Antikoagulation 2016: wann Mono-, Duale-, Tripletherapie?

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Typischer Fall

Ein Patient, 70 Jahre, kommt am Freitag Nachmittag nach stationärem Aufenthalt wegen KHK zur Verordnung seiner Medikation aus dem Krankenhaus in Ihre Praxis.

Er hat eine bekannte arterielle Hypertonie und eine Niereninsuffizienz (GFR 50), LV-EF 48%.

Im vorläufigen Arztbrief wird nach DES-Stenting der LAD eine Behandlung mit ASS + Clopidogrel für 12 Monate empfohlen.

Er erhält wegen Vorhofflimmerns seit vielen Jahren von Ihnen eine orale Antikoagulation mit einem Vitamin K-Antagonisten.

Typischer Fall: Stenting + Vorhofflimmern

Zunächst:

1. ASS + Clopidogrel + Falithrom
2. ASS + Falithrom
3. Clopidogrel + Falithrom
4. Ticagrelor + Falithrom
5. ASS + Clopidogrel + NOAK
6. ASS + NOAK
7. Clopidogrel + NOAK
8. Ticagrelor + NOAK
9. Sonstige Therapie

Typischer Fall: Stenting + Vorhofflimmern

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6. ASS + NOAK
7. Clopidogrel + NOAK
8. Ticagrelor + NOAK
9. Sonstige Therapie

Dann lebenslang:

1. ASS + Falithrom
2. Falithrom
3. ASS + Clopidogrel
4. Ticagrelor + Falithrom
5. ASS + NOAK
6. NOAK
7. Sonstige Therapie

Risikostratifizierung

⇨ **CHA_2DS_2-VASc Score**

4

(a) Risk factors for stroke and thrombo-embolism in non-valvular AF	
'Major' risk factors	'Clinically relevant non-major' risk factors
Previous stroke, TIA, or systemic embolism Age ≥75 years	Heart failure or moderate to severe LV systolic dysfunction (e.g. LV EF ≤ 40%) Hypertension - Diabetes mellitus Female sex - Age 65–74 years Vascular disease[a]
(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc (Note: maximum score is 9 since age may contribute 0, 1, or 2 points)	

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	9

ESC-Guidelines for the management of atrial fibrillation 2010, http://www.escardio.org

European Heart Journal Advance Access published August 27, 2016
European Heart Journal doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

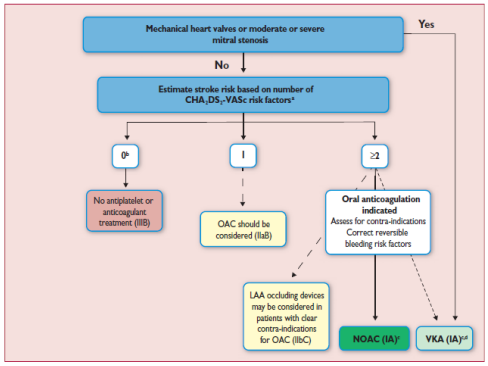
The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

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

Endorsed by the European Stroke Organisation (ESO)

European Heart Journal. doi:10.1093/eurheartj/ehw210.

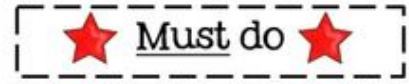
Vorhofflimmern: ESC-Leitlinien 2016



European Heart Journal. doi:10.1093/eurheartj/ehw210.

Vorhofflimmern: ESC-Leitlinien 2016

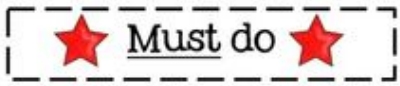
OAK bei **Männern** mit CHA_2DS_2-VASc Score **≥ 2** (I-A)



European Heart Journal. doi:10.1093/eurheartj/ehw210.

Vorhofflimmern: ESC-Leitlinien 2016

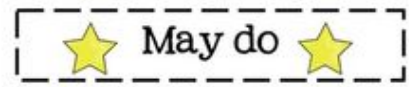
OAK bei **Frauen** mit CHA_2DS_2-VASc Score **≥ 3** (I-A)



European Heart Journal. doi:10.1093/eurheartj/ehw210.

Vorhofflimmern: ESC-Leitlinien 2016

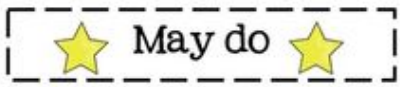
OAK bei **Männern** mit CHA_2DS_2-VASc Score **≥ 1** (IIa-B)



European Heart Journal. doi:10.1093/eurheartj/ehw210.

Vorhofflimmern: ESC-Leitlinien 2016

OAK bei **Frauen** mit CHA_2DS_2-VASc Score **≥ 2** (IIa-B)



European Heart Journal. doi:10.1093/eurheartj/ehw210.

HAS-BLED Bleeding Risk Score

4

⇨ **Blutungsrisiko bei Antikoagulation**

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

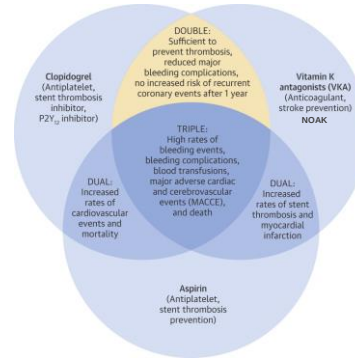
z.B. ASS, Clopidogrel, NSAR

ESC-Guidelines for the management of atrial fibrillation 2010, http://www.escardio.org

