What's new in Cardiology 2018

and some old achievements

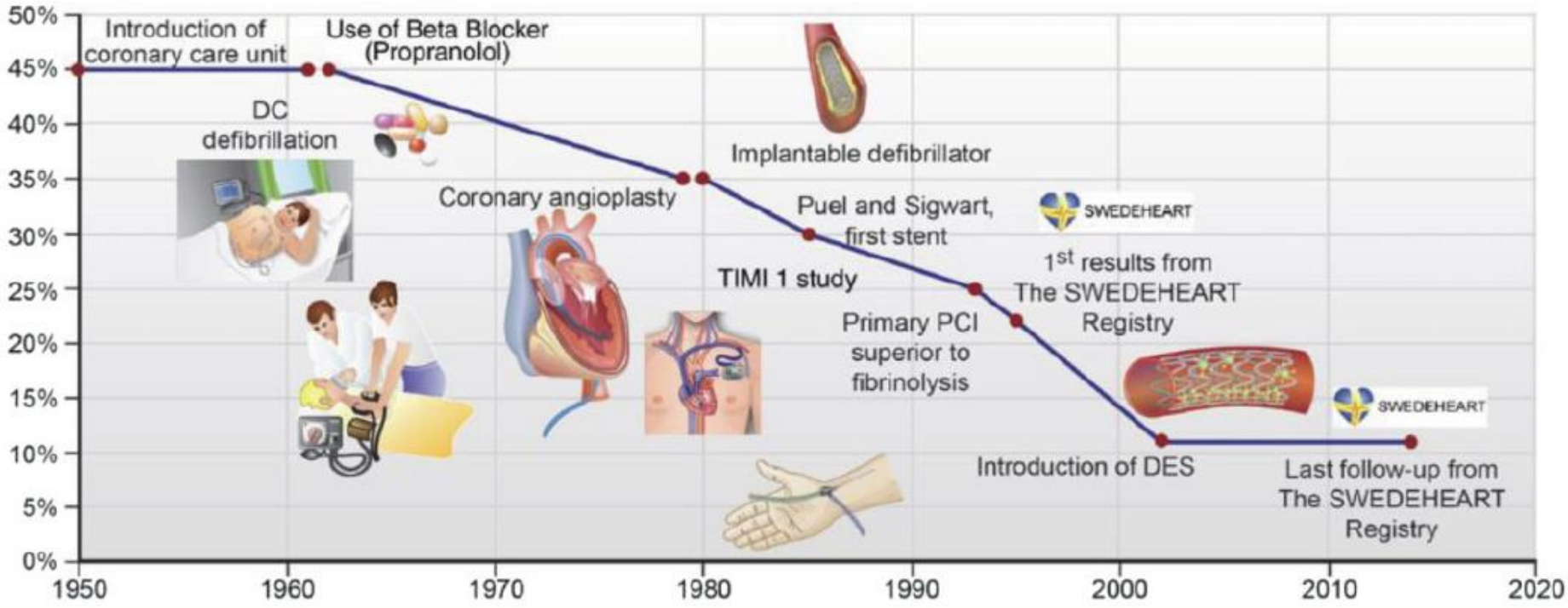


Figure 1 Change in mortality of acute myocardial infarction over time (from Luscher and Obeid[17]).

Prävention bei Diabetikern – Stellenwert von ASA in kontemporär behandelter Population

