Bezirksärzte - 25.09.2024

Antikoagulation bei kardiologischen Patienten

Assoz. Prof. PD Dr. Dirk von Lewinski

Abteilung für Kardiologie

Medizinische Universität Graz

Agenda

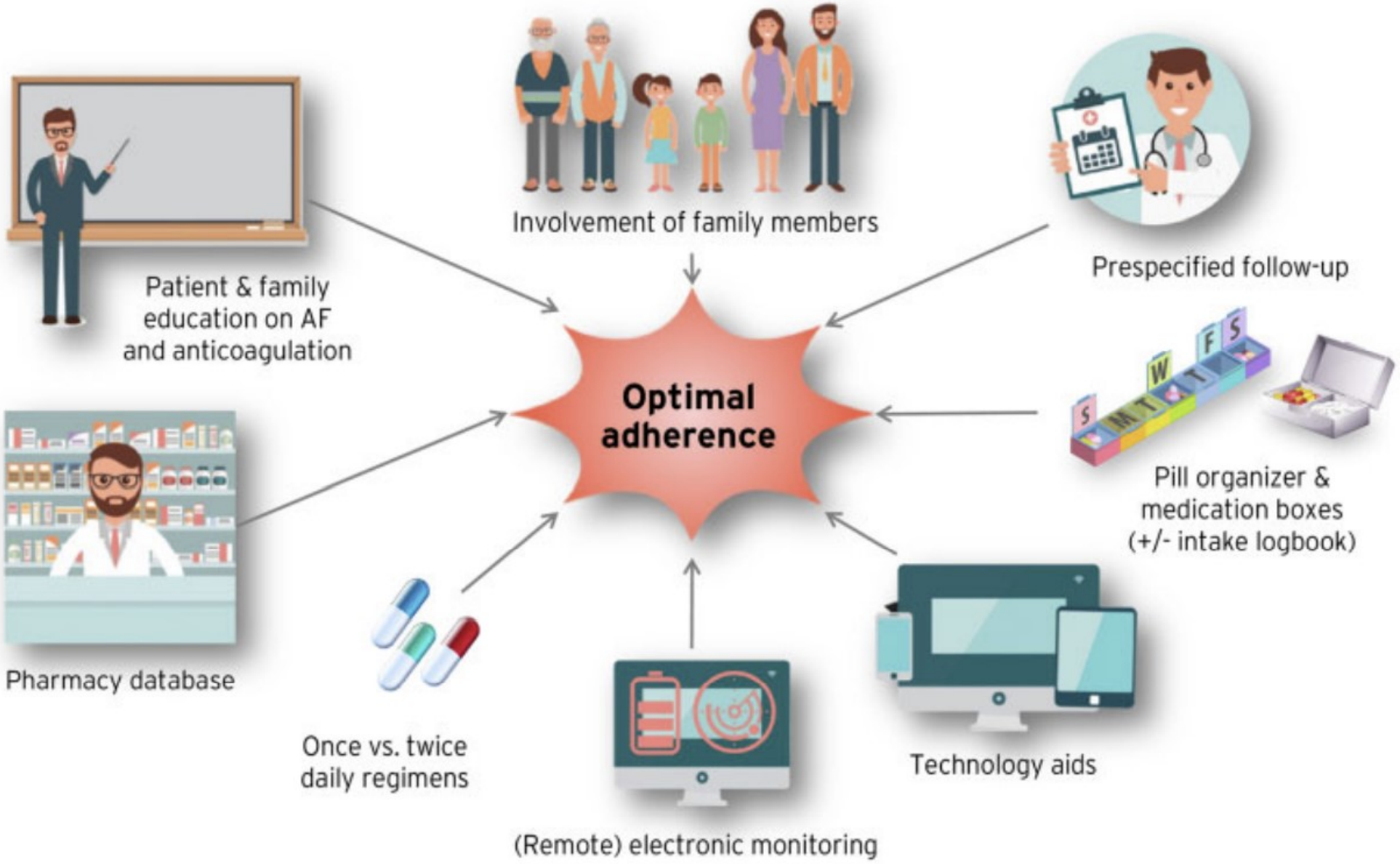
- VHF – ESC guideline
- Andere kardiologische Erkrankungen – Antikoagulation?

- Verwendung von NOAKs – EHRA statement
- Verwendung am LKH/MedUNI bei
  - PCI
  - TAVI
  - Deviceimplantation
  - Aktive Blutungen

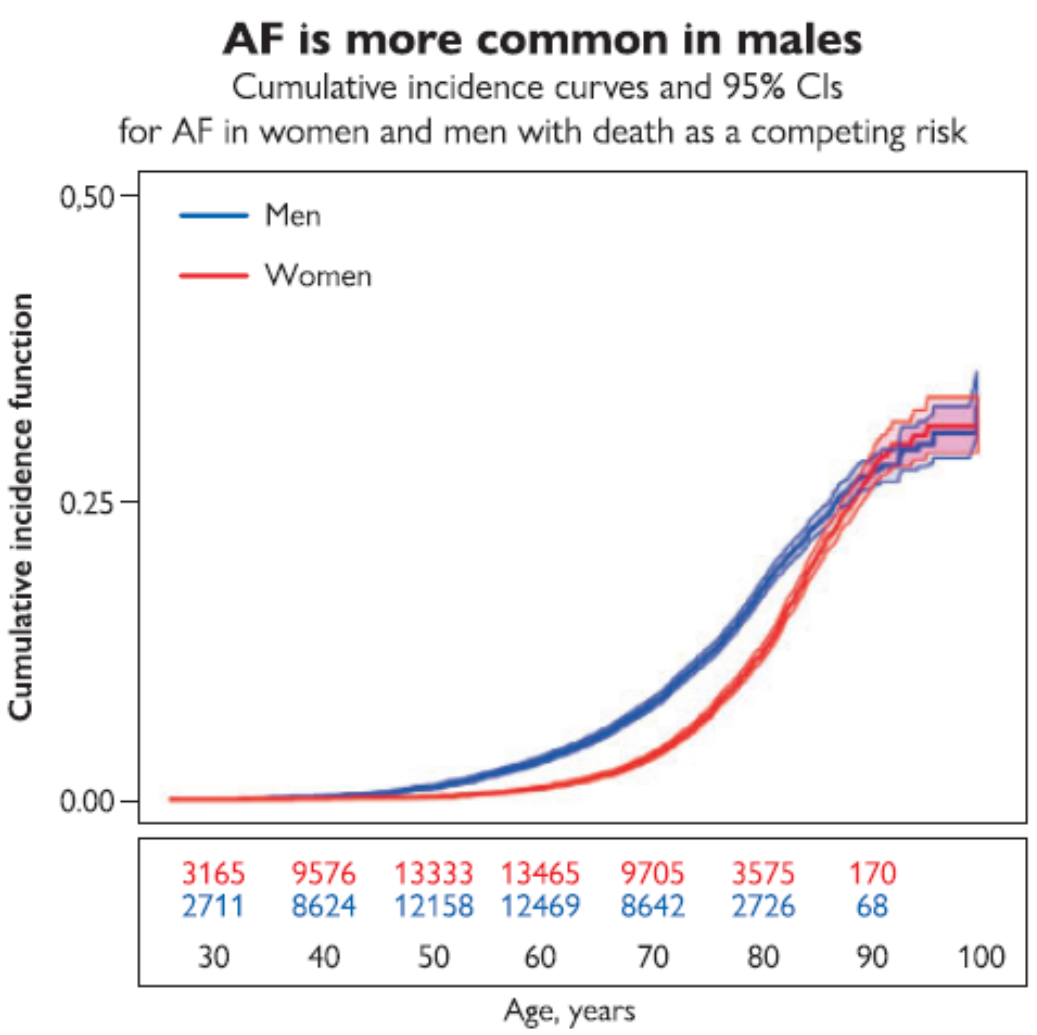
- AHRE (NOAH-Studie)

- MINS – Myocardial injury in non-cardiac surgery

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

Warum eigene Guidelines für Vorhofflimmern (VHFA)?



2-3fach erhöhte Mortalitätsrate

Ursache von 20-30% aller ischämischen Insulte

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

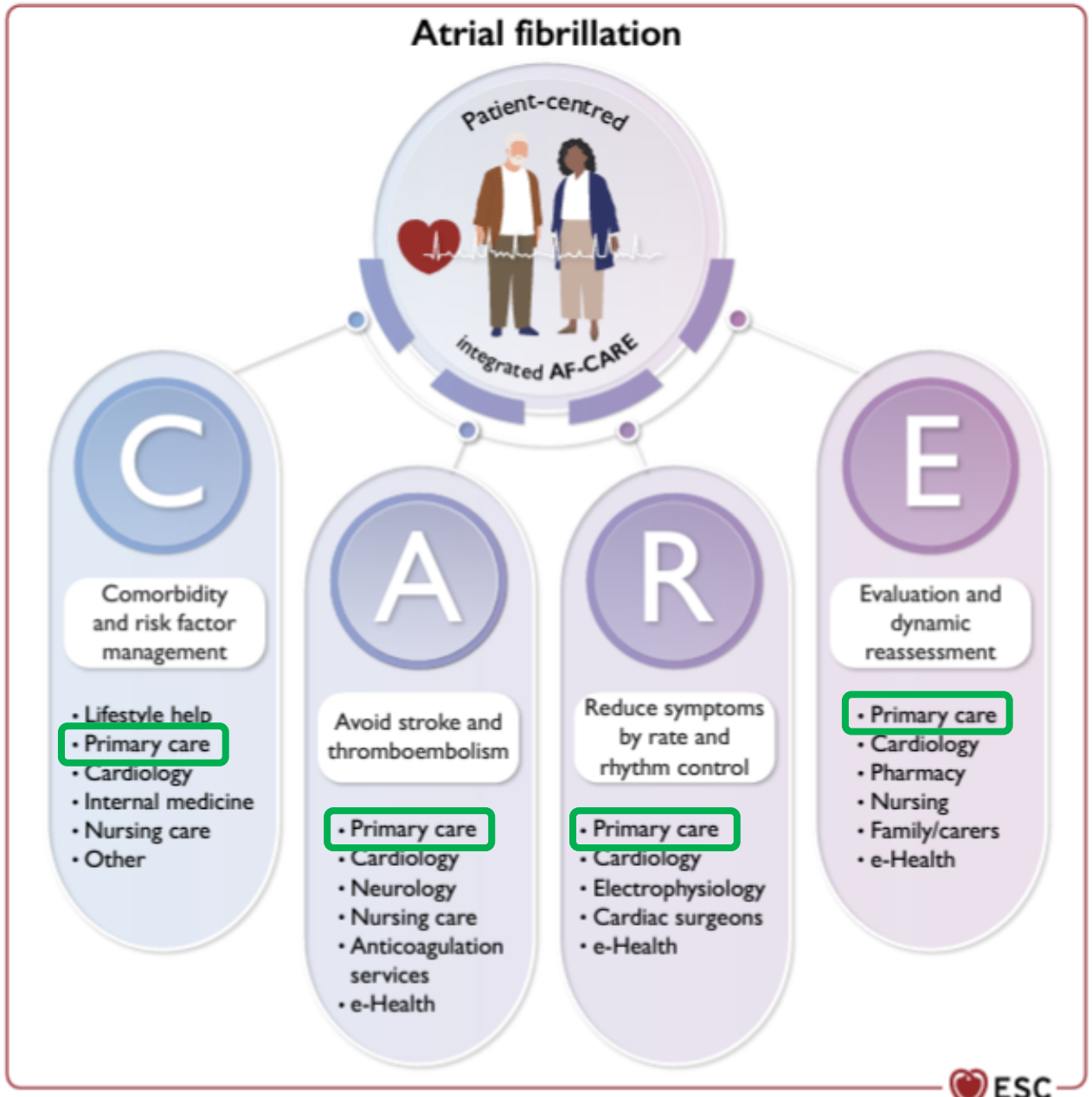
VHFA Guidelines 2020: Das „ABC“ der Therapie

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

2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

European Heart Journal (2024) **00**, 1–101

VHFA Guidelines 2024: Das „CARE“ der Therapie

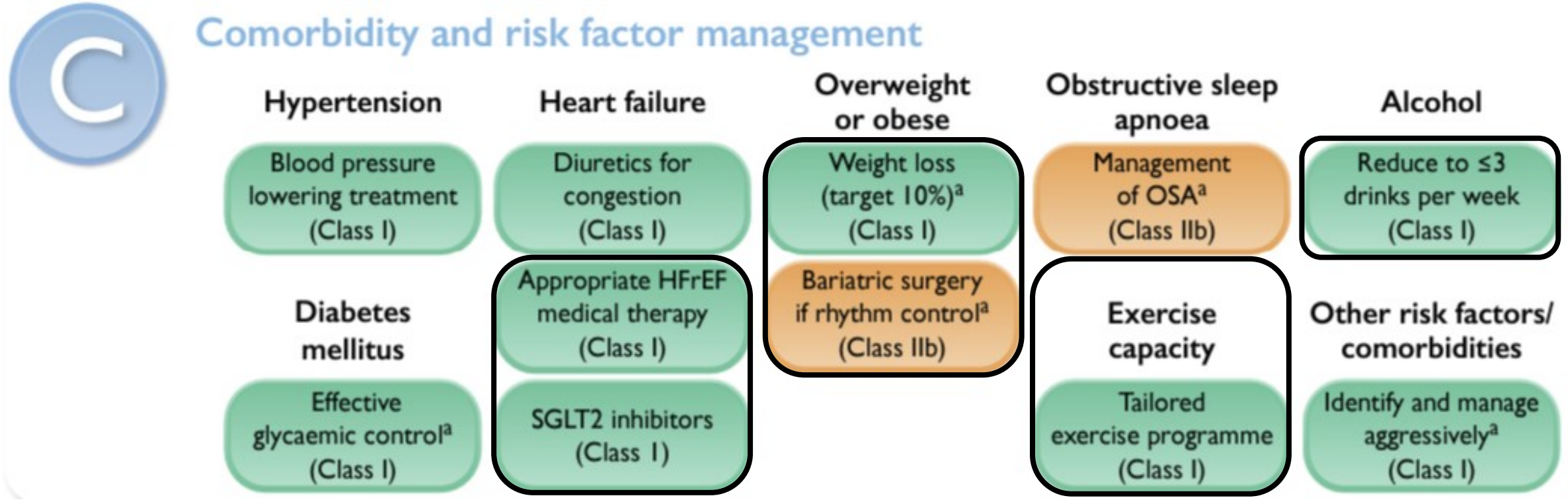


Was ist wichtiger geworden?