HAS-BLED Bleeding Risk Score

- **Erhöhtes Blutungsrisiko = HAS-BLED score ≥ 3**

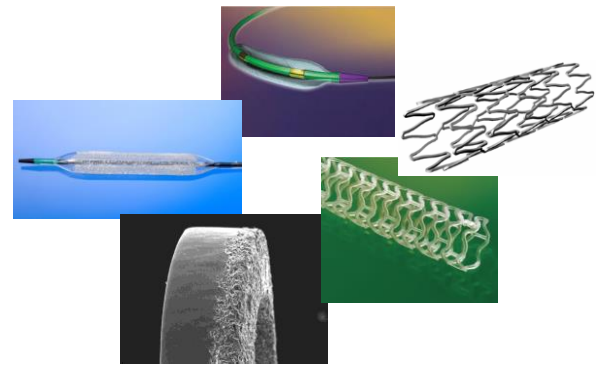
Kombinationen bei Vorhofflimmern & Koronarintervention



J Am Coll Cardiol. 2014;64(12):1270-1280

Faktor I: Intervention

Intervention

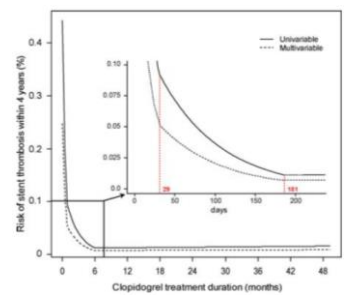


Intervention bei stabiler KHK

- **Bare-Metal Stents (BMS):**
  4 Wochen duale Thrombozytenaggregationshemmung (DAPT)
- **Neuere Drug-Eluting Stent (DES)-Generationen:**
  12 Monate → 6 Monate DAPT
- Target lesion revascularization
  Neuere DES-Generationen besser als BMS

Intervention bei stabiler KHK

Risiko für Stentthrombosen nach DES



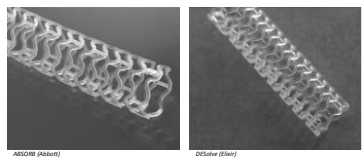
Schulz S et al. Eur Heart J 2009;30(22):2714–2721.

Medikamenten-beschichtete Ballonkatheter Drug-Coated Balloon (DCB)

Drug-Coated Balloon (DCB)

- IA-Indikation bei InStent-Restenosen
- De-novo Läsionen, Bifurkationen, Small vessel disease
- **4 Wochen DAPT**

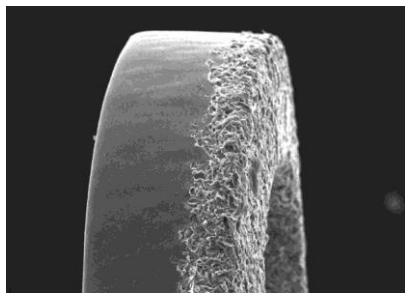
Drug-Eluting Bioresorbable Vascular Scaffold (BVS) Stent



Drug-Eluting Bioresorbable Vascular Scaffold (BVS) Stent

- De-novo Läsionen
- **(Mindestens) 12 Monate DAPT**
- Cave: Erhöhte Rate von Stentthrombosen (s. ABSORB II)

Drug-Coated Stent (DCS) = DES ohne Polymer



Selectively micro-structured surface holds drug in abluminal surface structures

Abizaid A et al. Circulation: Cardiovascular Interventions. 2010;3:384-393.

Drug-Coated Stent (DCS)

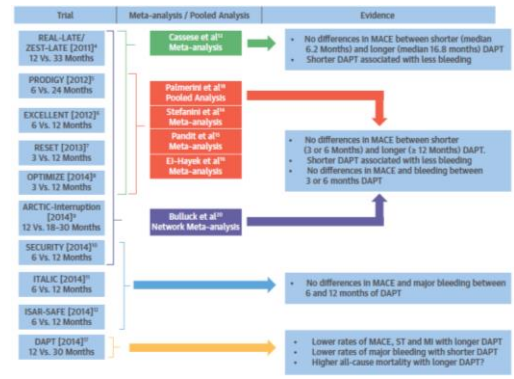
- Nach der Studienlage ist der DCS die bessere Alternative zum BMS
- De-novo Läsionen, InStent-Restenose
- **4 Wochen DAPT**

Faktor II:
Dauer der Thrombozytenaggregationshemmung
Elektive Indikation vs. Akutes Koronarsyndrom

Faktor IIA:
Elektive Indikation

Dauer und Umfang der Thrombozytenaggregationshemmung
im Wesentlichen abhängig von der Art der Koronarintervention (POBA, DCB, BMS, DES, DCS, BVS)

Dauer der Thrombozytenaggregationshemmung

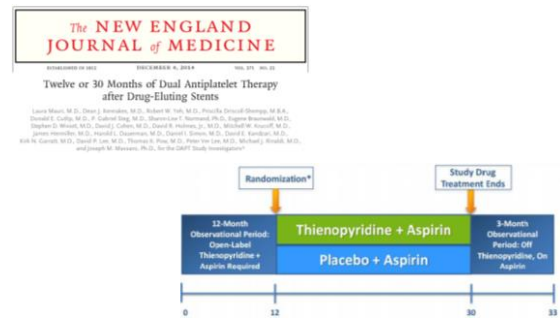


Dauer der Thrombozytenaggregationshemmung

Ist eine längere DAPT besser?

- ⇨ Kontroverse Ergebnisse
- ⇨ Empfehlung zu 'tailored therapies'
- ⇨ In der Regel:
  Verlängerung DAPT → Reduktion ischämischer Ereignisse
  zu Lasten von Blutungsereignissen

DAPT nach DES-Implantation bei stabiler KHK



Mauri L et al. N Engl J Med 2014;371:2155-66.

DAPT nach DES-Implantation bei stabiler KHK

Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.*

Outcome	Continued Thienopyridine (N=5020)	Placebo (N=4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

Mauri L et al. N Engl J Med 2014;371:2155-66.