ORIGINAL ARTICLE

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

26.8.2018 NEJM

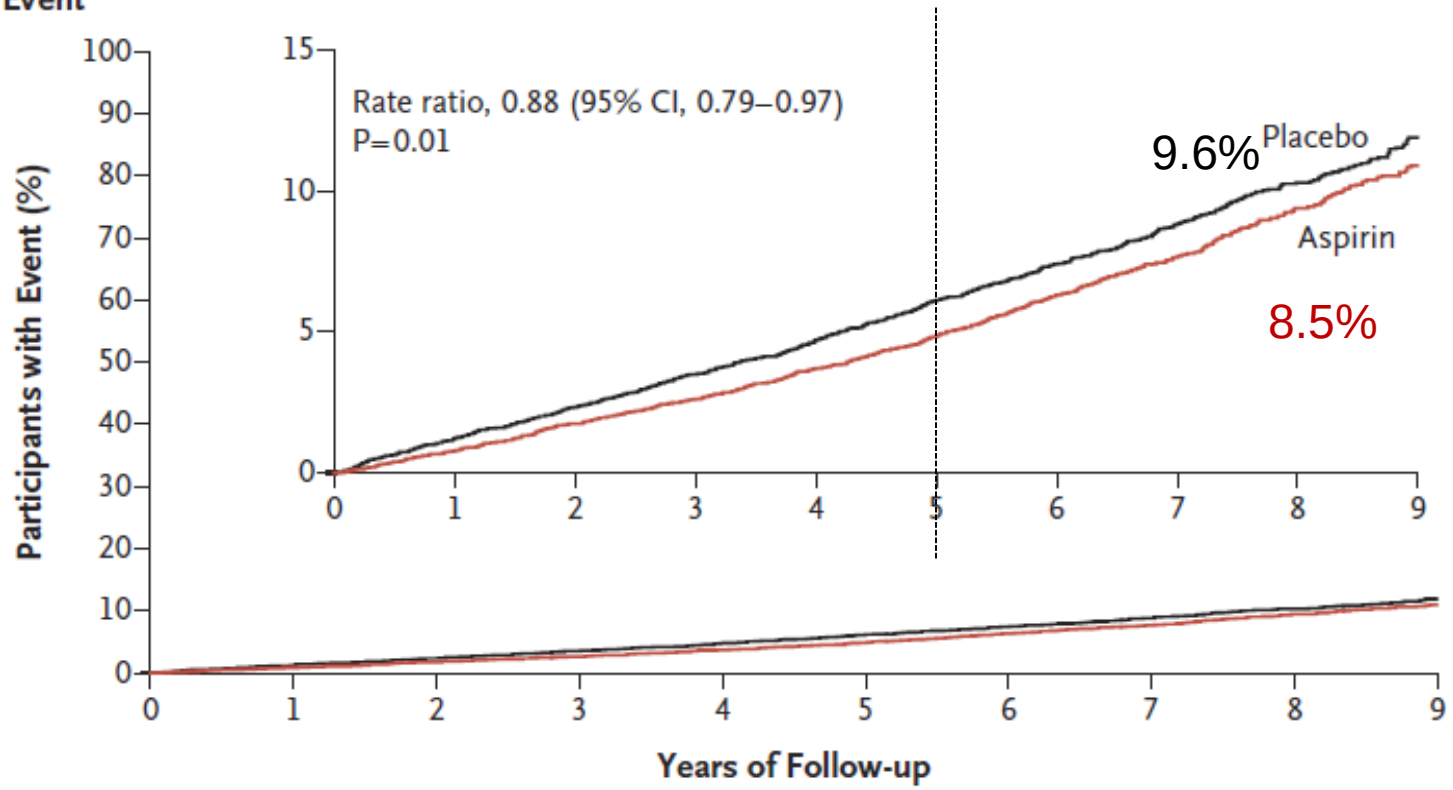
15’480 Pts, Diabetes ohne cv Erkrankung
Fu 7.4 J –,Alter Ø 63j,
gut balanciert bezügl. cv Risikofaktoren (40% low, 40% mid, 20%high risk)
Ca 1/3 vorgängig auf ASA, 75% unter Statinen, gute BD-Kontrolle

Endpunkte

Primär: erstes relevantes cv Ereignis (nfatal MI, nfatal CVI, TIA, vask.Tod)
Sekundär: GIT-Neoplasien, vask. Ereignisse/Revaskularisationen
Primärer safety EP: relev. Blutungen

Intervention: 100mg ASA/Placebo (1g n3-FS/Placebo)

