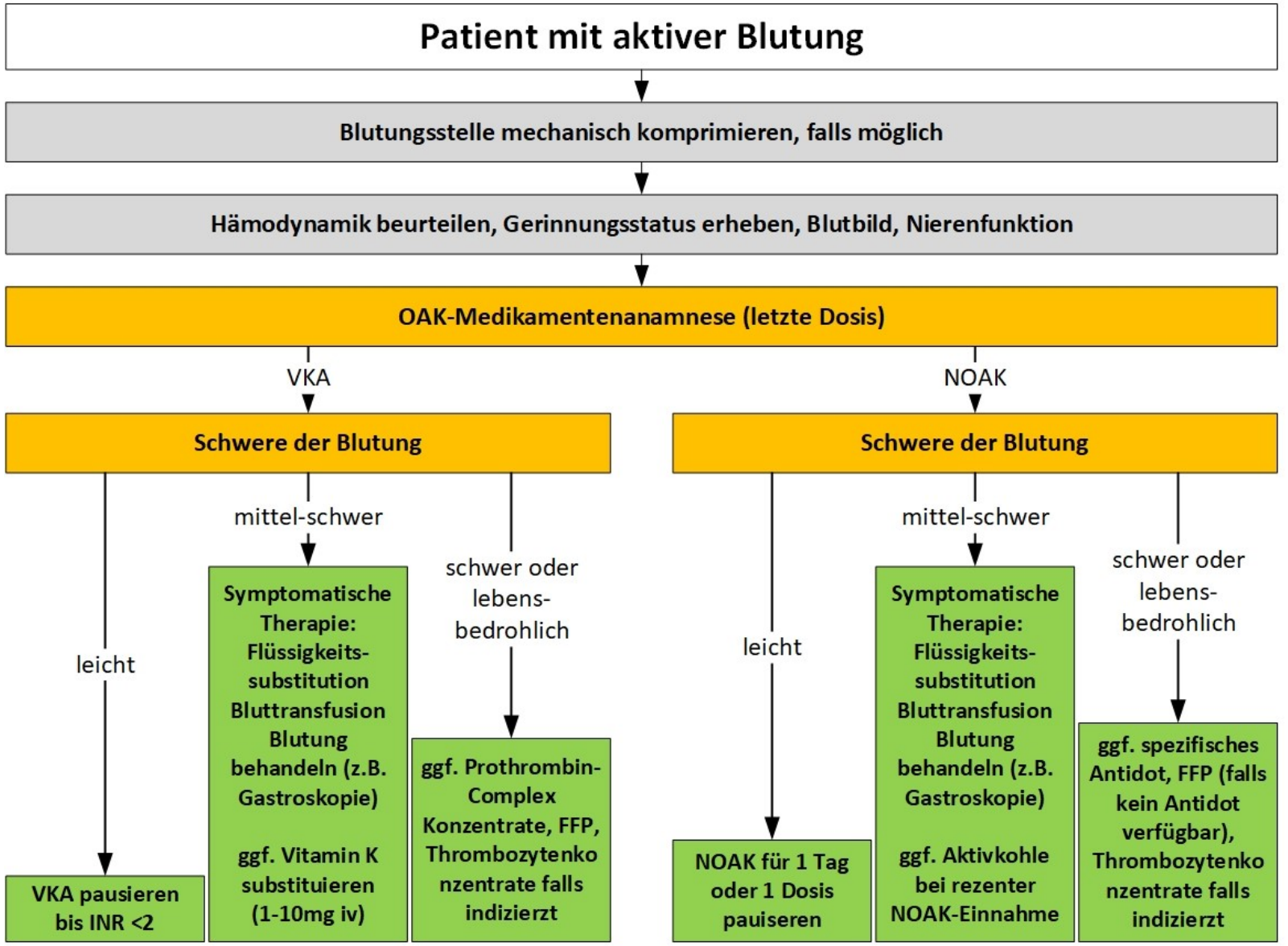




Antikoagulation + Blutung



Antikoagulation + Blutung



Grundlage

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 3826–3924
https://doi.org/10.1093/eurheartj/ehac270