DAPT nach DES-Implantation bei stabiler KHK

Table 3. Bleeding End Point during Month 12 to Month 30.*

Bleeding Complications	Continued Thienopyridine (N=4710)	Placebo (N=4649)	Difference	Two-Sided P Value for Difference
	no. of patients (%)		*percentage points (95% CI)*	
GUSTO severe or moderate†	119 (2.5)	73 (1.6)	1.0 (0.4 to 1.5)	0.001
Severe	38 (0.8)	26 (0.6)	0.2 (−0.1 to 0.6)	0.15
Moderate	81 (1.7)	48 (1.0)	0.7 (0.2 to 1.2)	0.004
BARC type 2, 3, or 5	263 (5.6)	137 (2.9)	2.6 (1.8 to 3.5)	<0.001
Type 2	145 (3.1)	72 (1.5)	1.5 (0.9 to 2.1)	<0.001
Type 3	122 (2.6)	68 (1.5)	1.1 (0.6 to 1.7)	<0.001
Type 5	7 (0.1)	4 (0.1)	0.1 (−0.1 to 0.2)	0.38

Mauri L et al. N Engl J Med 2014;371:2155-66.

Faktor IIB:
Akutes Koronarsyndrom

ESC Leitlinien 2014: STEMI

- **12 Monate DAPT**
- **ASS 100 mg + Prasugrel 10mg/d oder Ticagrelor 2x90mg/d**
  besser als Clopidogrel 75m/d
- ASS 75-100mg/d lebenslang

Recommendations	Class[a]	Level[b]	Ref[c]
Antiplatelet therapy			
ASA is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 80–150 mg i.v.) and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A	776,794
A $P2Y_{12}$ inhibitor is recommended in addition to ASA and maintained over 12 months unless there are contraindications such as excessive risk of bleeding. Options are:	I	A	–
• Prasugrel (60 mg loading dose, 10 mg daily dose) if no contraindication	I	B	
• Ticagrelor (180 mg loading dose, 90 mg twice daily) if no contraindication	I	B	
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B	

Windecker S et al. Eur Heart J 2014;35:2541–619.

ESC Leitlinien 2014: NSTEMI

- **12 Monate DAPT**
- **ASS 100 mg + Prasugrel 10mg/d oder Ticagrelor 2x90mg/d**
  besser als Clopidogrel 75m/d
- ASS 75-100mg/d lebenslang

Recommendations	Class[a]	Level[b]	Ref[c]
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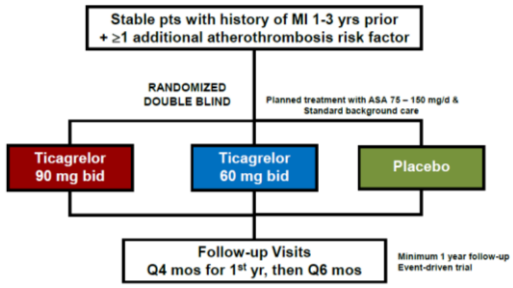
ASA is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 80–150 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A	774,776,794
A $P2Y_{12}$ inhibitor is recommended in addition to ASA, and maintained over 12 months unless there are contraindications such as excessive risk of bleeding. Options are:	I	A	337,341,825
• Prasugrel (60 mg loading dose, 10 mg daily dose) in patients in whom coronary anatomy is known and who are proceeding to PCI if no contraindication	I	B	7
• Ticagrelor (180 mg loading dose, 90 mg twice daily) for patients at moderate-to-high risk of ischaemic events, regardless of initial treatment strategy including those pre-treated with clopidogrel if no contraindication	I	B	
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated	I	B	825

Windecker S et al. Eur Heart J 2014;35:2541–619.

Wenn es um die Dauer der DAPT geht, …

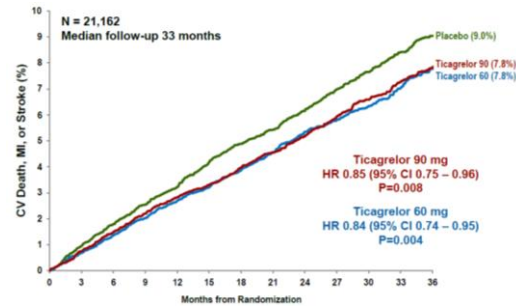
… das heißt, ‘Indikation zur einer längeren DAPT’ schlägt ‘Indikation zu einer kürzeren DAPT’.

PEGASUS-TIMI 54



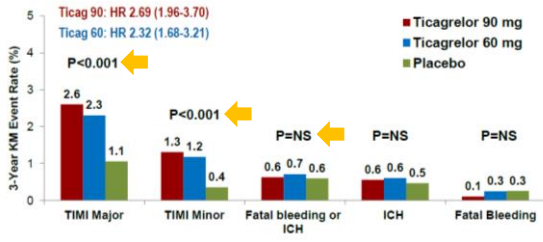
Bonaca MP et al. N Engl J Med 2015; 372:1791-1800.

PEGASUS-TIMI 54



Bonaca MP et al. N Engl J Med 2015; 372:1791-1800.

PEGASUS-TIMI 54



Bonaca MP et al. N Engl J Med 2015; 372:1791-1800.