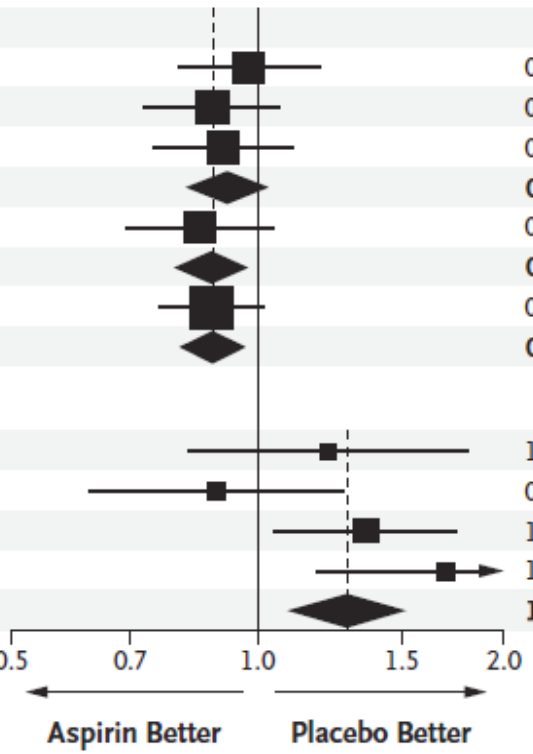
A First Serious Vascular Event

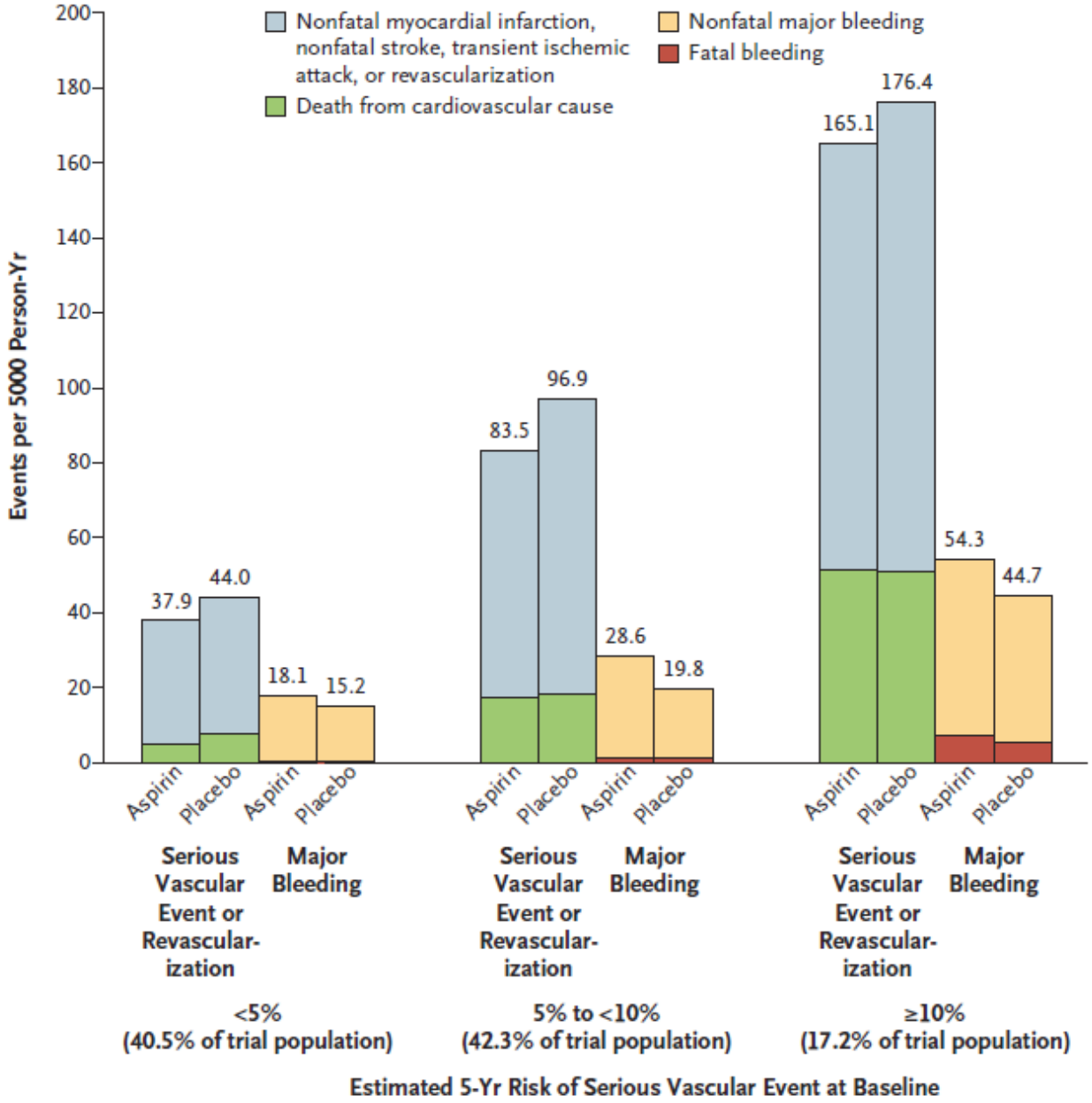


No. at Risk

Placebo	7740	7618	7486	7342	7188	7001	5771	3890	2200	1430
Aspirin	7740	7655	7536	7404	7252	7096	5825	3966	2222	1428
Cumulative benefit per 1000 participants in aspirin group		4±2	6±2	9±3	10±3	13±4	11±4	12±5	9±6	10±7

Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Value
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major bleeding	74 (1.0)	43 (0.6)	1.70 (1.18–2.44)	
Any major bleeding	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52)**	**0.003**





No. of Events per 5000 Person-Yr in Aspirin Group			
Serious vascular events avoided	5.7±3.7	11.2±5.4	4.9±12.9
Serious vascular events or revascularizations avoided	6.1±4.2	13.4±6.3	11.3±14.3
Major bleeding caused	2.8±2.6	8.9±3.2	9.6±7.5

Trotz erhöhtem cv Risiko hat Aspirin bei Diabetikern nur einen geringen präventiven Nutzen für cv Ereignisse, welcher durch erhöhtes Blutungsrisiko egalisiert wird

Dies bestätigt sich auch bei hohem Risiko

Stattdessen:Statine und Antihypertensiva !

Caveats/Ergänzungen

Therapie-Adhärenz: Nur ca 70%

Nutzen-Schaden : ca 50% Blutungen aus GIT → PPI!

Kein Wirkungsunterschied bei Pt > 70 kg (Lancet-Studie)

Kein Effekt auf Neoplasien (auch nicht GIT)

Kryptogener, vermutet emboligener stroke - Indikation für OAK?