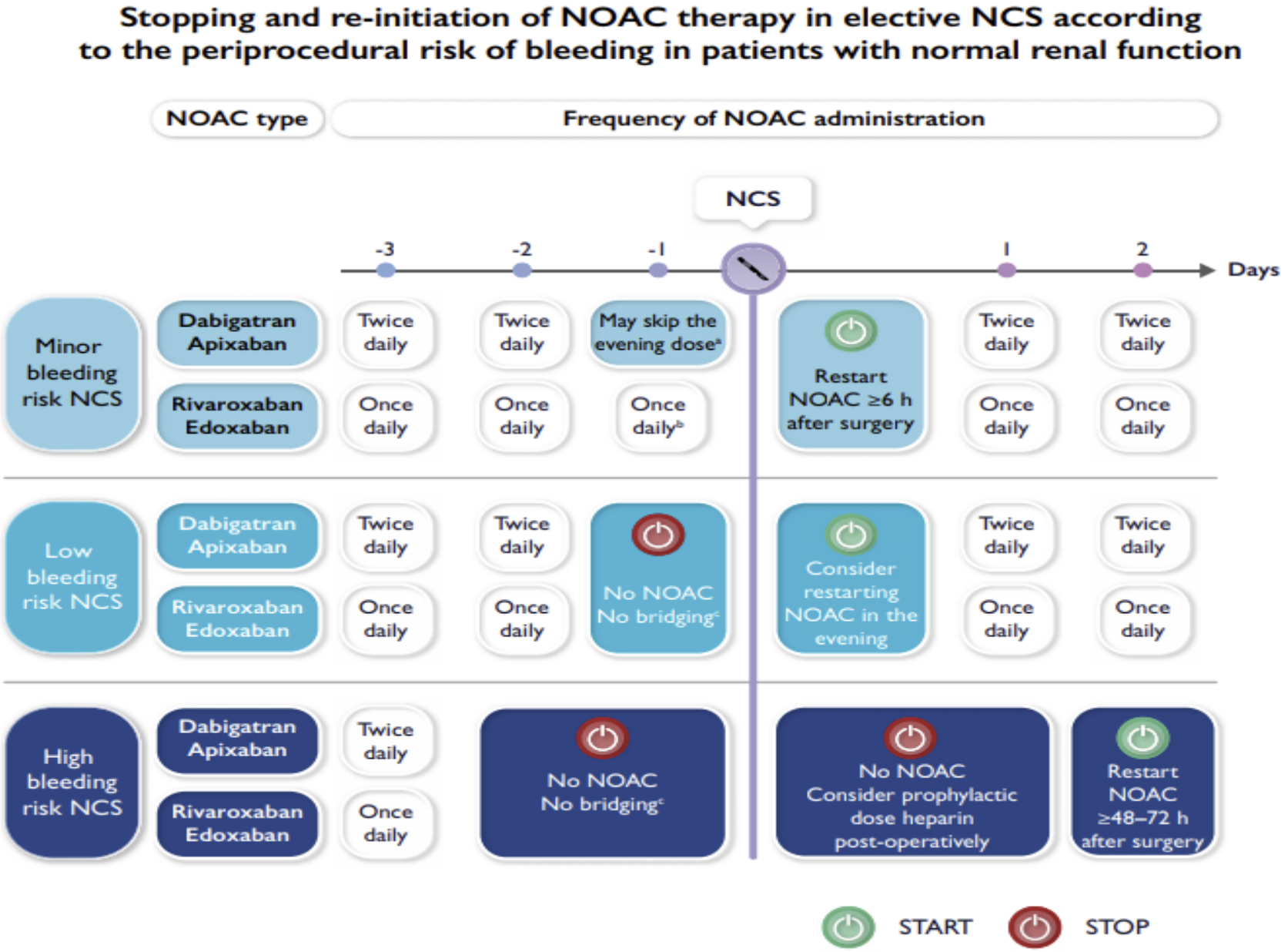
ESC GUIDELINES

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