DAPT Score

Variable	Punkte
Patientenmerkmale	
Alter	
≥ 75	-2
65 - <75	-1
< 65	0
Diabetes Mellitus	+1
Raucher	+1
Z.n. PCI oder Myokardinfarkt	+1
Herzinsuffizienz oder LVEF < 30%	+2
Index-Prozedur	
STEMI, NSTEMI	+1
PCI in Venenbypass	+2
Stentdiameter < 3mm	+1

Niedriger DAPT Score (< 2)
NNT um Ischämie zu vermeiden = 153
NNH um Blutung zu verursachen = 64

Hoher DAPT Score ≥ 2
NNT um Ischämie zu vermeiden = 34
NNH um Blutung zu verursachen = 272

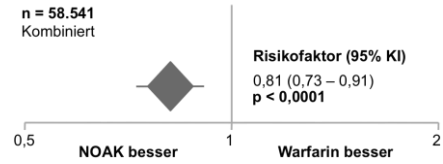
DAPT Score kann helfen, zu entscheiden, **wer sollte** und **wer sollte nicht** eine verlängerte DAPT-Therapie erhalten

Kereiakes DJ et al. J Am Coll Cardiol. 2016;67(21):2492-2502.

Faktor III:
Vorhofflimmern → Antikoagulation

NOAK als Klasse bieten eine bessere Schlaganfallprophylaxe als VKA

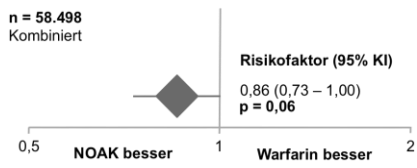
Schlaganfall oder systemische Embolien;
Metaanalyse aller NOAK Phase-III-Studien



Ruff CT et al. Lancet. 2014;383:955-62.

NOAK als Klasse zeigen einen deutlichen Trend zu weniger schweren Blutungen als VKA

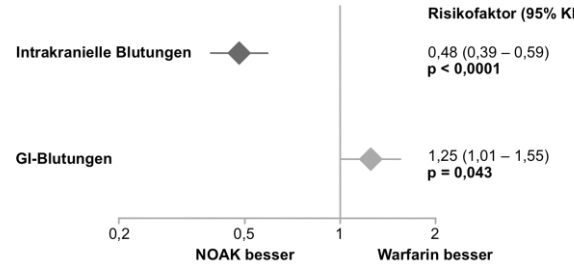
Schwere Blutungen;
Metaanalyse aller NOAK Phase-III-Studien



Ruff CT et al. Lancet. 2014;383:955-62.

Deutlich weniger ICB unter NOAK vs. VKA, aber verstärkt Gastrointestinale Blutungen

Metaanalyse aller NOAK Phase-III-Studien



Ruff CT et al. Lancet. 2014;383:955-62.

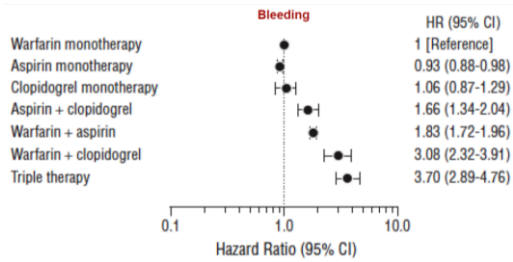
Faktor IV:
Triple Therapie & Blutungsrisiko

Triple Therapie in den Leitlinien 2016

"The **optimal combination** antithrombotic therapy or **duration of combination** therapy for AF patients undergoing percutaneous coronary intervention is **not known**,
but the continued bleeding risk suggests a **short duration**."

European Heart Journal. doi:10.1093/eurheartj/ehw210.

Risk of bleeding or ischemic stroke with single, dual, or triple therapy in patients with atrial fibrillation



Hansen ML, Archives of Internal Medicine 170, 1433-41 (2010)

Epidemiology and Prevention

Bleeding After Initiation of Multiple Antithrombotic Drugs, Including Triple Therapy, in Atrial Fibrillation Patients Following Myocardial Infarction and Coronary Intervention

A Nationwide Cohort Study

Morten Lamberts, MD; Jonas Bjerring Olesen, MD; Martin Huth Ruwald, MD; Carolina Malta Hansen, MD; Deniz Karasoy, MD; Søren Lund Kristensen, MD; Lars Køber, MD, DMSc; Christian Torp-Pedersen, MD, DMSc; Gunnar Hilmar Gislason, MD, PhD; Morten Lock Hansen, MD, PhD

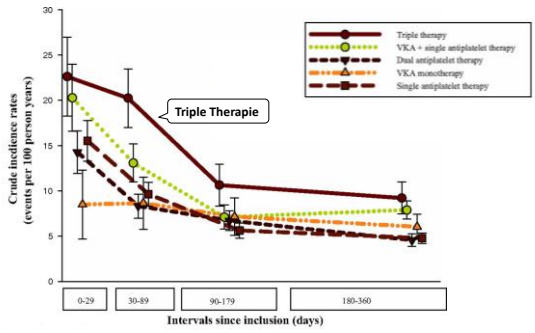
Background—Uncertainty remains over optimal antithrombotic treatment of patients with atrial fibrillation presenting with myocardial infarction and/or undergoing percutaneous coronary intervention. We investigated the risk and time frame for bleeding following myocardial infarction/percutaneous coronary intervention in patients with atrial fibrillation according to antithrombotic treatment.

Methods and Results—Patients with atrial fibrillation and admitted with myocardial infarction or for percutaneous coronary intervention between 2000 and 2009 (11 480 subjects, mean age 75.6 years [SD ± 10.3], males 60.9%) were identified by individual level linkage of nationwide registries in Denmark. Fatal or nonfatal (requiring hospitalization) bleeding was determined according to antithrombotic treatment regimen: triple therapy (TT) with vitamin K antagonist (VKA) + aspirin + clopidogrel, VKA + antiplatelet, and dual antiplatelet therapy with aspirin + clopidogrel. We calculated crude incidence rates and adjusted hazard ratios by Cox regression models. Within 1 year, 728 bleeding events were recorded (6.3%); 79 were fatal (0.7%). Within 30 days, rates were 22.6, 20.3, and 14.3 bleeding events per 100 person-years for TT, VKA + antiplatelet, and dual antiplatelet therapy, respectively. Both early (within 90 days) and delayed (90–360 days) bleeding risk with TT exposure in relation to VKA + antiplatelet was increased; hazard ratio 1.47 (1.04;2.08) and 1.36 (0.95;1.95), respectively. No significant difference in thromboembolic risk was observed for TT versus VKA + antiplatelet; hazard ratio, 1.15 (0.95;1.40).