- ➢ **Begleiterkrankungen beachten**
- ➢ **Ischämievermeidung**
- ➢ **Rhythmuserhalt**
- ➢ **Team-Ansatz**

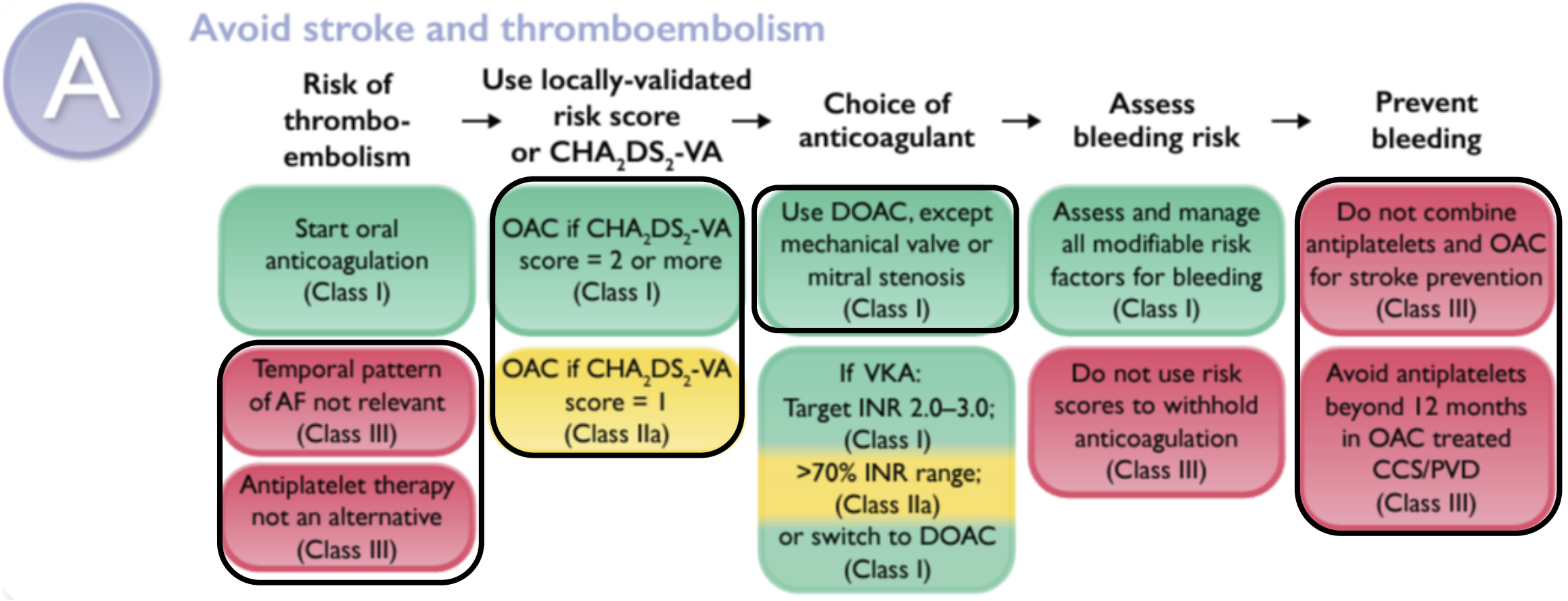
European Heart Journal (2024) **00**, 1–101

VHFA Guidelines 2024: permanentes Vorhofflimmern



- **4-Säulen Therapie bei HFrEF, SGLT2i für alle**
- **GLP1-RA werden auch hier Einzug erhalten**
- **(ambulante) Rehabilitation großzügig indiziert**
- **Mäßiger Alkoholkonsum**

VHFA Guidelines 2024: Das „CARE“ der Therapie



- **Bei VHF immer primär Antikoagulation**
- **Geschlecht spiel keine Rolle mehr**
- **Erste Wahl (immer) DOAK**
- **Möglichst wenig Plättchenhemmung**

European Heart Journal (2024) **00**, 1–101

VHFA Guidelines 2024: Das „CARE“ der Therapie

R — Reduce symptoms by rate and rhythm control

See patient pathways for:

- First-diagnosed AF
- Paroxysmal AF
- Persistent AF
- Permanent AF

Consider:

- Rate control drugs
- Cardioversion
- Antiarrhythmic drugs
- Catheter ablation
- Endoscopic/hybrid ablation
- Surgical ablation
- Ablate and pace

➢ **Abladieren!**

E — Evaluation and dynamic reassessment

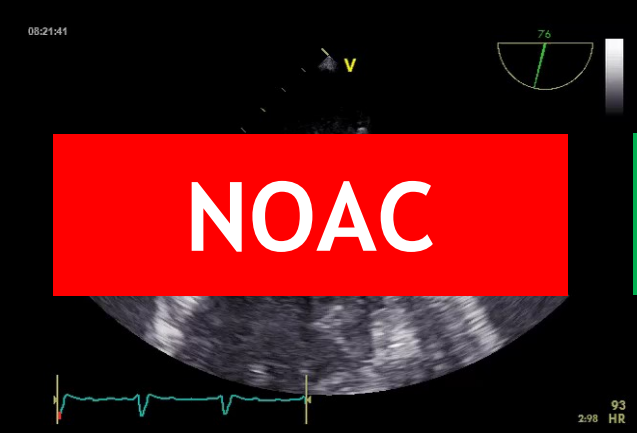
Re-evaluate when AF episodes or non-AF admissions

Regular re-evaluation: 6 months after presentation, and then at least annually or based on clinical need

- ECG, blood tests, cardiac imaging, ambulatory ECG, other imaging as needed
- Assess new and existing risk factors and comorbidities (Class I)
- Stratify risk for stroke and thromboembolism (Class I)
- Check impact of AF symptoms before and after treatment (Class I)
- Assess and manage modifiable bleeding risk factors (Class I)
- Continue OAC despite rhythm control if risk of thromboembolism (Class I)