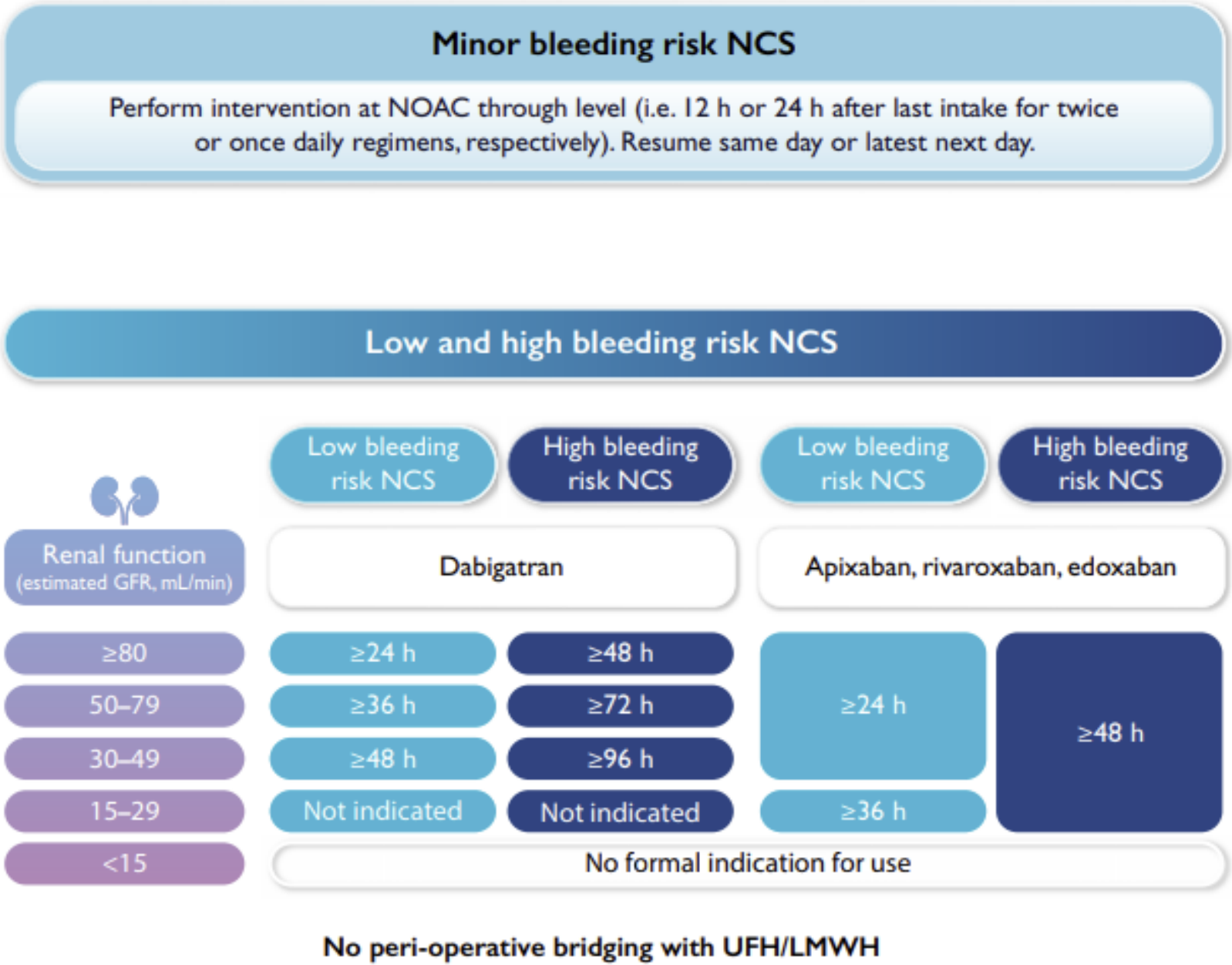
Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC)