ORIGINAL ARTICLE

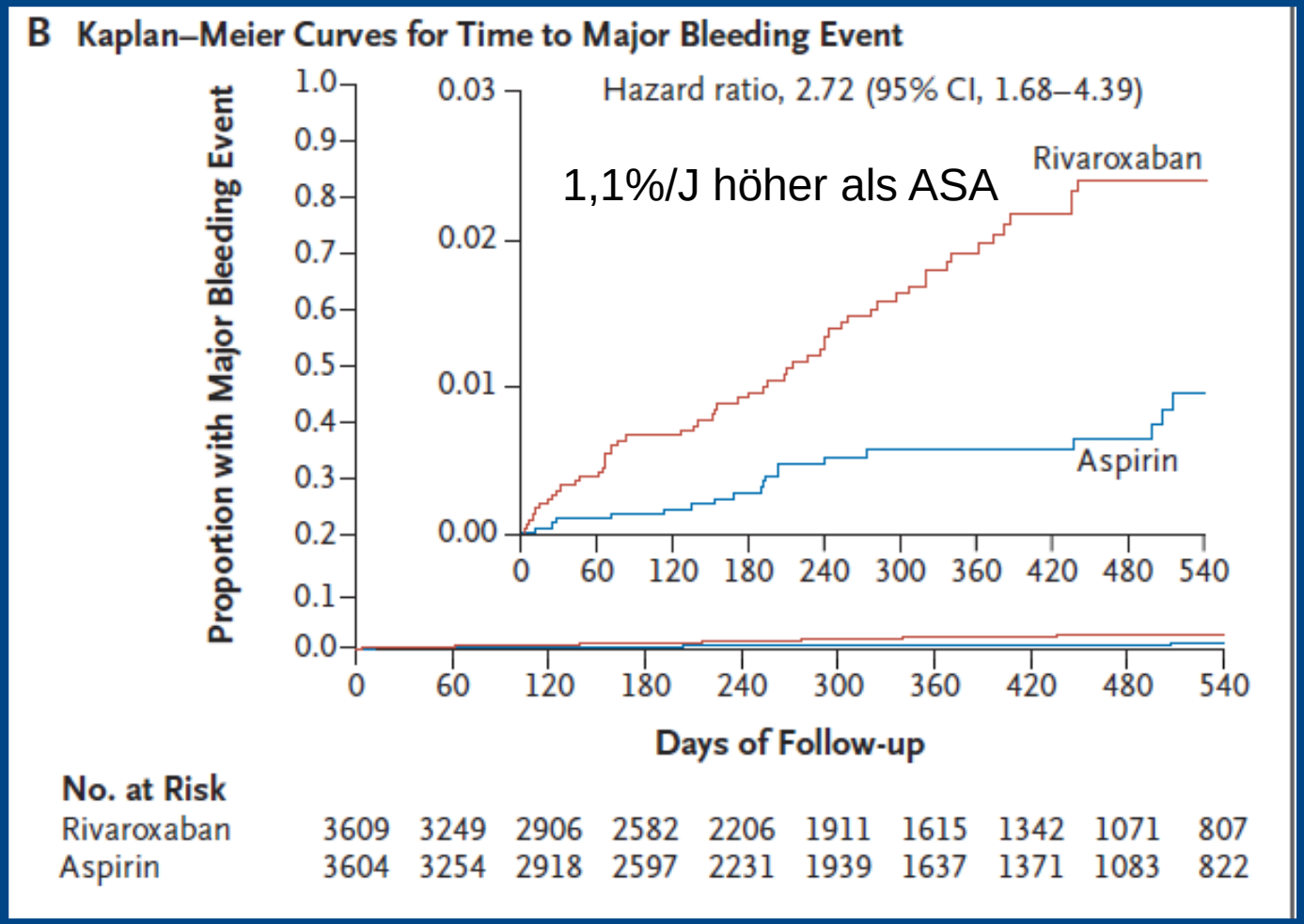
Rivaroxaban for Stroke Prevention after Embolic Stroke of Undetermined Source