European Heart Journal (2024) **00**, 1–101

Antikoagulation bei kardialen Erkrankungen

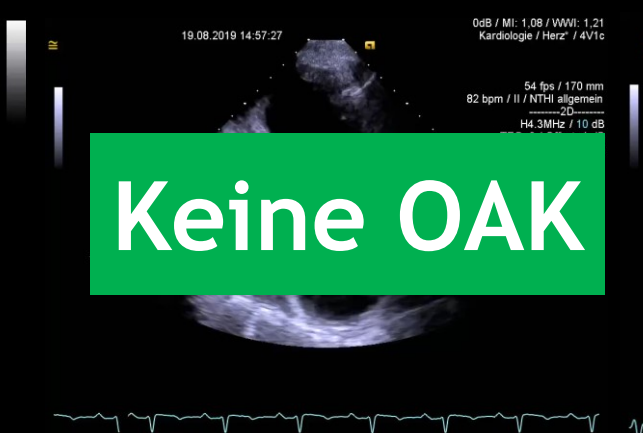


NOAC

Vorhofflimmern

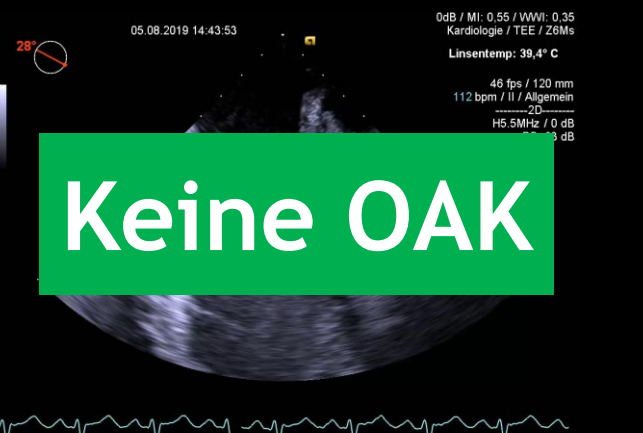
Keine OAK

Herzinsuffizienz



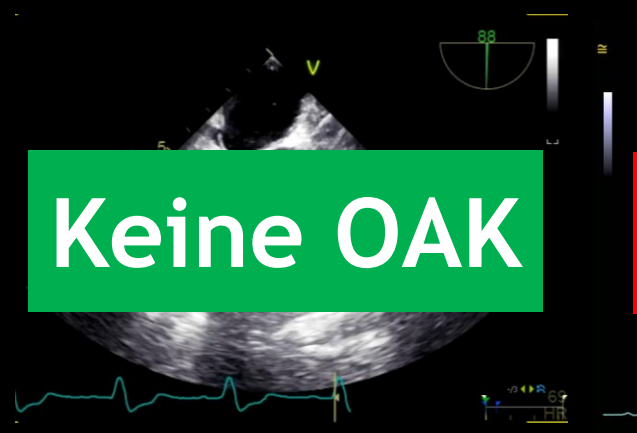
Keine OAK

Aneurysma



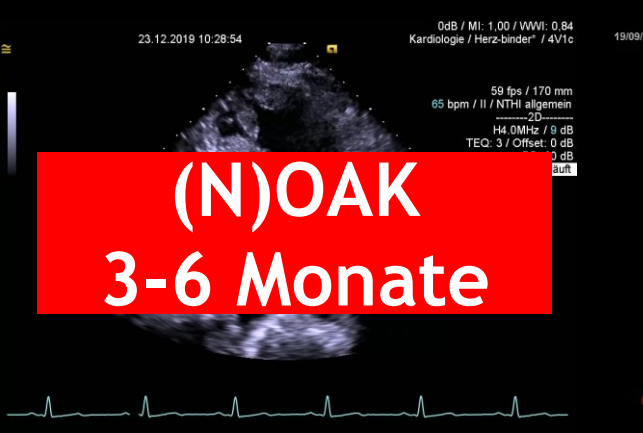
Keine OAK

Endokarditis



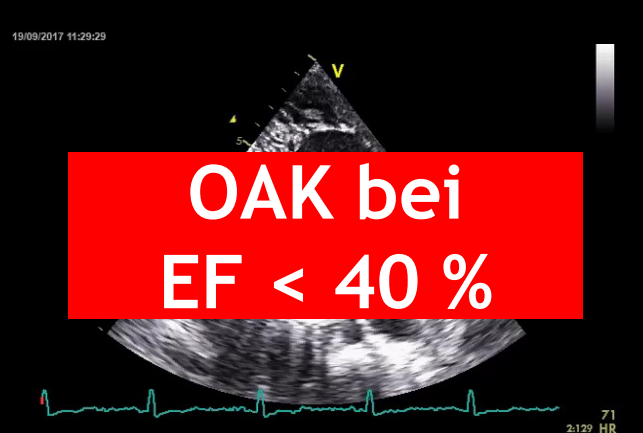
Keine OAK

PFO



(N)OAK 3-6 Monate

Ventrikelthrombus



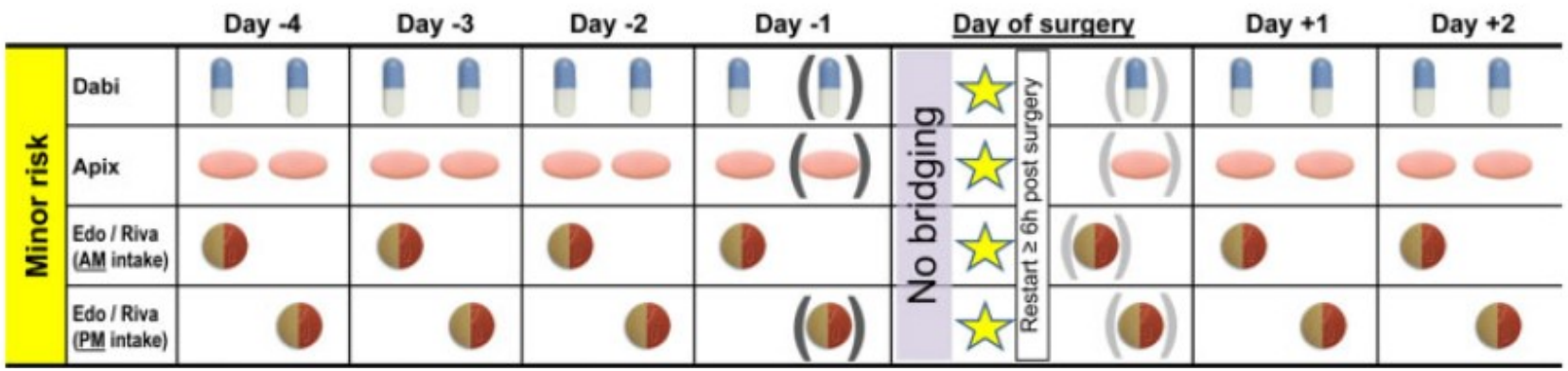
OAK bei EF < 40 %

LVNC

OAK

Klappenprothesen

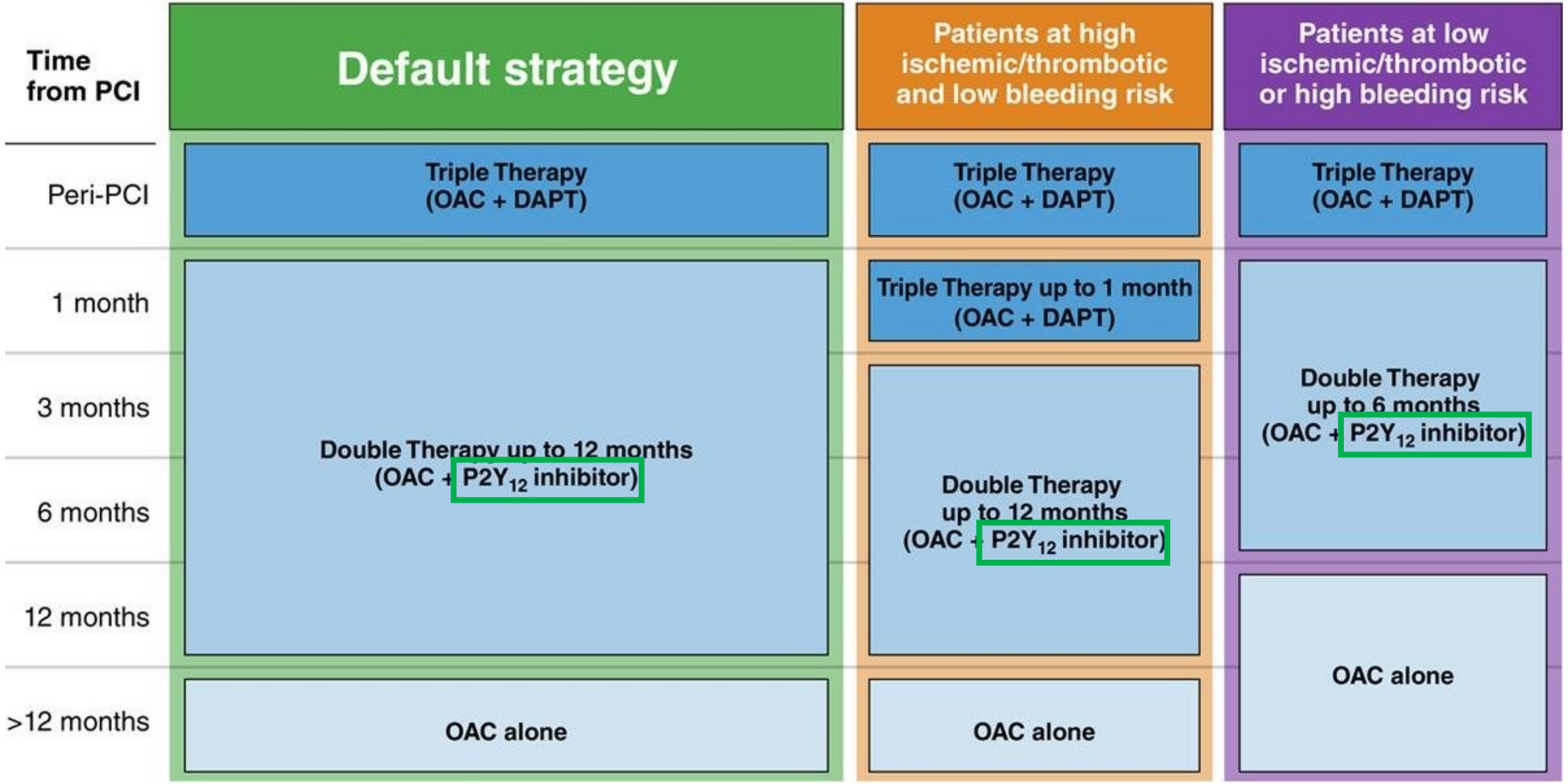
EHRA NOAC Practical Guide: Bridging



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



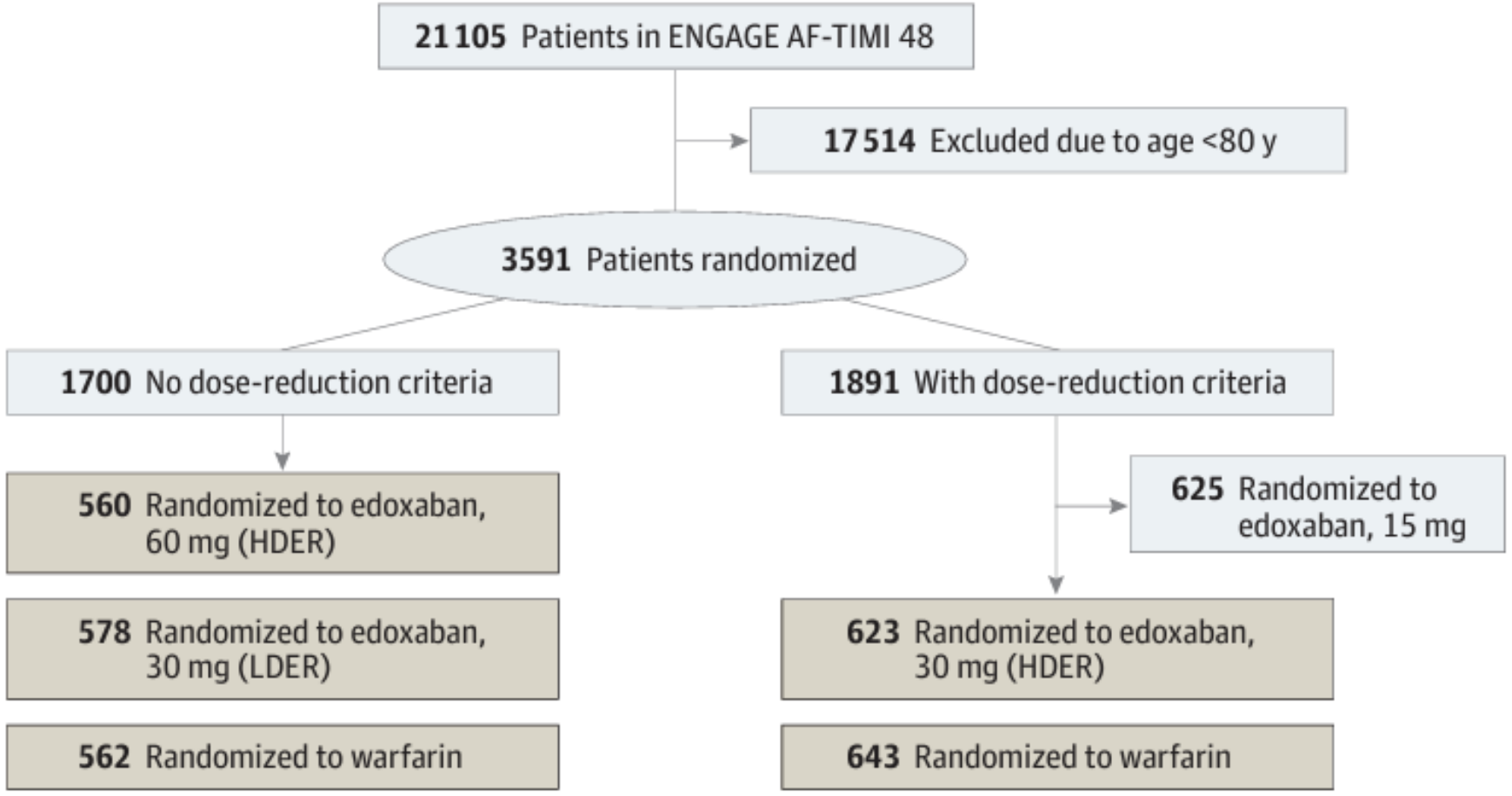
OAK: bei GFR<15 | metallische Herzklappe!

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

Dosierung Edoxaban

Dose Reduction of Edoxaban in Patients 80 Years and Older With Atrial Fibrillation

ENGAGE-AF TIMI 48 - post-hoc Analyse – Subanalyse bei > 80 Jahre alten Patienten (N = 2966)

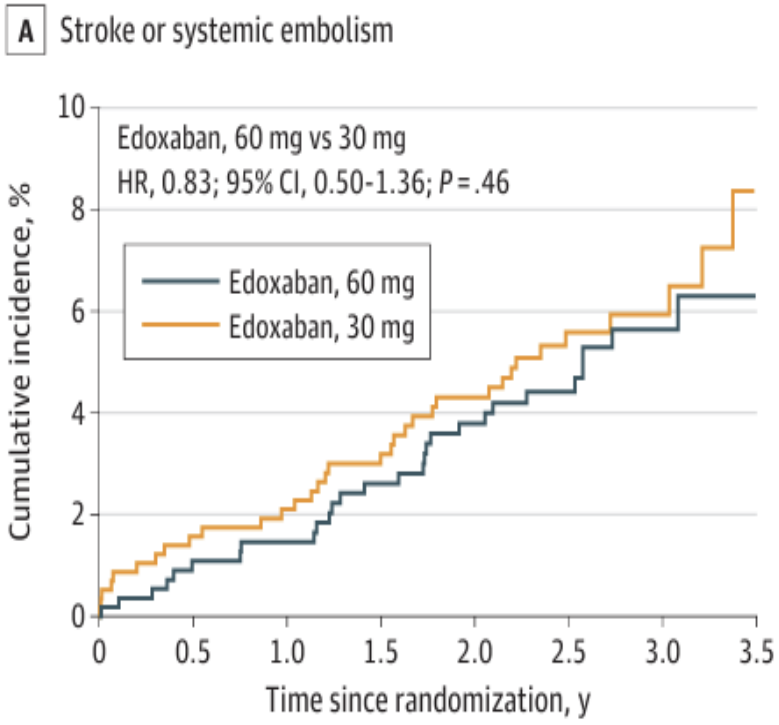


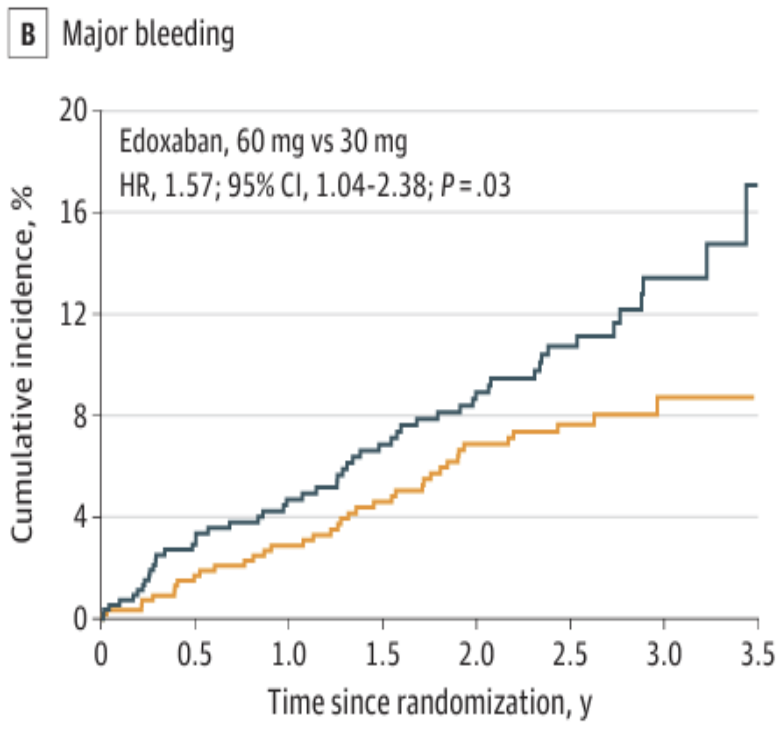
JAMA Cardiol. 2024;9(9):817-825.