VHFA: Antikoagulation

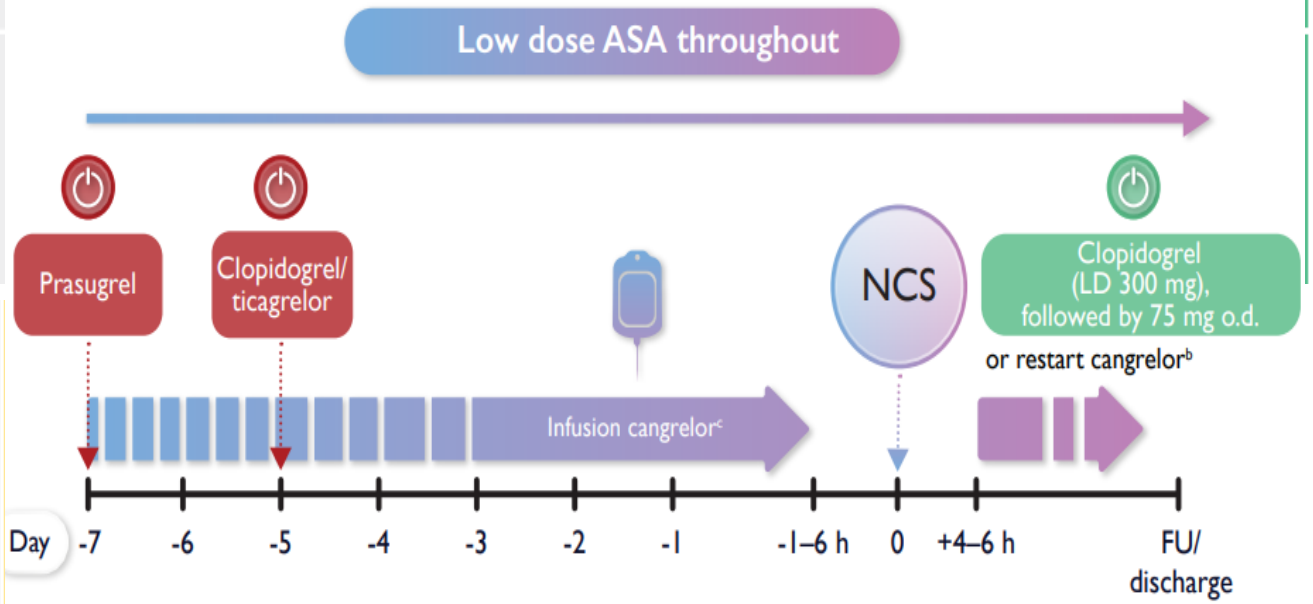


Timing of last NOAC dose before elective NCS according to renal function



ESC Leitlinie non-cardiac surgery 2022

Antiplatelets			
Consideration should be given to performing non-urgent NCS in patients who have had recent DES implantation no sooner than 12 months following the intervention. This delay may be reduced to 6 months for the new-generation DES.	IIa	Elektive nicht kardiale Operationen sollten nach PCI um 6 Monate und nach ACS um 12 Monate verschoben werden	I
It is recommended that aspirin be continued for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life-threatening surgical bleeding on aspirin is unacceptably high.	I	After elective PCI, it is recommended to delay time-sensitive NCS until a minimum of 1 month of DAPT treatment has been given.	I
Continuation of aspirin, in patients previously thus treated, may be considered in the peri-operative period, and should be based on an individual decision that depends on the peri- operative bleeding risk, weighed against the risk of thrombotic complications.			
In patients treated with $P2Y_{12}$ inhibitors, who need to undergo surgery, postponing surgery for at least 5 days after cessation of ticagrelor and clopidogrel—and for 7 days in the case of prasugrel—if clinically feasible, should be considered unless the patient is at high risk of an ischaemic event.			