Conclusions—High risk of bleeding is immediately evident with TT after myocardial infarction/percutaneous coronary intervention in patients with atrial fibrillation. A continually elevated risk associated with TT indicates no safe therapeutic window, and TT should only be prescribed after thorough bleeding risk assessment of patients. (***Circulation***. **2012;126:1185-1193.**)

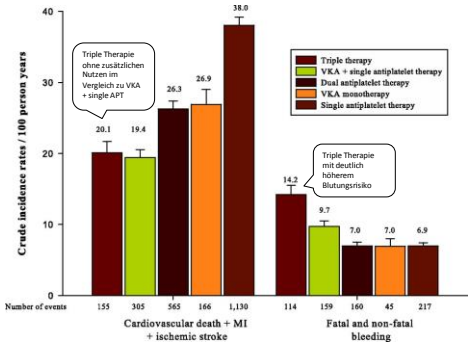
Lamberts M et al. Circulation 2012; 126: 1185-1193.

Bleeding After Initiation of Multiple Antithrombotic Drugs
Including Triple Therapy, in AF Patients Following MI and Coronary Intervention



Lamberts M et al. Circulation 2012; 126: 1185-1193.

Bleeding After Initiation of Multiple Antithrombotic Drugs
Including Triple Therapy, in AF Patients Following MI and Coronary Intervention



Lamberts M et al. Circulation 2012; 126: 1185-1193.

Bei Vorhofflimmern
nach elektiver Koronarintervention mit Stenting:
Triple-Therapie mit ASS, Clopidogrel und OAK
1 Monat
IIa B

European Heart Journal. doi:10.1093/eurheartj/ehw210.

Bei Vorhofflimmern
nach akutem Koronarsyndrom und Koronarintervention mit Stenting:
Triple-Therapie mit ASS, Clopidogrel und OAK
1-6 Monate
IIa C

European Heart Journal. doi:10.1093/eurheartj/ehw210.

Bei Vorhofflimmern
nach akutem Koronarsyndrom
Ø Koronarintervention, Ø Stentimplantation:
Duale Therapie mit ASS oder Clopidogrel und OAK
bis zu 12 Monate
IIa C

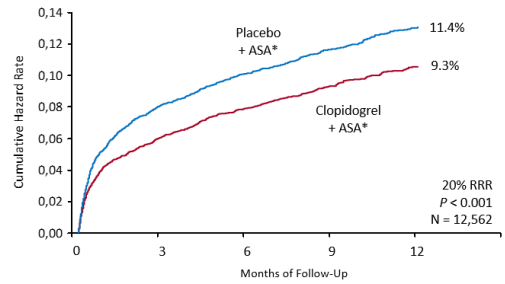
European Heart Journal. doi:10.1093/eurheartj/ehw210.

Bei geplanten Interventionen/Operationen:
Besser Fortführung der OAK als "switching" oder "bridging" zu anderen Antikoagulantien
→ reduziert das periinterventionelle Blutungsrisiko.

European Heart Journal. doi:10.1093/eurheartj/ehw210.

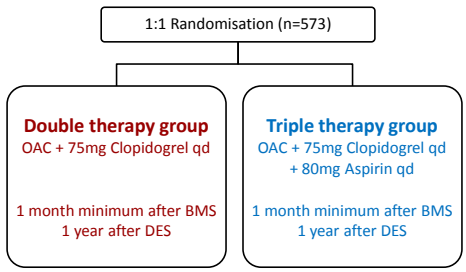
Faktor V:
Können wir auf Aspirin verzichten?

CURE: Primary End Point - MI/Stroke/CV Death



The CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

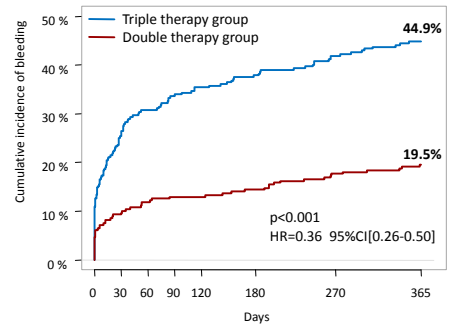
WOEST



Follow up: 1 year
Primary Endpoint: The occurence of all bleeding events (TIMI criteria)
Secondary Endpoints:
- Combination of stroke, death, myocardial infarction, stent thrombosis and TLR
- All individual components of primary and secondary endpoints

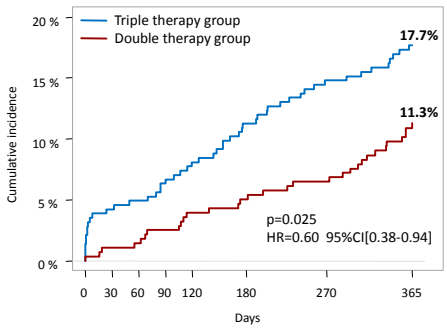
Dewilde WJ et al. Lancet. 2013 Mar 30;381(9872):1107-15.

WOEST
Primärer Endpunkt: Gesamtzahl der TIMI-Blutungen



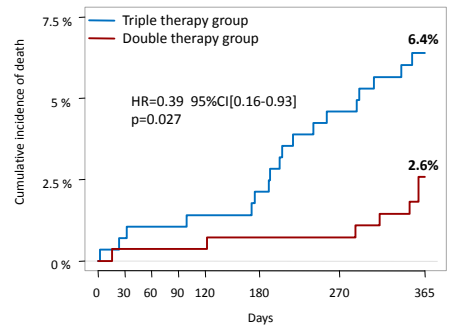
Dewilde WJ et al. Lancet. 2013 Mar 30;381(9872):1107-15.