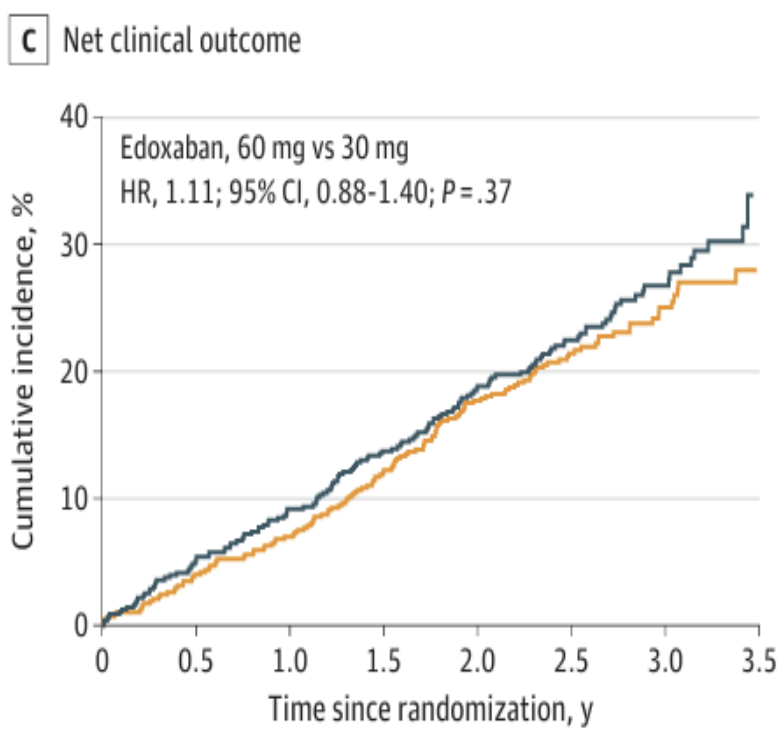
Dosierung Edoxaban

Dose Reduction of Edoxaban in Patients 80 Years and Older With Atrial Fibrillation

ENGAGE-AF TIMI 48 - post-hoc Analyse – Subanalyse bei > 80 Jahre alten Patienten (N = 296)







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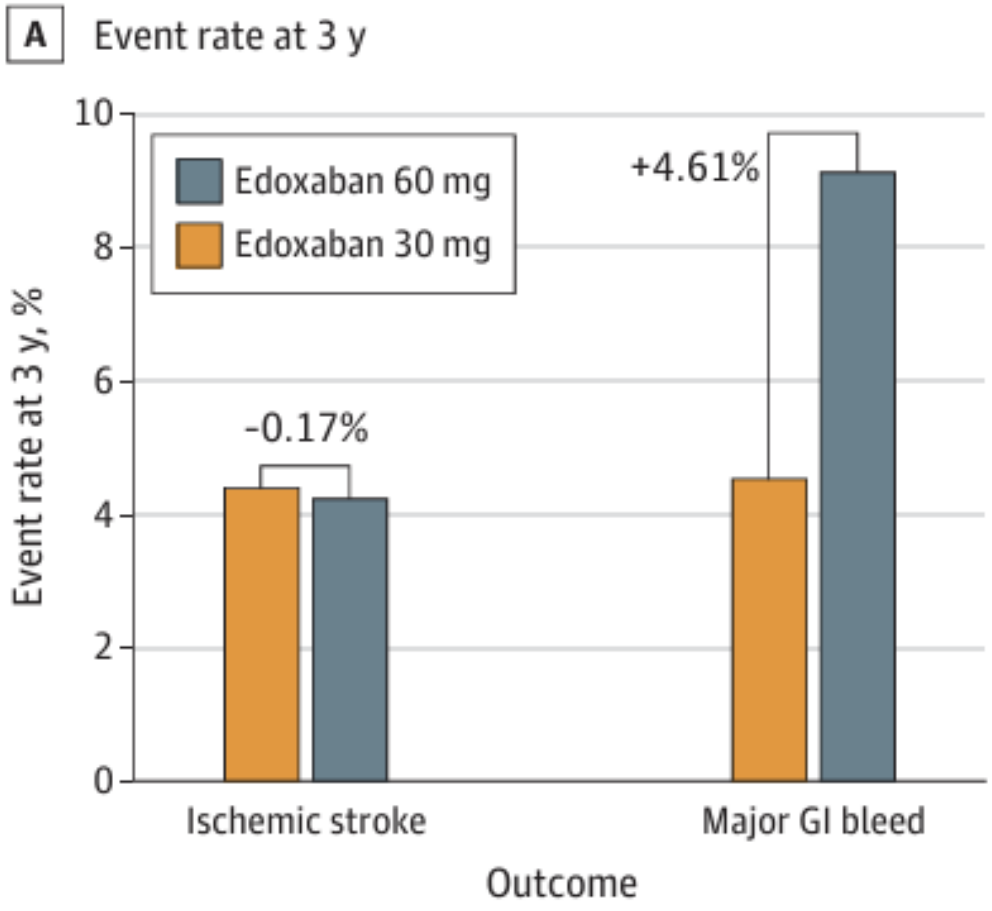
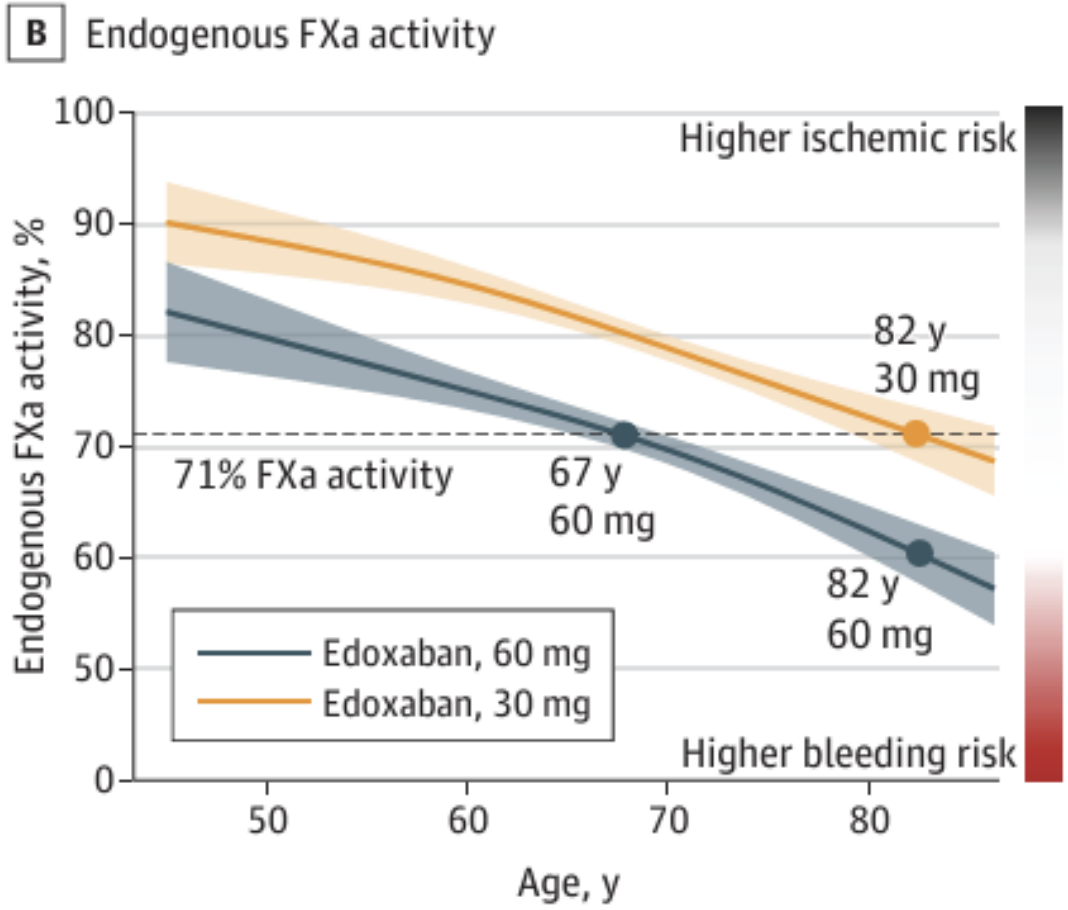




Krea-Clearance < 50 mL/min., Gewicht < 60kg, starke P-Glykoprotein Inhibitoren

JAMA Cardiol. 2024;9(9):817-825.

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

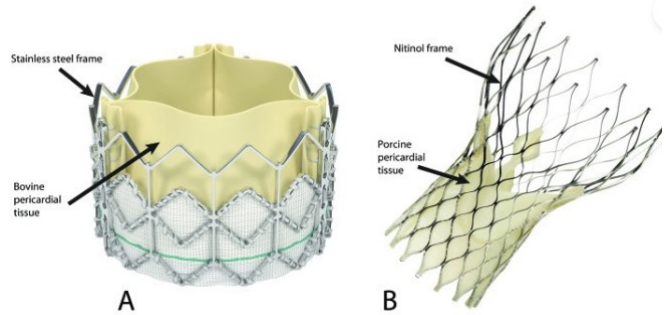
OAC Monotherapie
O

(DAPT)
A und C
oder
SAPT
A oder C

O OAC (präferentiell NOAKs, alternativ VKAs)

A Aspirin 75-100mg täglich

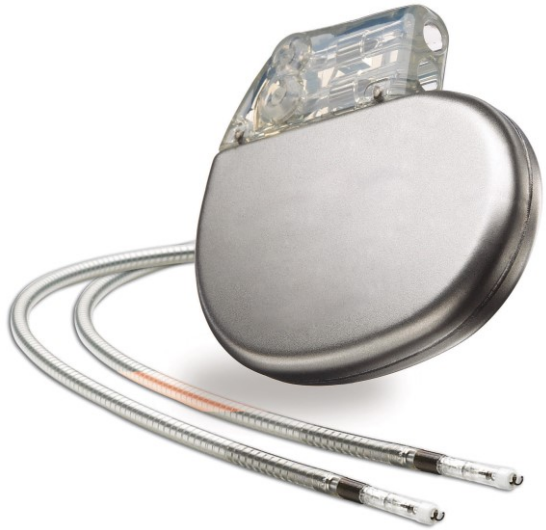
C Clopidogrel 75mg täglich



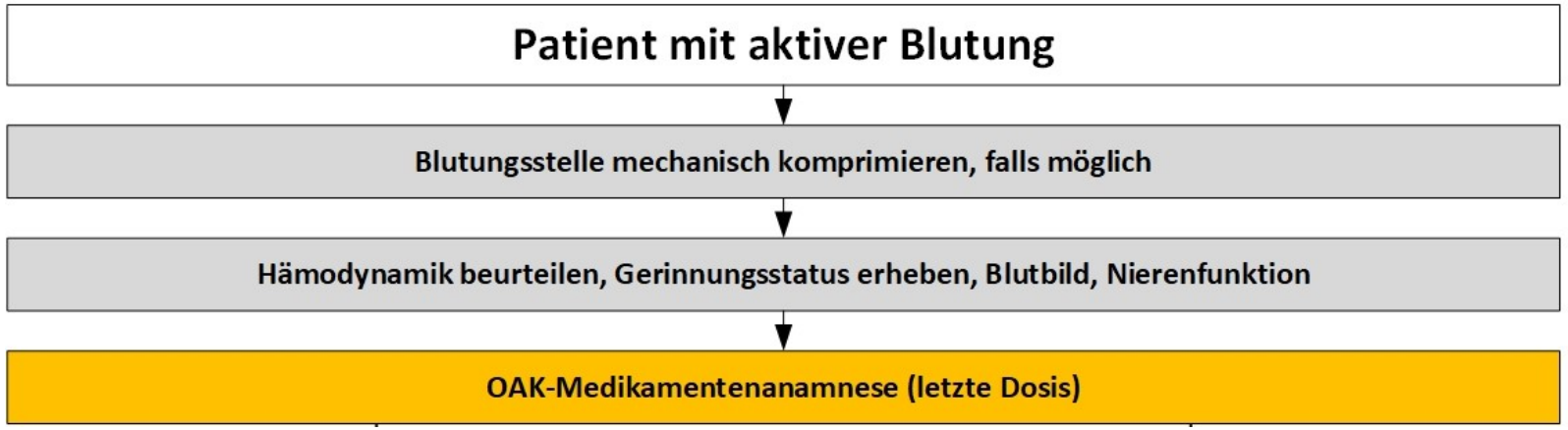
NOAKs und Deviceimplantation - SOP UHZ Graz

- 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

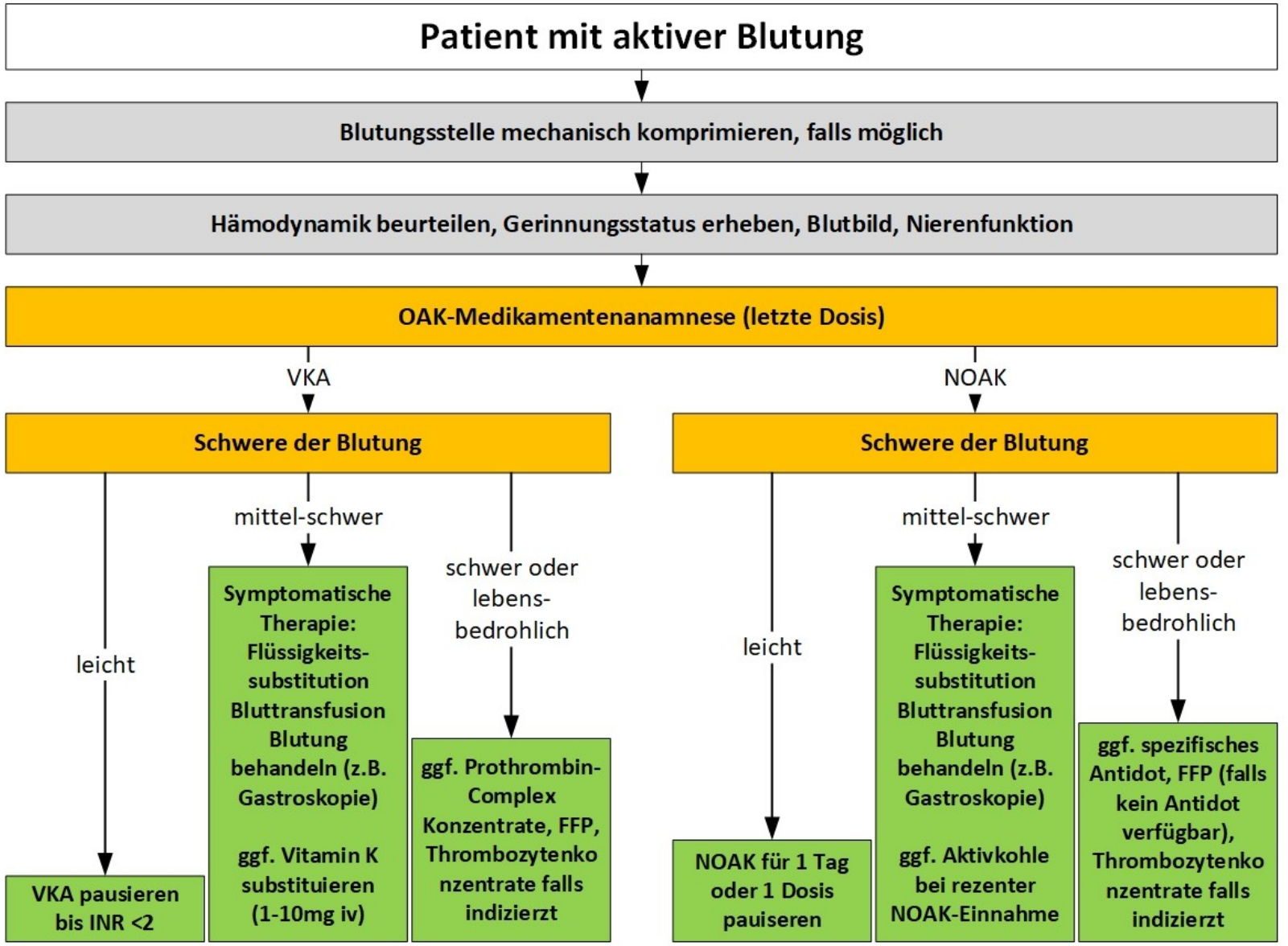
	Dabigatran		Apixaban - Edoxaban - Rivaroxaban	
No perioperative bridging with LMWH / UFH				
Minor risk procedures: - Perform procedure at NOAC trough level (i.e., 12 h / 24 h after last intake). - Resume same day or latest next day.				
	Low risk	**High risk**	**Low risk**	**High risk**
CrCl ≥80 ml/min	≥ 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			