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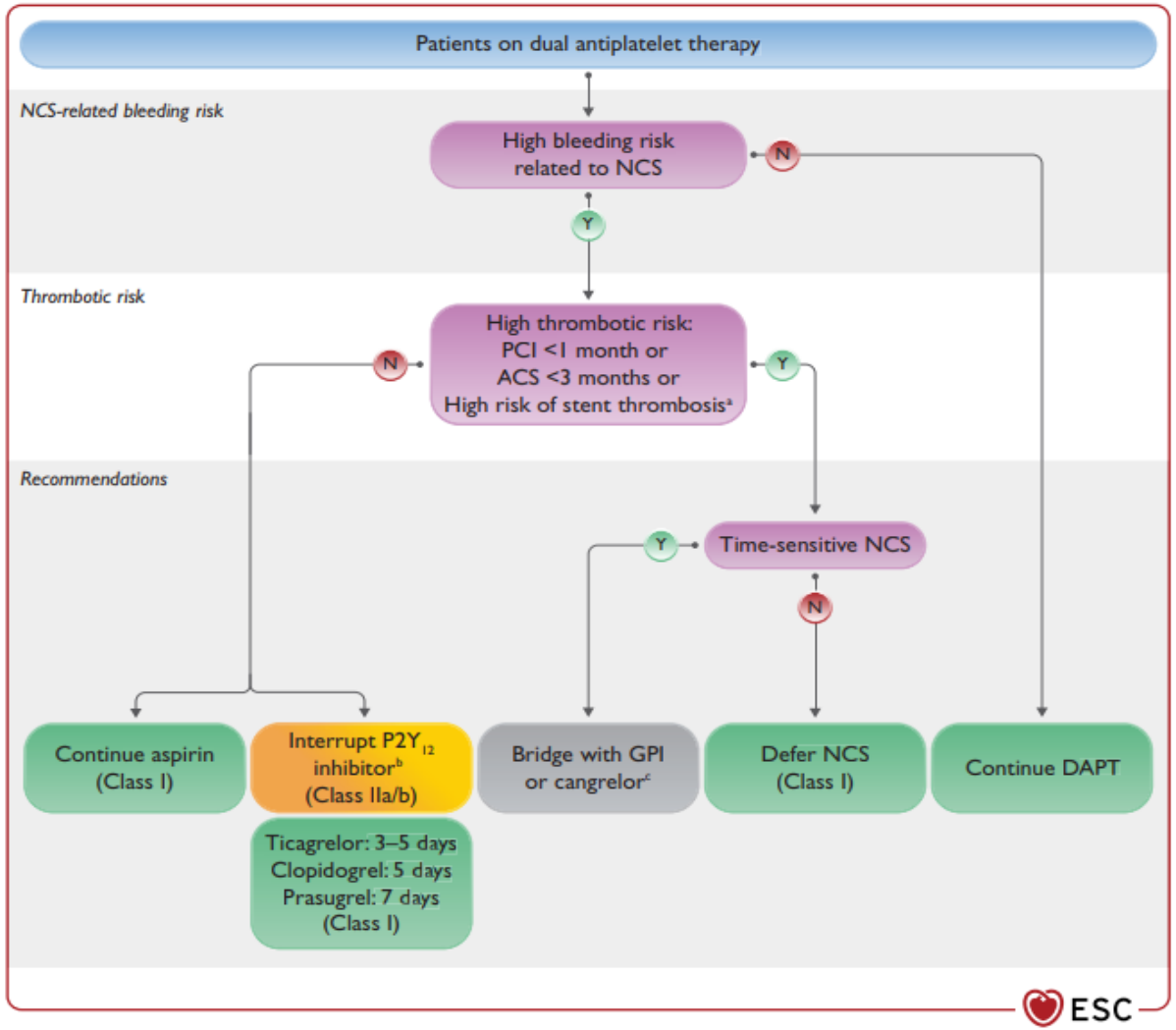