WOEST
Sekundärer Endpunkt (Tod, MI, TVR, Schlaganfall, ST)



Dewilde WJ et al. Lancet. 2013 Mar 30;381(9872):1107-15.

WOEST
Gesamtsterblichkeit



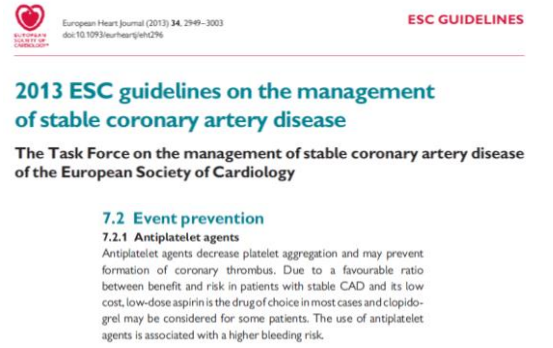
Dewilde WJ et al. Lancet. 2013 Mar 30;381(9872):1107-15.

2014 Consensus Document

Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS)

"Although it might be premature to abandon aspirin after stent implantation in AF patients requiring OAC based solely on the results of WOEST, **dual therapy with OAC and clopidogrel may be considered as an alternative to triple therapy in selected AF patients at low risk of stent thrombosis/recurrent cardiac events.**"

Lip G al. EHJ 2014.



European Heart Journal (2013) 34, 2949–3003
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

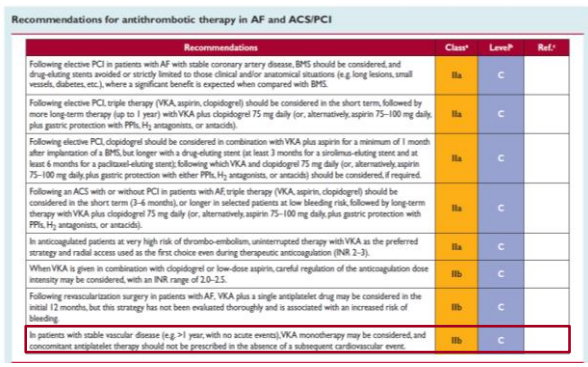
7.2 Event prevention

7.2.1 Antiplatelet agents

Antiplatelet agents decrease platelet aggregation and may prevent formation of coronary thrombus. Due to a favourable ratio between benefit and risk in patients with stable CAD and its low cost, low-dose aspirin is the drug of choice in most cases and clopidogrel may be considered for some patients. The use of antiplatelet agents is associated with a higher bleeding risk.

European Heart Journal (2013) 34, 2949–3003

Bei stabiler KHK ohne PCI und ohne ACS ..



Recommendations for antithrombotic therapy in AF and ACS/PCI

Recommendations	Class[a]	Level[b]	Ref.[c]
Following elective PCI in patients with AF with stable coronary artery disease, BMS should be considered, and drug-eluting stents avoided or strictly limited to those clinical and/or anatomical situations (e.g. long lesions, small vessels, diabetes, etc.), where a significant benefit is expected when compared with BMS.	IIa	C	
Following elective PCI, triple therapy (VKA, aspirin, clopidogrel) should be considered in the short term, followed by more long-term therapy (up to 1 year) with VKA plus clopidogrel 75 mg daily (or, alternatively, aspirin 75–100 mg daily, plus gastric protection with PPIs, H_2 antagonists, or antacids).	IIa	C	
Following elective PCI, clopidogrel should be considered in combination with VKA plus aspirin for a minimum of 1 month after implantation of a BMS, but longer with a drug-eluting stent (at least 3 months for a sirolimus-eluting stent and at least 6 months for a paclitaxel-eluting stent); following which VKA and clopidogrel 75 mg daily (or, alternatively, aspirin 75–100 mg daily, plus gastric protection with either PPIs, H_2 antagonists, or antacids) should be considered, if required.	IIa	C	
Following an ACS with or without PCI in patients with AF, triple therapy (VKA, aspirin, clopidogrel) should be considered in the short term (3–6 months), or longer in selected patients at low bleeding risk, followed by long-term therapy with VKA plus clopidogrel 75 mg daily (or, alternatively, aspirin 75–100 mg daily, plus gastric protection with PPIs, H_2 antagonists, or antacids).	IIa	C	
In anticoagulated patients at very high risk of thrombo-embolism, uninterrupted therapy with VKA as the preferred strategy and radial access used as the first choice even during therapeutic anticoagulation (INR 2–3).	IIa	C	
When VKA is given in combination with clopidogrel or low-dose aspirin, careful regulation of the anticoagulation dose intensity may be considered, with an INR range of 2.0–2.5.	IIb	C	
Following revascularization surgery in patients with AF, VKA plus a single antiplatelet drug may be considered in the initial 12 months, but this strategy has not been evaluated thoroughly and is associated with an increased risk of bleeding.	IIb	C	
In patients with stable vascular disease (e.g. >1 year, with no acute events), VKA monotherapy may be considered, and concomitant antiplatelet therapy should not be prescribed in the absence of a subsequent cardiovascular event.	IIb	C	

European Heart Journal (2010) 31, 2369–2429

Bei **stabiler KHK und Vorhofflimmern**
können wir bei oraler Antikoagulation (mit VKA)
auf ASS verzichten
- dies gilt auch für die periphere arterielle Verschlusskrankheit.
.

European Heart Journal. doi:10.1093/eurheartj/ehw210.