Antikoagulation + Blutung

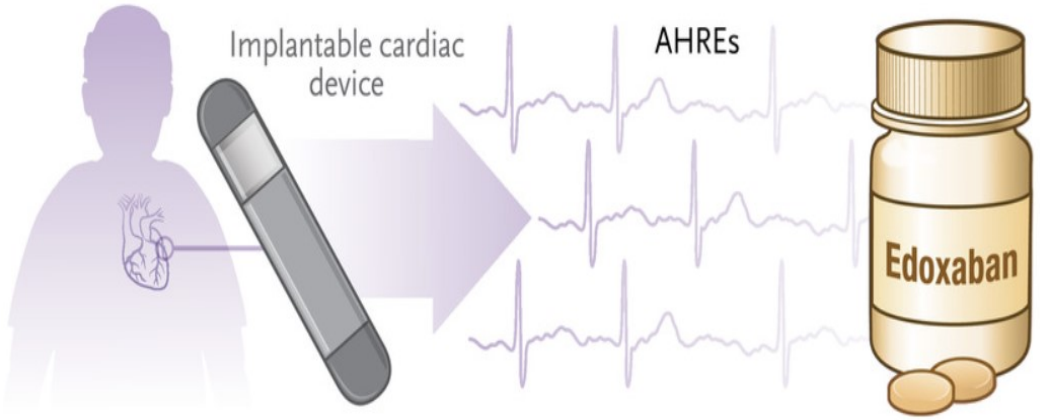


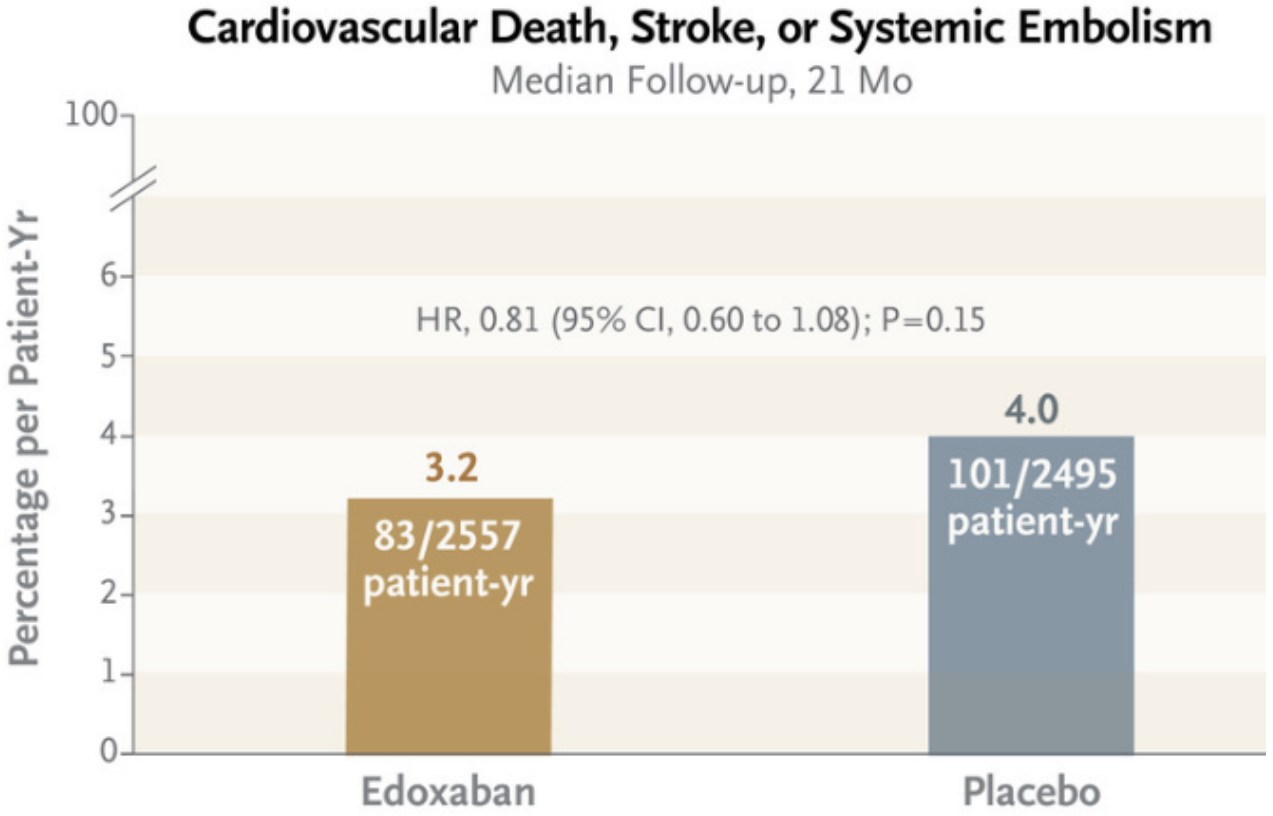
Antikoagulation + Blutung



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.

Grundlage

ESC European Society of Cardiology

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

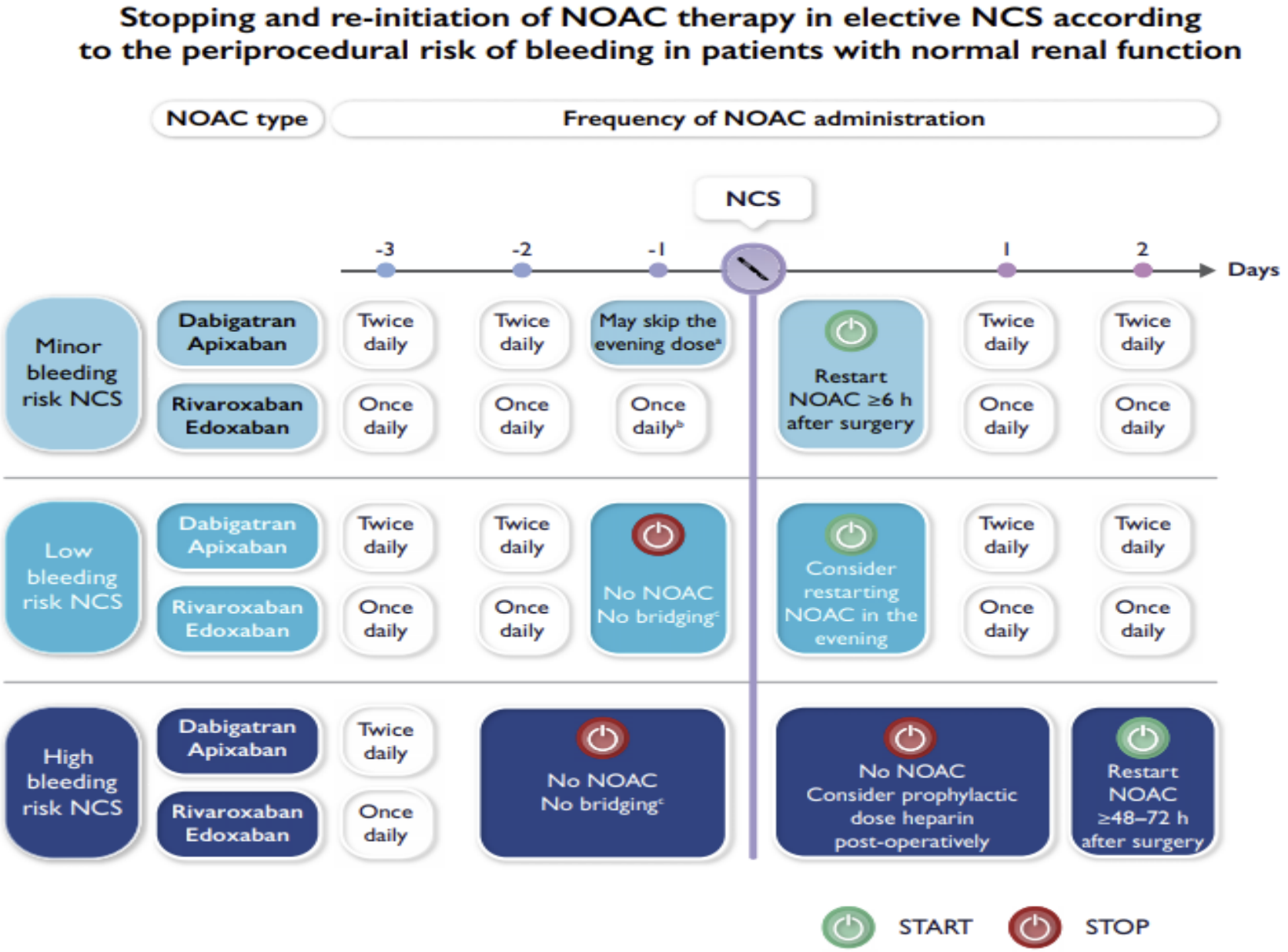
ESC GUIDELINES

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

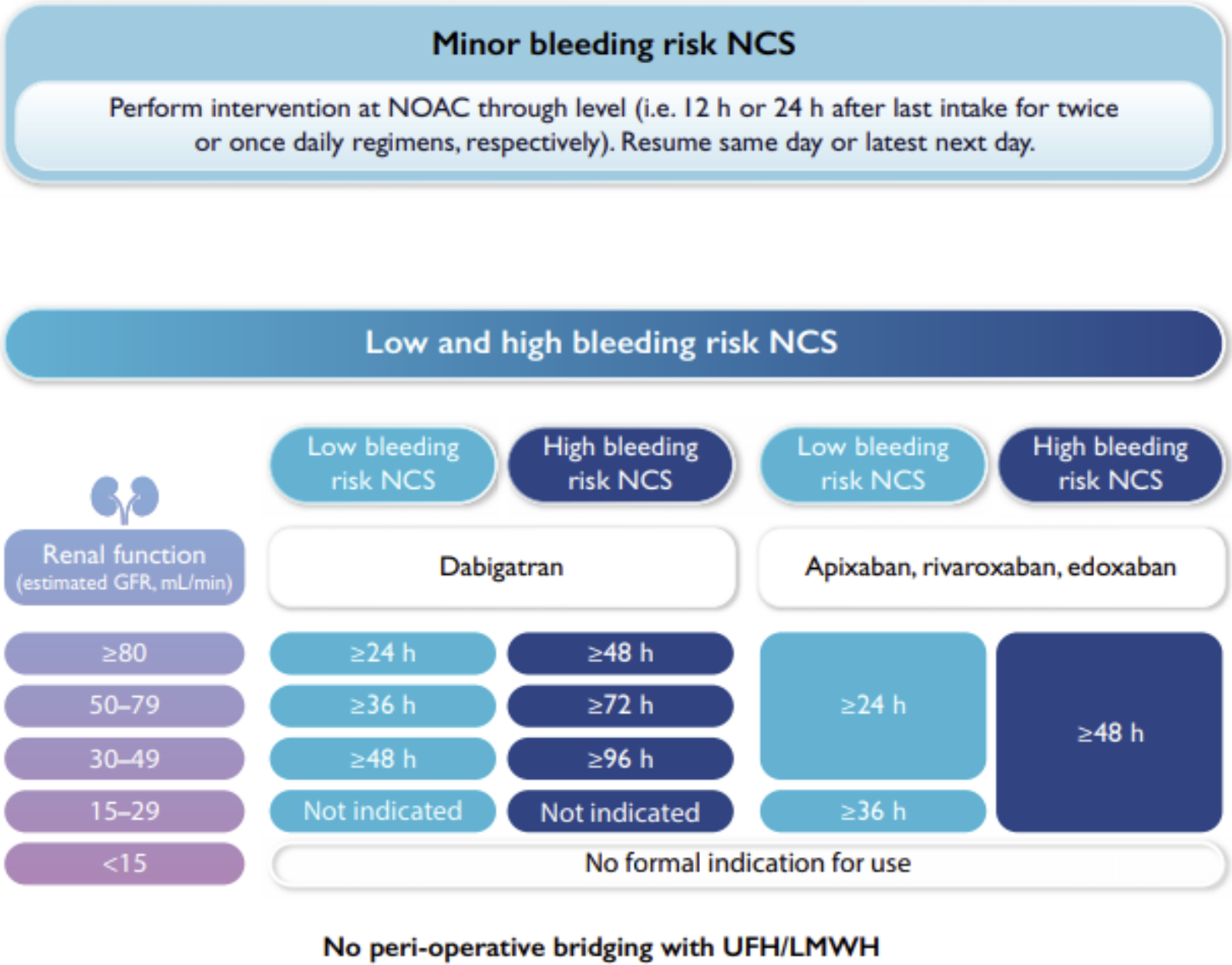
Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