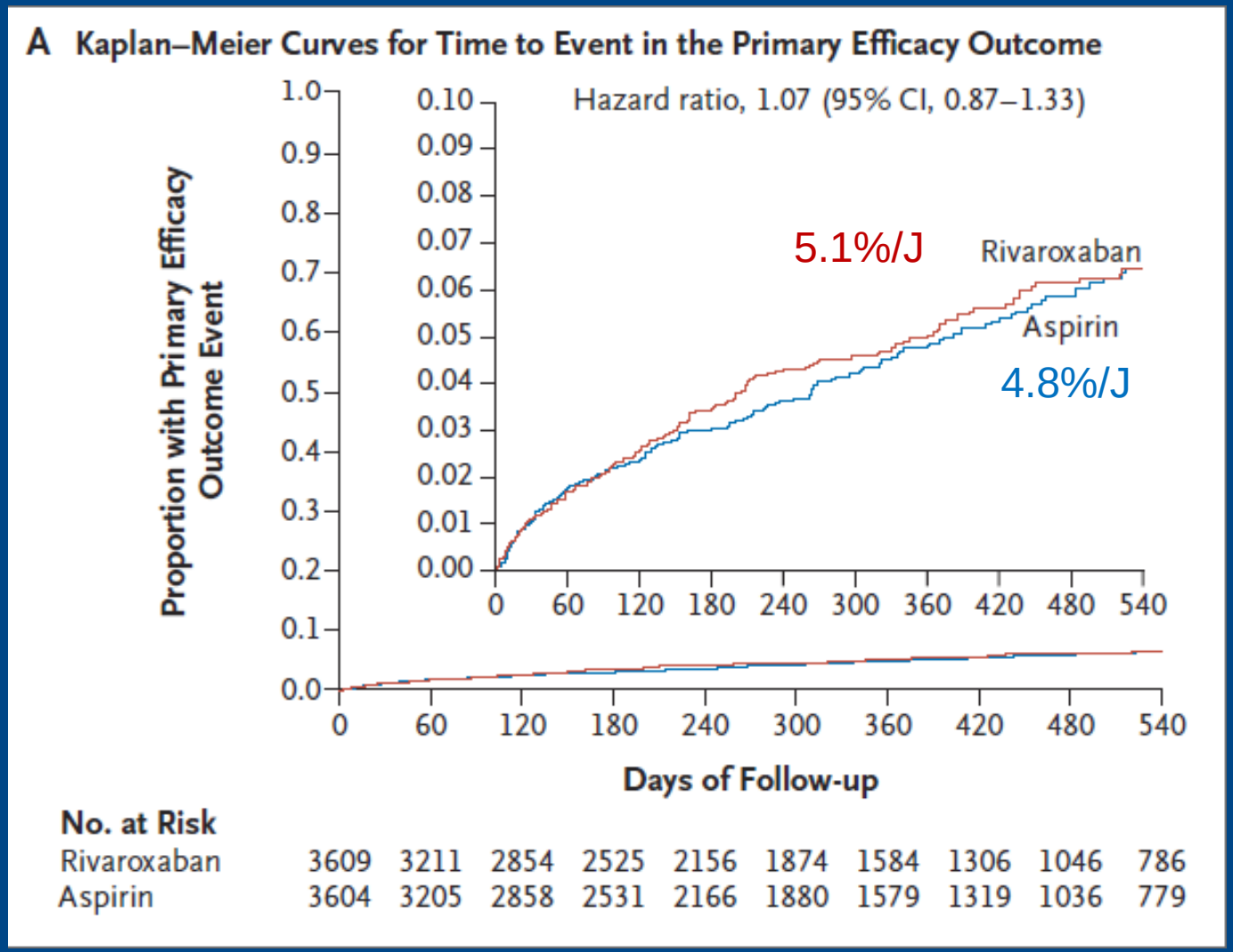
NAVIGATE ESUS NEJM 7.6.2018

- 7213 Pts. nach CVI (7d-6mo,nicht lakunär), vermutet embolisch ohne Ursachennachweis (zB keine Stenose ≥ in ass. Gefäss, kein VHFli, kein kard.Emboliequelle), Ø 67j, älter als 49j, 50-59J +≥ 1 cv RF

  80% aHT, 25% Dm,28% St.n.CVI,7% PFO
- Multizentrisch
- **Endpunkt**
- Erstes Rezidiv CVI/system. Embolie
- Intervention: Rivaroxaban 15 mg vs ASA 100mg

Am 5.10.2017 Studienabbruch wegen Exzess-Blutungen ohne Hinweis auf verbesserte Effizienz nach durchschnittlich 11 Monaten fu




A Kaplan–Meier Curves for Time to Event in the Primary Efficacy Outcome
Hazard ratio, 1.07 (95% CI, 0.87–1.33)
5.1%/J
Rivaroxaban
Aspirin
4.8%/J
Proportion with Primary Efficacy Outcome Event
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0 60 120 180 240 300 360 420 480 540
Days of Follow-up
No. at Risk
Rivaroxaban 3609 3211 2854 2525 2156 1874 1584 1306 1046 786
Aspirin 3604 3205 2858 2531 2166 1880 1579 1319 1036 779

Auch kein Effekt auf sekundäre cv Endpunkte

Table 2. Efficacy Outcomes.*

Outcome	Rivaroxaban Group (N=3609)	Aspirin Group (N=3604)	Hazard Ratio (95% CI)†
	no. of patients (annualized rate)		
Primary efficacy outcome: any recurrent stroke or systemic embolism	172 (5.1)	160 (4.8)	1.07 (0.87–1.33)
Secondary efficacy outcomes			
Any recurrent stroke‡	171 (5.1)	158 (4.7)	1.08 (0.87–1.34)
Ischemic stroke‡	158 (4.7)	156 (4.7)	1.01 (0.81–1.26)
Hemorrhagic stroke§	13 (0.4)	2 (0.1)	6.50 (1.47–28.8)
Systemic embolism	1 (<0.1)	2 (0.1)	0.50 (0.05–5.51)
Any recurrent stroke, myocardial infarction, death from cardiovascular causes, or systemic embolism¶	207 (6.2)	195 (5.8)	1.06 (0.87–1.29)
Any disabling stroke	41 (1.2)	29 (0.8)	1.42 (0.88–2.28)
Myocardial infarction	17 (0.5)	23 (0.7)	0.74 (0.39–1.38)
Death from any cause	65 (1.9)	52 (1.5)	1.26 (0.87–1.81)
Death from cardiovascular causes¶	34 (1.0)	23 (0.7)	1.48 (0.87–2.52)