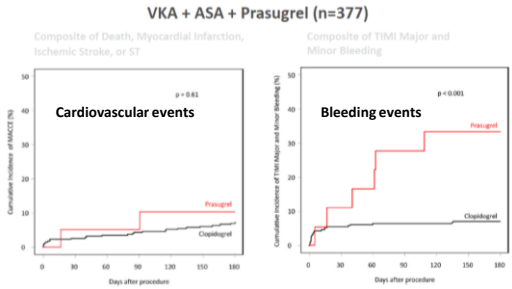
Duale Therapie mit
OAK (VKA oder NOAK) plus Clopidogrel 75 mg/d
kann bei ausgewählten Patienten
eine **Alternative zur initialen Triple-Therapie** sein.
IIa B

European Heart Journal. doi:10.1093/eurheartj/ehw210.

Faktor VI:
Typ des Thrombozytenaggregationshemmers in der Triple-Therapie

Typ der P2Y12-Inhibition

6-month regimen of aspirin and oral anticoagulation with either prasugrel or clopidogrel after DES



Sarafoff N et al. J Am Coll Cardiol 2013;61:2060–6.

Typ der P2Y12-Inhibition

Wenn Triple-Therapie: Clopidogrel
Prasugrel und Ticagrelor sollten vermieden werden.

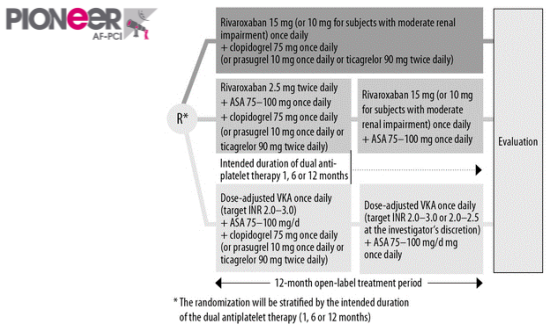
European Heart Journal. doi:10.1093/eurheartj/ehw210.

Faktor VII:
NOAKs & Triple Therapie

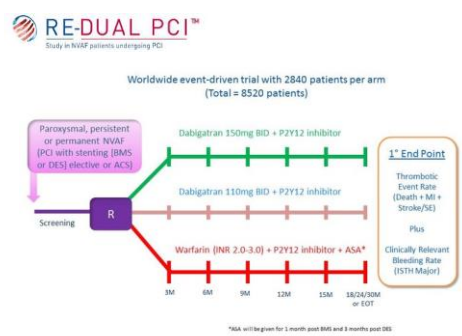
RE-LY Studie (Untergruppenanalyse):
Single APT + 110 mg Dabigatran
im Vergleich zu APT + Warfarin und APT + 150 mg Dabigatran
die Gruppe mit dem geringsten Blutungsrisiko

European Heart Journal. doi:10.1093/eurheartj/ehw210.

NOAKs & Triple Therapie



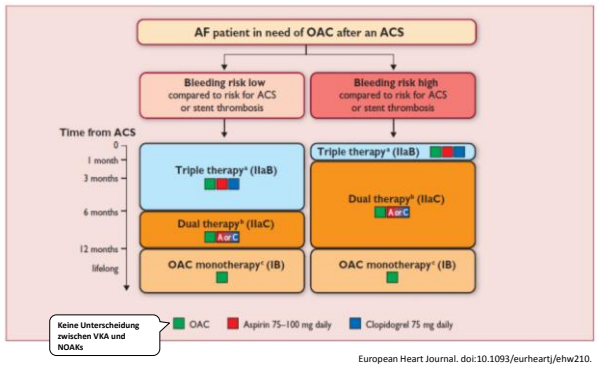
NOAKs & Triple Therapie



Schlussfolgerungen

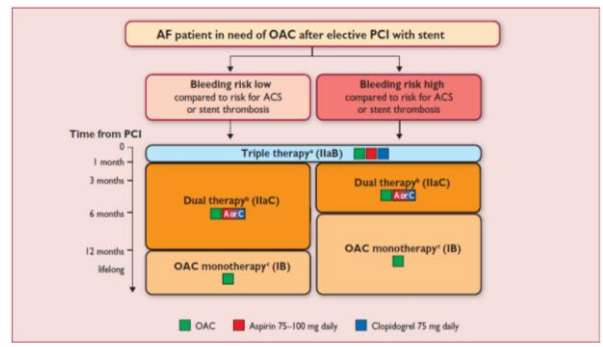
Einfache Schemata für alle
(z.B. 4 Wochen Triple, dann OAK)
vs.
Individualisierte Entscheidungen

ESC-Empfehlungen bei Akutem Koronarsyndrom



European Heart Journal. doi:10.1093/eurheartj/ehw210.

ESC-Empfehlungen nach Koronarintervention



European Heart Journal. doi:10.1093/eurheartj/ehw210.

Alle Patienten erhalten nach einer Koronarintervention einen **Stentpass**, in dem Empfehlungen zur Dauer und Art der OAK und Thrombozytenaggregationshemmung dokumentiert werden (müssen)!
Ggf. Rücksprache mit Zentrum/Operateur

European Heart Journal. doi:10.1093/eurheartj/ehw210.