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

VHFA: Antikoagulation

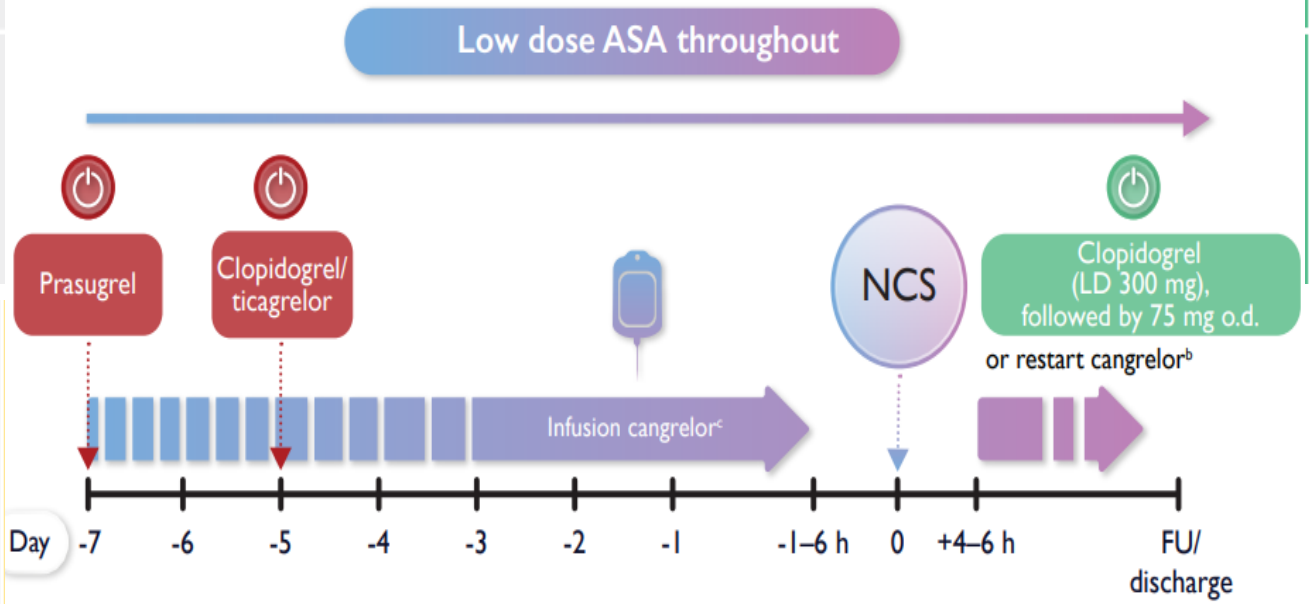


Timing of last NOAC dose before elective NCS according to renal function



ESC Leitlinie non-cardiac surgery 2022

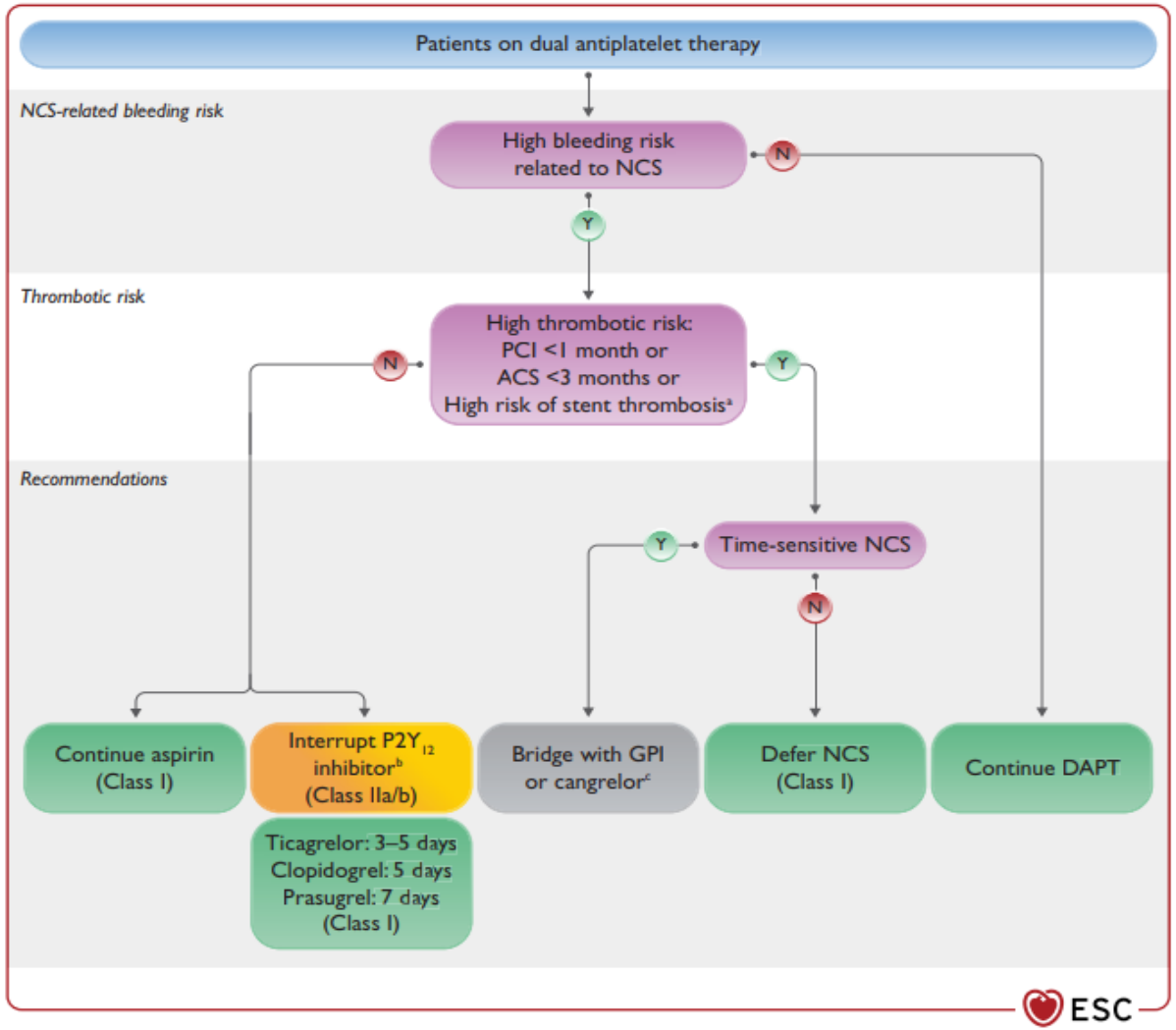
Antiplatelets			
Consideration should be given to performing non-urgent NCS in patients who have had recent DES implantation no sooner than 12 months following the intervention. This delay may be reduced to 6 months for the new-generation DES.	IIa	Elektive nicht kardiale Operationen sollten nach PCI 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.			



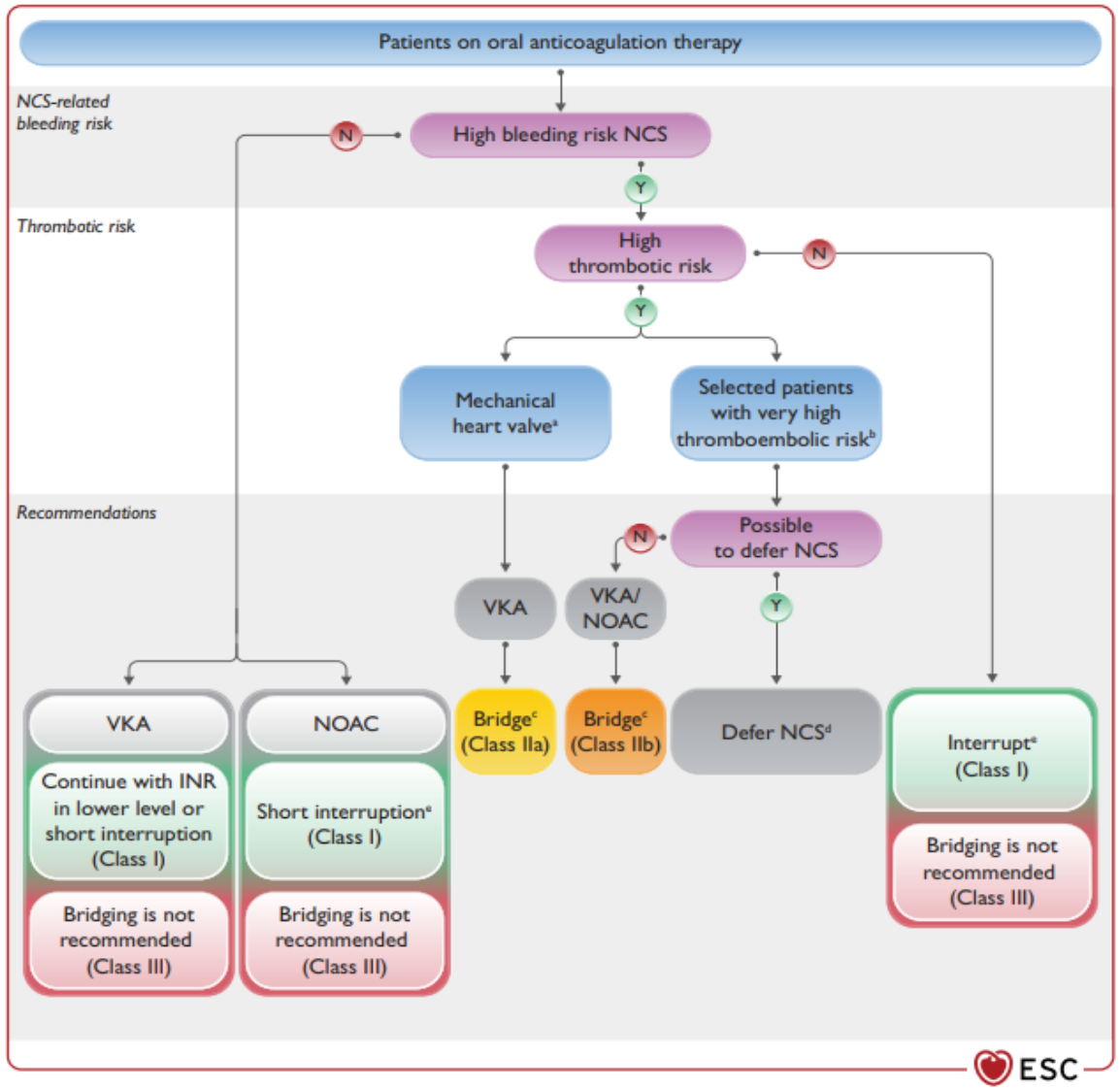
European Heart Journal (2022) **00**, 1–99

ESC Leitlinie non-cardiac surgery 2022

Pat. unter DAPT



Pat. unter OAK



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]

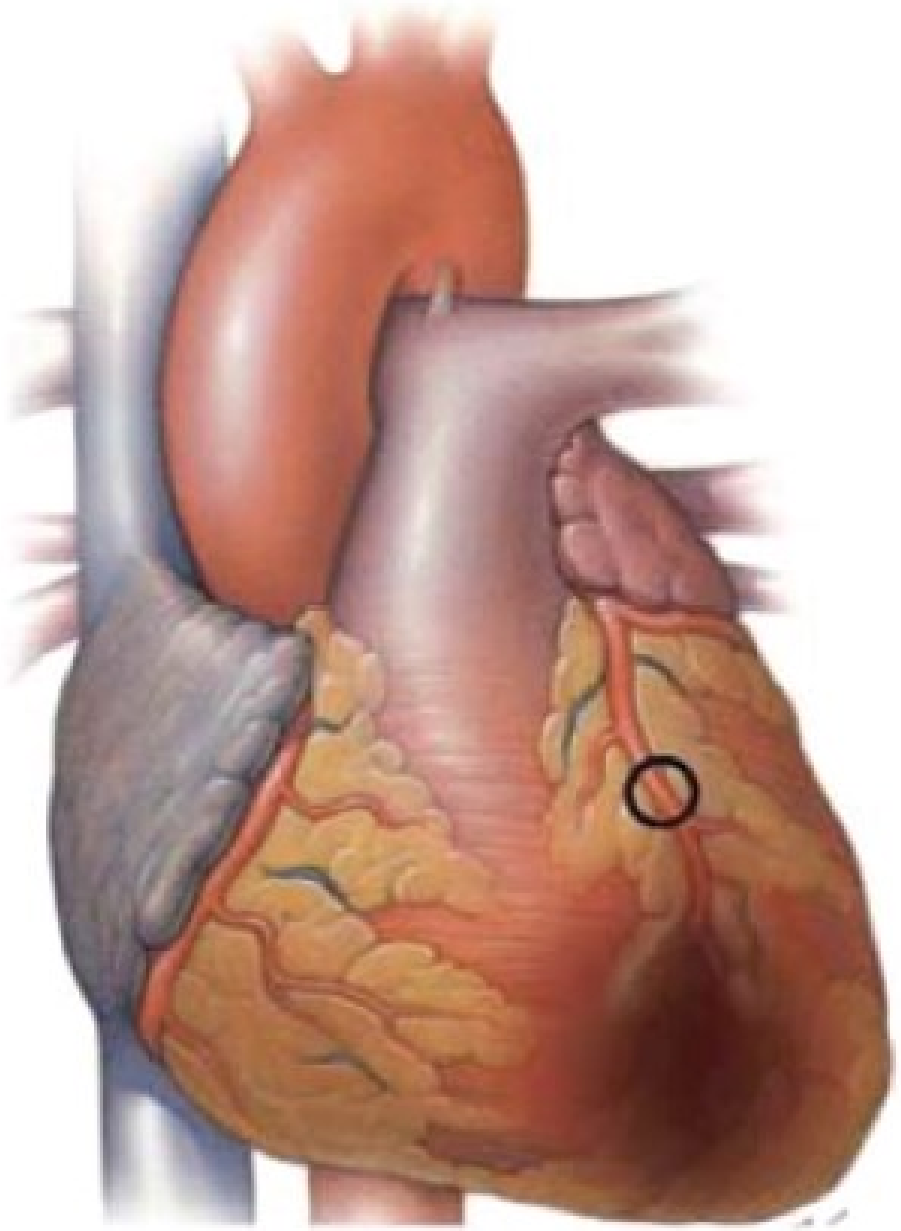
	hsTnT Thresholds, ng/L					
	<5	5 to <14	14 to <20	20 to <65	65 to <1000	≥1000
Patients, No. (%)	5318 (24.4)	8750 (40.1)	2530 (11.6)	4049 (18.6)	1118 (5.1)	54 (0.2)
Deaths, No. (%)	6 (0.1)	40 (0.5)	29 (1.1)	123 (3.0)	102 (9.1)	16 (29.6)
Adjusted hazard ratio (95% CI)	1 [Reference]	3.73 (1.58-8.82)	9.11 (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