- Rivaroxaban bezüglich Nettoeffekt ASA hier unterlegen
- Adäquates Procedere bei kryptogenem stroke immer noch diskutabel,
- Kryptogen ≠ vermutet emboligen (?)
- Weitere Studien mit unterschiedlichen OAKs/Dosierung folgen
- *Zur Erinnerung:*
- *COMPASS trial (stabile cv Erkrankung) : ASA + 2x2,5 mg Rivaroxaban effizienter; mehr Blutungen – netto kein Vorteil*
- *Rivaroxaban 2x5 ohne ASA : nicht effizienter, mehr Blutungen*

Vorhofflimmern und Koronar-intervention
DAPT oder OAK ?

ESC European Society of Cardiology

European Heart Journal (2018) **39**, 1726–1735
doi:10.1093/eurheartj/ehy162

META-ANALYSIS

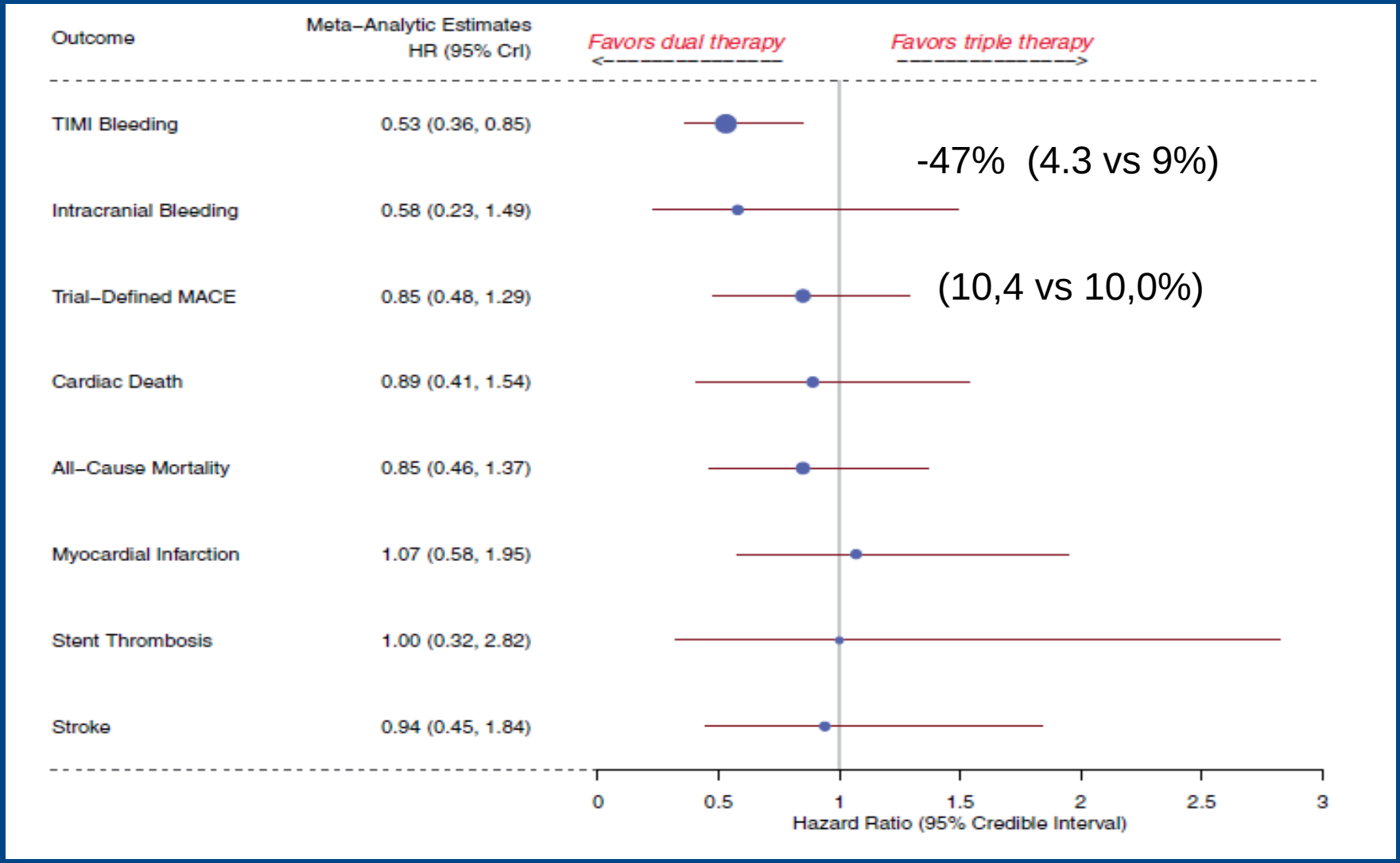
Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials