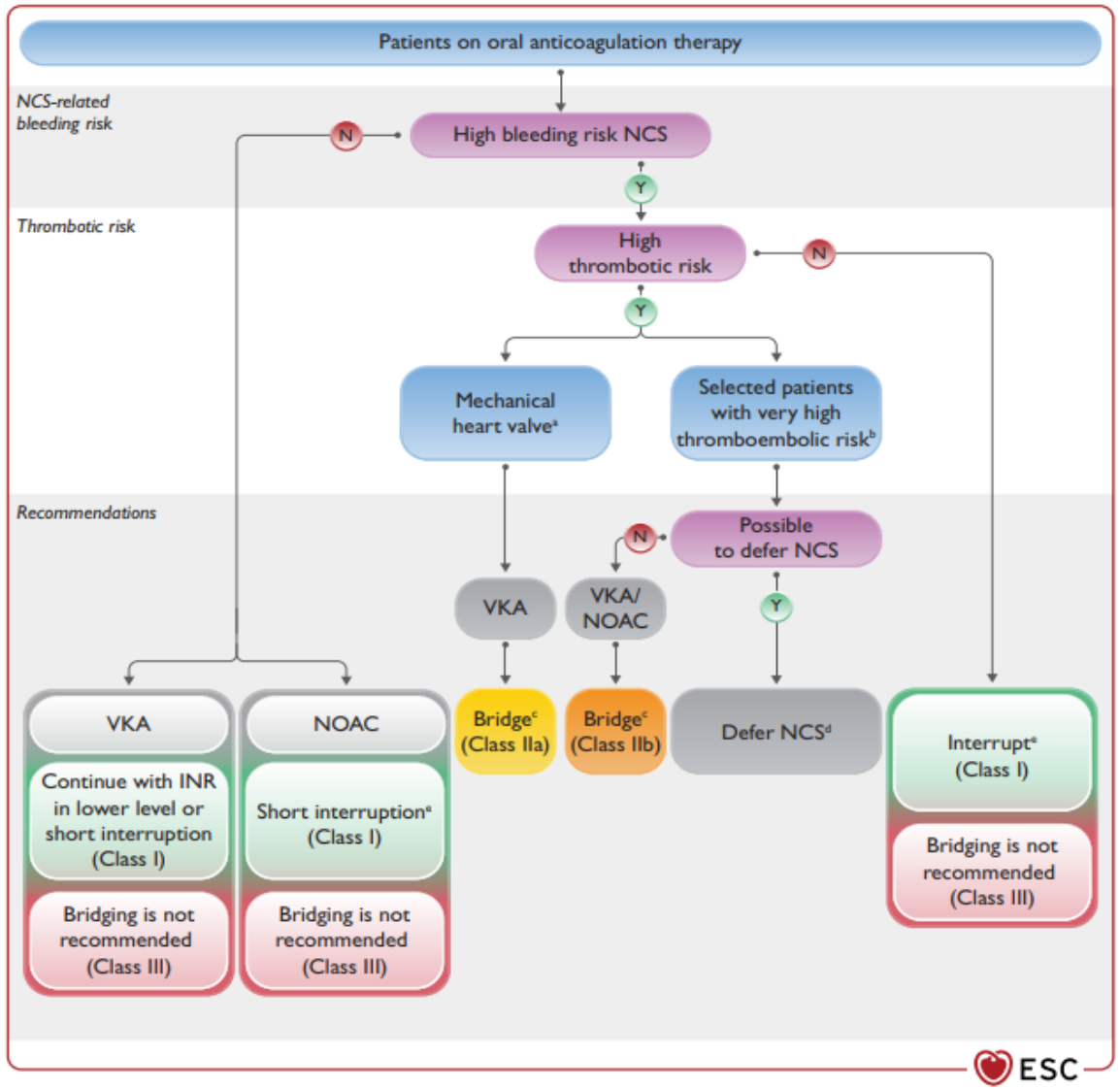
ESC Leitlinie non-cardiac surgery 2022