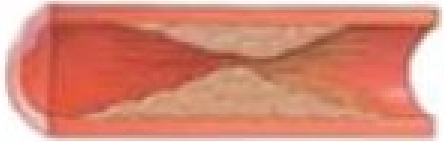
Plaque rupture with thrombus

MI Type 1

Vasospasm or endothelial dysfunction

MI Type 2

Fixed atherosclerosis and supply-demand imbalance

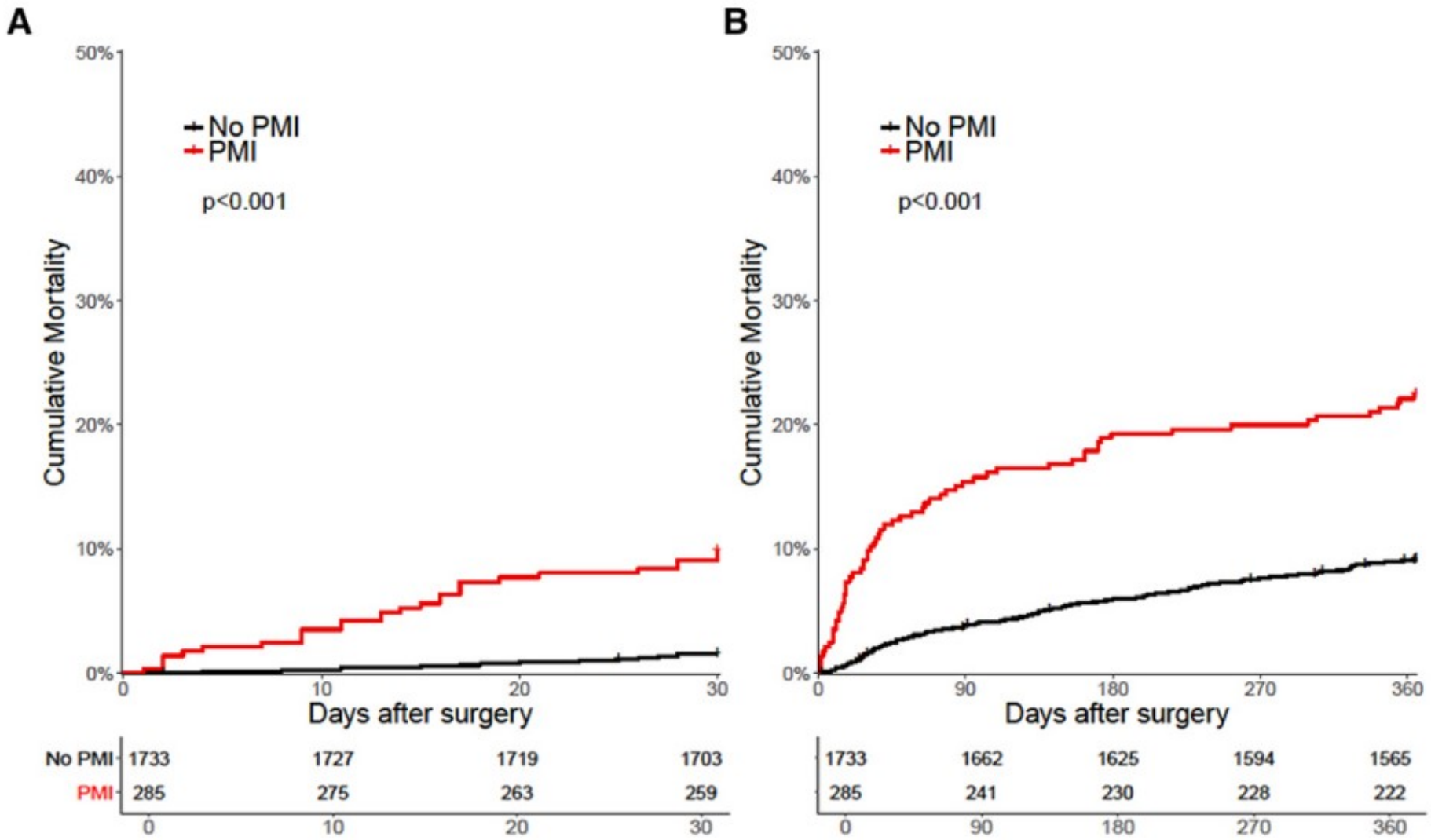


MI Type 2

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

MINS - NTproBNP

10 402 Patienten > 45 Jahre mit noncardiac surgery
Wertigkeit des baseline-NTproBNP

Variable	All Patients, *n* (%) (*n* = 10 402)	Preoperative NT-proBNP Threshold			
		<100 pg/mL, *n* (%) (*n* = 5356)	100 to <200 pg/mL, *n* (%) (*n* = 1843)	200 to <1500 pg/mL, *n* (%) (*n* = 2608)	≥1500 pg/mL, *n* (%) (*n* = 595)
Age					
45–64 y	5426 (52.2)	3707 (69.2)	767 (41.6)	793 (30.4)	159 (26.7)
65–74 y	2857 (27.5)	1270 (23.7)	632 (34.3)	805 (30.9)	150 (25.2)
≥75 y	2119 (20.4)	379 (7.1)	444 (24.1)	1010 (38.7)	286 (48.1)
Men	5204 (50.0)	2777 (51.8)	812 (44.1)	1277 (49.0)	338 (56.8)
Surgery					
Major vascular	654 (6.3)	203 (3.8)	120 (6.5)	250 (9.6)	81 (13.6)
Major general	1859 (17.9)	922 (17.2)	356 (19.3)	479 (18.4)	102 (17.1)
Major thoracic	277 (2.7)	152 (2.8)	46 (2.5)	71 (2.7)	8 (1.3)
Major urologic/gynecologic	1440 (13.8)	777 (14.5)	242 (13.1)	351 (13.5)	70 (11.8)
Major orthopedic	2632 (25.3)	1239 (23.1)	536 (29.1)	711 (27.3)	146 (24.5)
Major neurologic	524 (5.0)	271 (5.1)	100 (5.4)	131 (5.0)	22 (3.7)
Low-risk	3467 (33.3)	2049 (38.3)	539 (29.2)	702 (26.9)	177 (29.7)
Urgent/emergent	455 (4.4)	159 (3.0)	63 (3.4)	168 (6.4)	65 (10.9)

Ann Intern Med. 2020;172:96-104.

MINS - NTproBNP

10 402 Patienten > 45 Jahre mit noncardiac surgery
Wertigkeit des baseline-NTproBNP

Table 2. Incidence of 30-Day Outcomes, by Preoperative NT-proBNP Values*

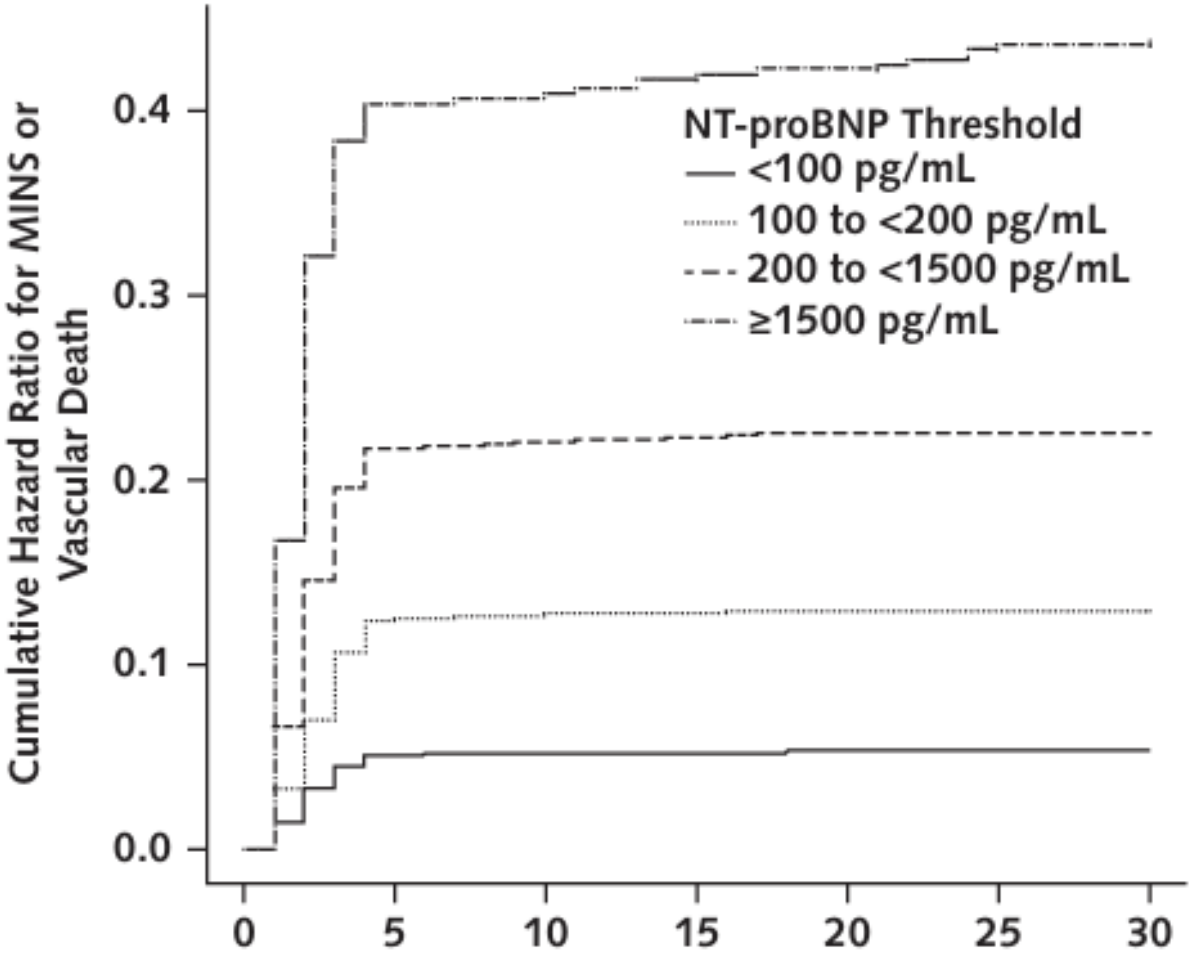
Variable	All Patients (*n* = 10 402)	Preoperative NT-proBNP Threshold			
		<100 pg/mL (*n* = 5356)	100 to <200 pg/mL (*n* = 1843)	200 to <1500 pg/mL (*n* = 2608)	≥1500 pg/mL (*n* = 595)
Composite of vascular death or MINS					
Events, *n* (incidence [95% CI], %)†	1269 (12.2 [11.6–12.8])	278 (5.2 [4.6–5.8])	226 (12.3 [10.8–13.8])	542 (20.8 [19.2–22.3])	223 (37.5 [33.5–41.3])
Adjusted HR (95% CI)	–	1.00	2.27 (1.90–2.70)	3.63 (3.13–4.21)	5.82 (4.81–7.05)
Composite of all-cause mortality or MI					
Events, *n* (incidence [95% CI], %)†	446 (4.3 [3.9–4.7])	92 (1.7 [1.4–2.1])	55 (3.0 [2.2–3.8])	205 (7.9 [6.8–8.9])	94 (15.8 [12.8–18.7])
Adjusted HR (95% CI)	–	1.00	1.57 (1.12–2.19)	3.64 (2.83–4.69)	5.35 (3.91–7.34)
MINS					
Events, *n* (incidence [95% CI], %)†	1237 (11.9 [11.3–12.5])	272 (5.1 [4.5–5.7])	223 (12.1 [10.6–13.6])	529 (20.3 [18.7–21.8])	213 (35.8 [31.9–39.6])
Adjusted HR (95% CI)	–	1.00	2.29 (1.91–2.73)	3.62 (3.12–4.21)	5.70 (4.69–6.92)
MI					
Events, *n* (incidence [95% CI], %)†	378 (3.6 [3.3–4.0])	82 (1.5 [1.2–1.9])	46 (2.5 [1.8–3.2])	175 (6.7 [5.7–7.7])	75 (12.6 [9.9–15.3])
Adjusted HR (95% CI)	–	1.00	1.47 (1.02–2.10)	3.46 (2.64–4.53)	4.68 (3.32–6.60)
All-cause mortality					
Events, *n* (incidence [95% CI], %)†	88 (0.8 [0.7–1.0])	14 (0.3 [0.1–0.4])	13 (0.7 [0.3–1.1])	37 (1.4 [1.0–1.9])	24 (4.0 [2.4–5.6])
Adjusted HR (95% CI)	–	1.00	2.41 (1.13–5.14)	4.12 (2.20–7.73)	8.40 (4.10–17.23)
Vascular death					
Events, *n* (incidence [95% CI], %)†	54 (0.5 [0.4–0.7])	11 (0.2 [0.1–0.3])	8 (0.4 [0.1–0.7])	18 (0.7 [0.4–1.0])	17 (2.9 [1.5–4.2])
Adjusted HR (95% CI)	–	1.00	1.84 (0.74–4.59)	2.41 (1.11–5.21)	6.75 (2.90–15.70)

Ann Intern Med. 2020;172:96-104.