Harsh B. Golwala[1], Christopher P. Cannon[1,2], Ph. Gabriel Steg[3], Gheorghe Doros[2,4], Arman Qamar[1], Stephen G. Ellis[5], Jonas Oldgren[6], Jurrien M. ten Berg[7], Takeshi Kimura[8], Stefan H. Hohnloser[9], Gregory Y.H. Lip[10], and Deepak L. Bhatt[1]*

Table I Baseline characteristics of patients in intention-to-treat analysis of randomized trials included in the analysis

5317 Pts

	WOEST[12]		ISAR-TRIPLE[13]		PIONEER AF-PCI[14]		RE-DUAL PCI[15]			Combined	
	DAT ($n = 279$)	TAT ($n = 284$)	DAT ($n = 307$)	TAT ($n = 307$)	DAT ($n = 709$)	TAT ($n = 706$)	DAT ($n = 981$) Dabigatran 110 mg	DAT ($n = 763$) Dabigatran 150 mg	TAT ($n = 981$)	DAT ($n = 3039$)	TAT ($n = 2278$)
Age (years)	70.3 (7.0)	69.5 (8.0)	73.9 (7.7)	73.3 (8.7)	70.4 (9.1)	69.9 (8.7)	71.5 (8.9)	68.6 (7.6)	71.7 (8.9)	70.9	71.1
Female (%)	23	18	25	21	26	27	26	22	24	25	23
BMI (kg/m^2)	27.5 (4.3)	27.9 (4.2)	27.5 (4.2)	27.9 (4.6)	28.6 (25.7–32.4)	29.0 (25.8–32.8)	NR	NR	NR	27.9	28.2
Diabetes (%)	24	25	28	24	29	31	37	34	39	32	32
Hypertension (%)	69	68	77	76	73	75	NR	NR	NR	73	74
Dyslipidaemia (%)	68	72	74	75	43	45	NR	NR	NR	56	58%
Current smoker (%)	22	15	9	10	5	7	NR	NR	NR	10	9
History of MI (%)	34	35	29	25	20	22	24	24	27	25	26
History of CABG (%)	20	26	24	17	NR	NR	10	10	11	13	15
History of PCI (%)	31	36	NR	NR	NR	NR	33	31	35	32	35
PPI use (%)	34	39	NR	NR	39	37	NR	NR	NR	37	37
Type of index event (%)											
ACS	25	30	33	31	51	52	52	51	48	47	45
Non-ACS	75	70	67	69	49	48	48	49	52	53	55
Type of stent (%)											
Drug-eluting stent	65	64	99	99	65	66	82	81	84	79	79
Bare-metal stent	32	30	1	0	33	32	15	16	13	19	19
Drug-eluting and bare-metal stents	1	4	0	0	2	2	2	1	1	1	1
PTCA/no stent	2	1	1	1	0	0	1	1	1	1	1
Indication for oral anti coagulation (%)											
Atrial fibrillation	69	69	83	85	100	100	100	100	100	96	95
Mechanical valve	10	11	6	9	0	0	0	0	0%	1	2
Other	20	20	12	6	0	0	0	0	0	3	3
CHA_2DS_2-VASc score (%)											
≤2	NR	NR	5	7	27	21	23	32	20	25	18
>2	NR	NR	95	93	73	79	77	68	80	75	82
HAS-BLED score (%)											
<3	NR	NR	NR	NR	28	29	33	41	29	34	29
≥3	NR	NR	NR	NR	72	71	67	56	71	66	71


Outcome
Meta–Analytic Estimates
HR (95% CrI)
Favors dual therapy
Favors triple therapy
TIMI Bleeding
0.53 (0.36, 0.85)
-47% (4.3 vs 9%)
Intracranial Bleeding
0.58 (0.23, 1.49)
Trial–Defined MACE
0.85 (0.48, 1.29)
(10,4 vs 10,0%)
Cardiac Death
0.89 (0.41, 1.54)
All–Cause Mortality
0.85 (0.46, 1.37)
Myocardial Infarction
1.07 (0.58, 1.95)
Stent Thrombosis
1.00 (0.32, 2.82)
Stroke
0.94 (0.45, 1.84)
0
0.5
1
1.5
2
2.5
3
Hazard Ratio (95% Credible Interval)

Vice versa: Koronarintervention bei Pts mit etabliertem VHFli

Table 3 Triple vs. dual antithrombotic therapy after myocardial infarction in patients with atrial fibrillation undergoing PCI (data from Batra *et al.*,[46] DAPT was used as reference treatment)

	Triple therapy	ASA + warfarin	Clopidogrel + warfarin
Cardiovascular outcome adjusted HR			
0–90 days	0.86 (0.70–1.07)	0.82 (0.54–1.26)	0.90 (0.68–1.19)
91–365 days	0.78 (0.58–1.05)	0.62 (0.48–0.79)	0.68 (0.49–0.95)
Major bleeds adjust. HR			
0–90 days	2.16 (1.48–3.13)	1.30 (0.60–2.85)	1.28 (0.71–2.32)
91–365 days	1.61 (0.98–2.66)	1.01 (0.63–1.62)	1.08 (0.57–2.04)

Was sagen die guidelines?