Pat. unter DAPT



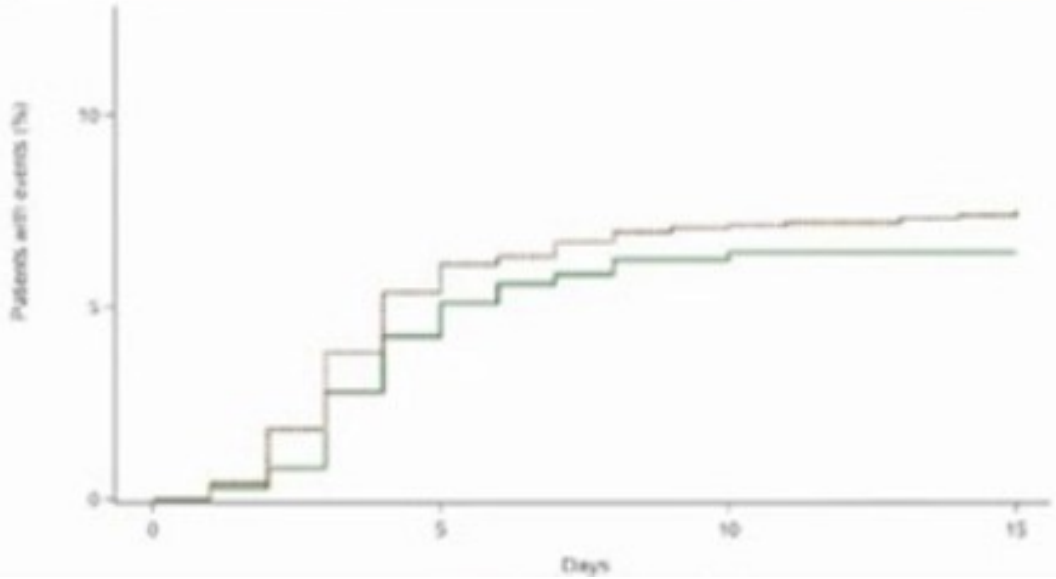
Pat. unter OAK

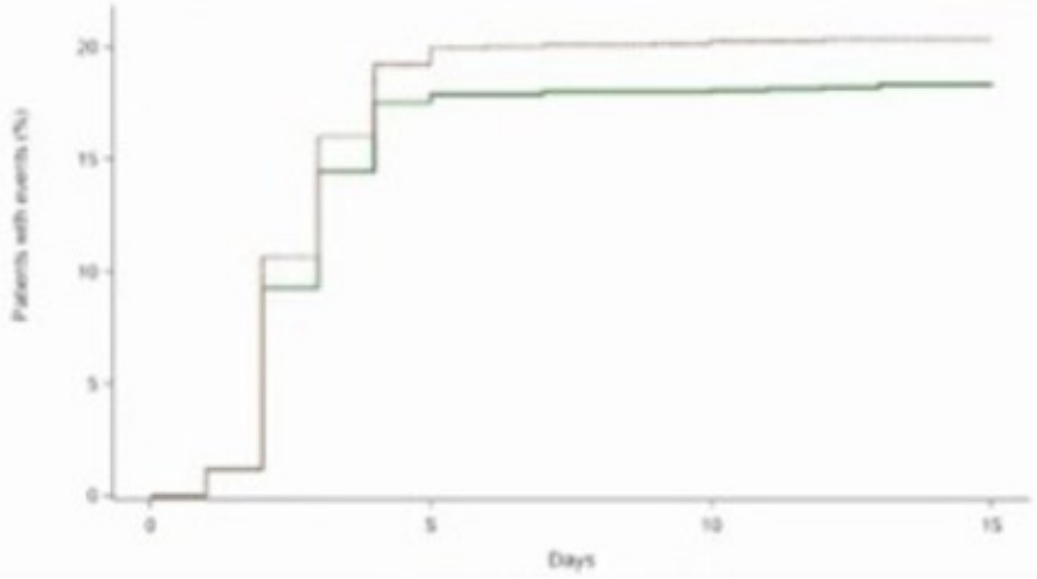


Colchizin perioperativ bei non-cardiac surgery (COP-AF)

Co-primary outcomes

	Colchicine (N=1608)	Placebo (N=1601)	Hazard Ratio (95% CI)	P Value
Clinically important perioperative AF	103 (6.4)	120 (7.5)	0.85 (0.65-1.10)	0.22
Myocardial injury after noncardiac surgery	295 (18.3)	325 (20.3)	0.89 (0.76-1.05)	0.16





Lancet. 2023 Nov 4;402(10413):1627-1635.

Zusammenfassung

- Adhärenz ist entscheidend für den therapeutischen Erfolg
- Das Vorhofflimmerrisiko ist hoch, insb. Bei Männern
- A$_{\text{ntikoagulation}}$ B$_{\text{essere Symptomkont.}}$ C$_{\text{omorbiditäten}}$ Schema ist zentral bei der Therapie
- Tripletherapie nur noch sehr kurz verwenden
- Bridging nur in Ausnahmefällen
- P2Y12-Hemmer 7 (Prasu) bzw. 5 (Tica, Clopi) Tage vor OP absetzen