ORIGINAL RESEARCH Annals of Internal Medicine
Preoperative *N*-Terminal Pro-B-Type Natriuretic Peptide and Cardiovascular Events After Noncardiac Surgery

MINS - NTproBNP

10 402 Patienten > 45 Jahre mit noncardiac surgery
Wertigkeit des baseline-NTproBNP



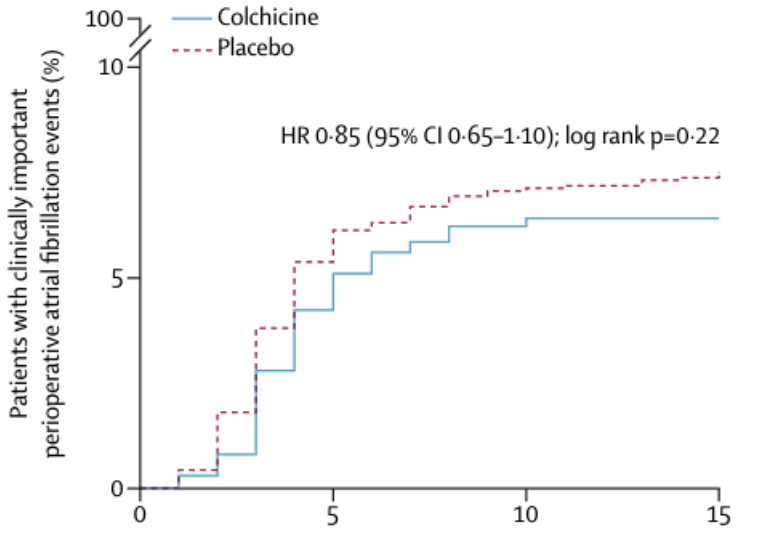
Ann Intern Med. 2020;172:96-104.

MINS - Colchizin

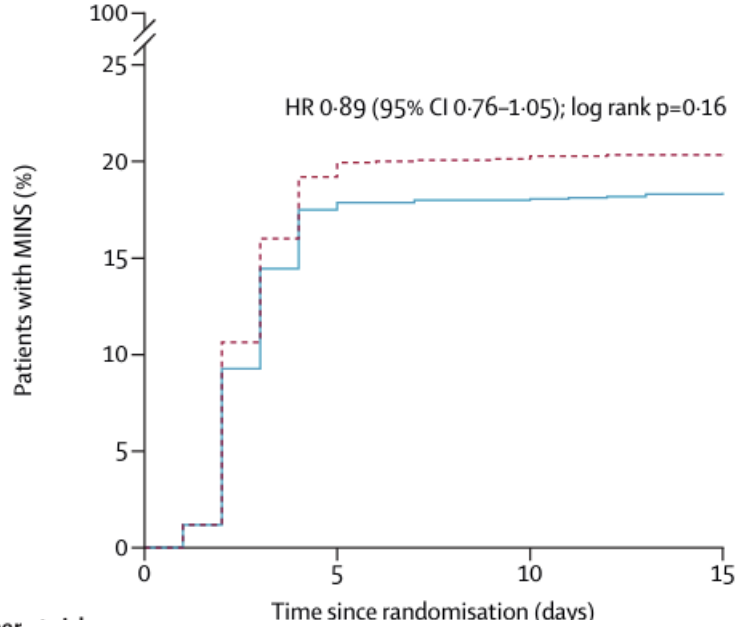
Effect of colchicine on perioperative atrial fibrillation and myocardial injury after non-cardiac surgery in patients undergoing major thoracic surgery (COP-AF):

COP-AF: 3209 Patienten (Ø 68 Jahre) mit großer „non-cardiac“-Operation
0,5mg Colchizin 1-0-1 vs Placebo

	Colchicine group (n=1608)	Placebo group (n=1601)
Age, years	68·3 (7·3)	68·3 (7·1)
Sex		
Female	777 (48·3%)	776 (48·5%)
Male	831 (51·7%)	825 (51·5%)
Ethnicity		
White or Caucasian	1332 (82·8%)	1331 (83·1%)
BMI, kg/m²	27·0 (5·3)	27·2 (5·4)
Medications taken within 24 h before surgery		
Aspirin	155 (9·6%)	141 (8·8%)
ACE inhibitor or ARB	310 (19·3%)	305 (19·1%)
β blocker	232 (14·4%)	224 (14·0%)
Rate-controlling calcium channel blocker	28 (1·7%)	23 (1·4%)
Statin	551 (34·3%)	498 (31·1%)



	Events/participants (%)		HR (95% CI)	$p_{interaction}$
	Colchicine (n=1608)	Placebo (n=1601)		
Age, years				0·085
<65	15/536 (2·8%)	28/524 (5·3%)	0·52 (0·28–0·97)	
≥65	88/1072 (8·2%)	92/1077 (8·5%)	0·95 (0·71–1·28)	
Surgical approach				<0·0001
Thoracoscopic	43/1219 (3·5%)	77/1178 (6·5%)	0·53 (0·36–0·77)	
Non-thoracoscopic	60/374 (16·0%)	43/410 (10·5%)	1·59 (1·07–2·35)	



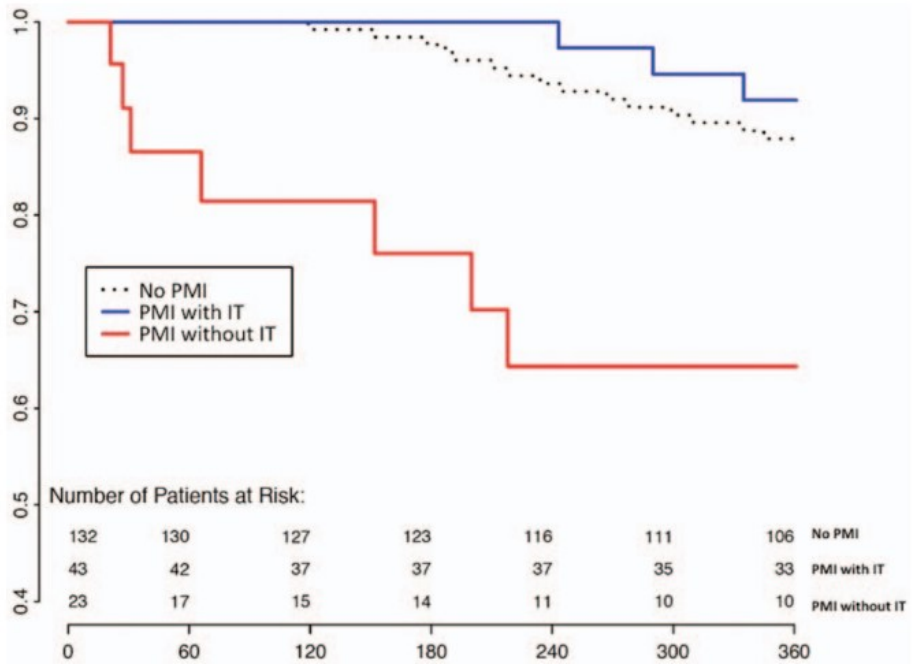
	Events/participants (%)		HR (95% CI)	$p_{interaction}$
	Colchicine (n=1608)	Placebo (n=1601)		
Age, years				0·77
<65	75/536 (14·0%)	85/524 (16·2%)	0·85 (0·62–1·18)	
≥65	220/1072 (20·5%)	240/1077 (22·3%)	0·90 (0·75–1·09)	
Surgical approach				0·041
Thoracoscopic	188/1219 (15·4%)	220/1178 (18·7%)	0·80 (0·66–0·98)	
Non-thoracoscopic	107/374 (28·6%)	105/410 (25·6%)	1·15 (0·87–1·53)	

Lancet 2023; 402: 1627–35

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.

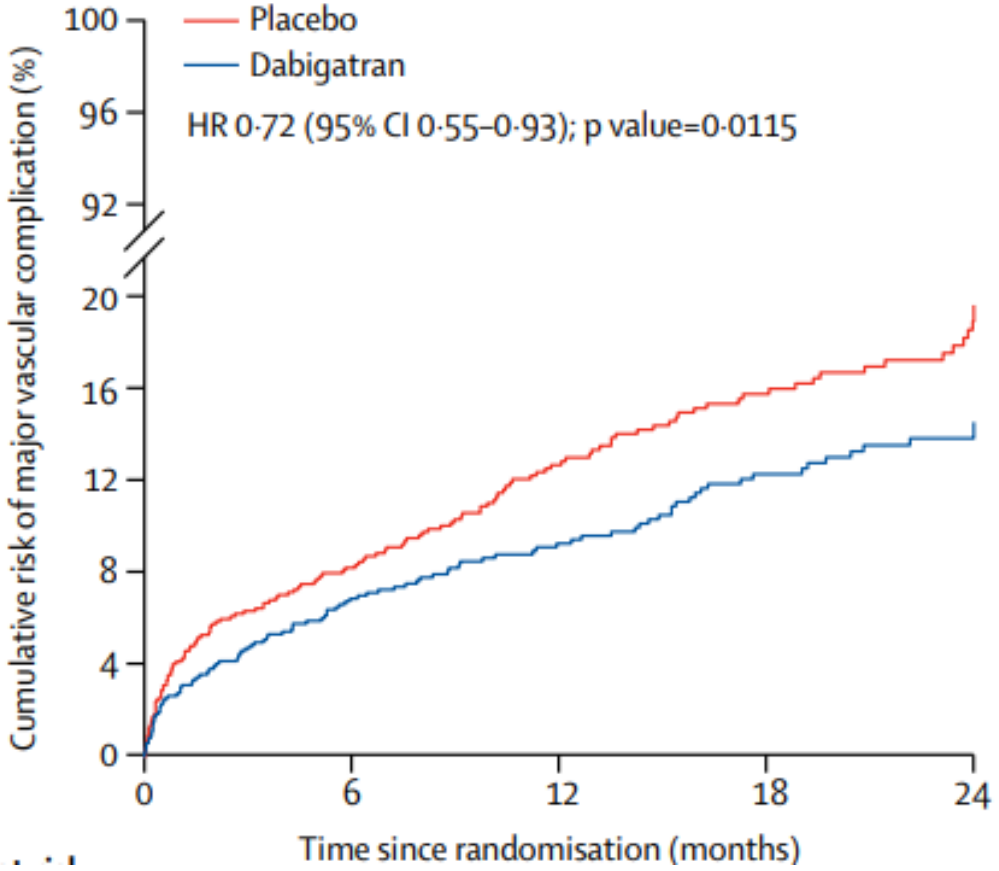


(Anesth Analg 2014;119:1053–63)

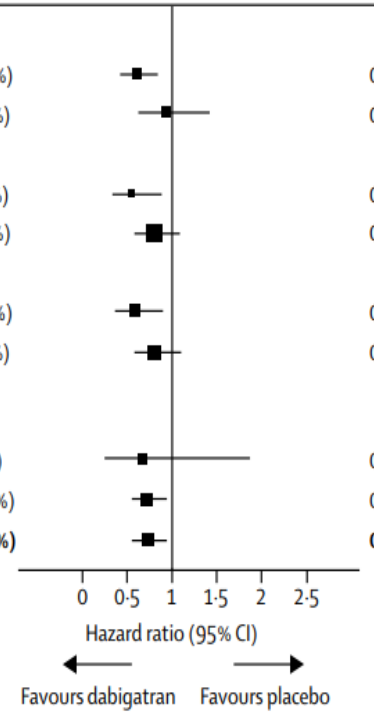
Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial

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

Zusammenfassung

- Neues CARE Schema ist zentral bei der Therapie
- Keine Unterscheidung nach Geschlecht bei VHF mehr
- Begleiterkrankungen therapieren!
- Tripletherapie nur noch sehr kurz verwenden
- Bridging nur in Ausnahmefällen
- AHRE sind keine Indikation für Antikoagulation
- Perioperativer Myokardschaden ist häufig und gefährlich
- Patienten müssen intensiviert behandelt werden – positive Daten für TASS, Statin und NOAK