ESC European Society of Cardiology

European Heart Journal (2018) **39**, 213–254
doi:10.1093/eurheartj/ehx419

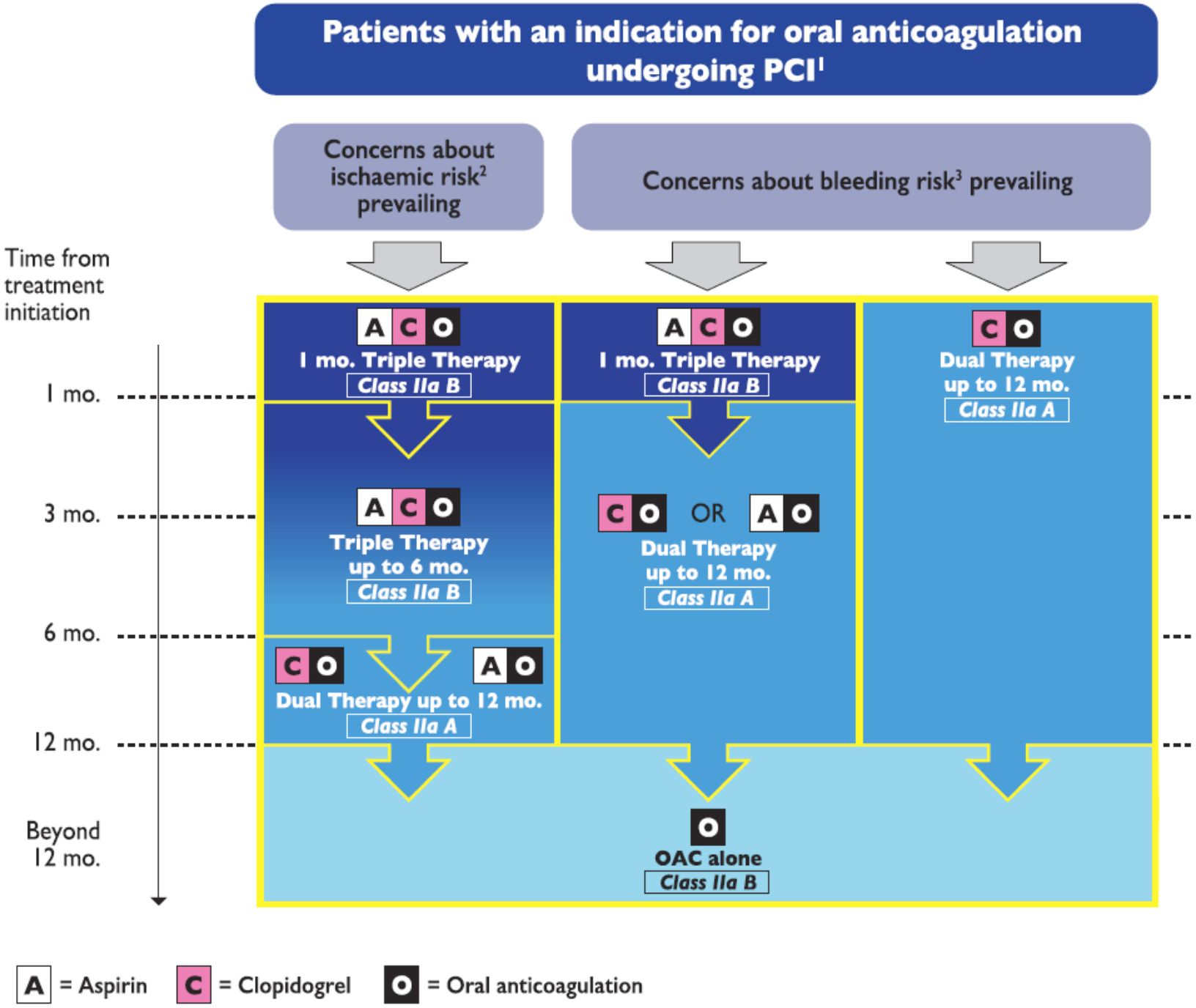
ESC GUIDELINES

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)

Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

• Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, HAS-BLED) with a focus on modifiable risk factors.
• Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
• Consider the use of NOACs instead of VKA.
• Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.
• Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.[a]
• Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
• Use low-dose (≤ 100 mg daily) aspirin.
• Routine use of PPIs.


Patients with an indication for oral anticoagulation undergoing PCI[1]
Concerns about ischaemic risk[2] prevailing
Concerns about bleeding risk[3] prevailing
Time from treatment initiation
1 mo.
3 mo.
6 mo.
12 mo.
Beyond 12 mo.
A C O
1 mo. Triple Therapy
Class IIa B
A C O
1 mo. Triple Therapy
Class IIa B
C O
Dual Therapy up to 12 mo.
Class IIa A
A C O
Triple Therapy up to 6 mo.
Class IIa B
C O OR A O
Dual Therapy up to 12 mo.
Class IIa A
C O
A O
Dual Therapy up to 12 mo.
Class IIa A
O
OAC alone
Class IIa B
A = Aspirin
C = Clopidogrel
O = Oral anticoagulation