"EVB-KARD/ANG-Empfehlungen": TAH & OAK bei komplexen kardiologischen Interventionen

Device	Vor der Intervention	Nach der Intervention
TAVI (Corevalve®) *Based on: Bocksch et al. Kardiologie up2date. 2012;8:188-192.*	– Am Vortag 500 mg ASS + 300 mg Clopidogrel – INR vor Intervention < 2,0	– **Standard** (Pat. ohne Ind. OAK, TAVI ohne PCI): 100 mg/d ASS + 75 mg/d Clopidogrel für 6 Monate (min. 15 d.) - danach ASS – **Indikation zur OAK**: Clopidogrel + Falithrom (INR-Ziel 2-2,5 bei Vorhofflimmern, 3,0 bei mechanischer Mitralklappe, keine NOAKs) für 6 Monate (min. 15 Tage) - danach OAK – **TAVI + PCI BMS**: ASS + Clopidogrel 6 Monate (min. 30 d.) - danach ASS – **TAVI + PCI DES**: ASS + Clopidogrel 12 Monate (min. 90 d.) - danach ASS – **TAVI + PCI DES + AFib**: Monat 1-6: Falithrom (INR-Ziel 2-2,5) + ASS + Clopidogrel, Monat 7-12: Falithrom + Clopidogrel, danach OAK
MitraClip® *Based on: Boekstegers et al. Kardiologe. 2013;7:91–104.*	– Am Vortag 500 mg ASS + 300 mg Clopidogrel – INR vor Intervention < 2,0	– **Standard** (Pat. ohne Ind. OAK, MitraClip ohne PCI): 100 mg/d ASS für 6 Monate + 75 mg/d Clopidogrel für 1 Monat – **Indikation zur OAK:** Clopidogrel oder ASS für 1 Monat + Falithrom (INR-Ziel 2-2,5 bei Vorhofflimmern, 2,5-3,0 bei mechanischer Aortenklappe, keine NOAKs) - danach OAK
PFO-/ASD-Verschluss	– Am Vortag 500 mg ASS + 300 mg Clopidogrel	– **Standard**: 100 mg/d ASS + 75 mg/d Clopidogrel für 3 Monate – TEE nach 3 Monaten (bei Restshunt: ASS + Clopidogrel für weitere 3 Monate, kein Restshunt: ASS für weitere 3 Monate) – **Indikation zur OAK**: INR-Ziel 2-2,5 bei Vorhofflimmern, 2,5-3,0 bei mechanischer Aortenklappe, 3,0 bei mechanischer Mitralklappe, für 6 Monate zusätzlich 75 mg/d Clopidogrel
LAA-Verschluss (Watchman®) *Based on: Meier B et al. Euro-Intervention 2015;10:1109-112.*	– Am Vortag 500 mg ASS + 300 mg Clopidogrel – INR vor Intervention < 2,0	– **HAS-BLED 0-2:** 100 mg/d ASS lebenslang, OAK (INR-Ziel 2-2,5) für 6 Wochen, dann 75 mg/d Clopidogrel bis Ende 6 Monate nach Prozedur – **HAS-BLED ≥ 3:** 100 mg/d ASS lebenslang, 75 mg/d Clopidogrel für 6 Monate – TEE nach 6 Monaten (bei Restshunt: ASS + Clopidogrel, kein Restshunt: ASS lebenslang)

Bonaventura, TAH & OAK bei kardiologischen Diagnosen und Interventionen - Potsdam, Version 5.0, 06/2016

"EVB-KARD/ANG-Empfehlungen": TAH & OAK bei PVI, Device-Therapie und RDN

Device	Vor der Implantation	Nach der Implantation
PVI	– INR vor Intervention < 2,0 – Bei NOAKs 48 Stunden Pause vor PVI – Ggf. überlappend Heparin (UFH/NMH)	– Beginn OAK am Folgetag – Ggf. überlappend Heparin (UFH/NMH) – OAK für 3 Monate (Ziel INR 2,0-2,5), weitere OAK nach CHA_2DS_2-VASc Score
Schrittmacher, ICD, CRT, Event-Rekorder	– INR vor Intervention ≤ 2,0 – Bei Vorhofflimmern: Letzte Heparingabe am Vorabend – Bei mechanischen Herzklappen und anderen Indikationen: Rücksprache mit HKL	– Beginn OAK nach Rücksprache mit Operateur – Überlappende Gaben von UFH/NMH zurückhaltend
Renale Denervation *Based on: Mahfoud et al. Kardiologe. 2013;7:429-434.*	– Am Vortag 100 mg ASS	– **Standard**: 100 mg/d ASS für 4 Wochen

Die **Dauer der Kombinationstherapie**, insbesondere der Triple-Therapie, sollte **so kurz wie nötig** gehalten werden … und dabei eine Ausgleich der Risiken für Blutungen und Koronarereignisse angestrebt werden.

IIa B

Typischer Fall

Ein Patient, 70 Jahre, kommt am Freitag Nachmittag nach stationärem Aufenthalt wegen KHK zur Verordnung seiner Medikation aus dem Krankenhaus in Ihre Praxis.

Er hat eine bekannte arterielle Hypertonie und eine Niereninsuffizienz (GFR 50), LV-EF 48%.

Im vorläufigen Arztbrief wird nach DES-Stenting der LAD eine Behandlung mit ASS + Clopidogrel für 12 Monate empfohlen.

Er erhält wegen Vorhofflimmerns seit vielen Jahren von Ihnen eine orale Antikoagulation mit einem Vitamin K-Antagonisten.

Risikostratifizierung

4

⇨ **CHA_2DS_2-VASc Score**

(a) Risk factors for stroke and thrombo-embolism in non-valvular AF	
'Major' risk factors	'Clinically relevant non-major' risk factors
Previous stroke, TIA, or systemic embolism Age ≥75 years	Heart failure or moderate to severe LV systolic dysfunction (e.g. LV EF ≤ 40%) Hypertension - Diabetes mellitus Female sex - Age 65–74 years Vascular disease[a]
(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc (Note: maximum score is 9 since age may contribute 0, 1, or 2 points)	

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

ESC-Guidelines for the management of atrial fibrillation 2010, http://www.escardio.org

HAS-BLED Bleeding Risk Score

4

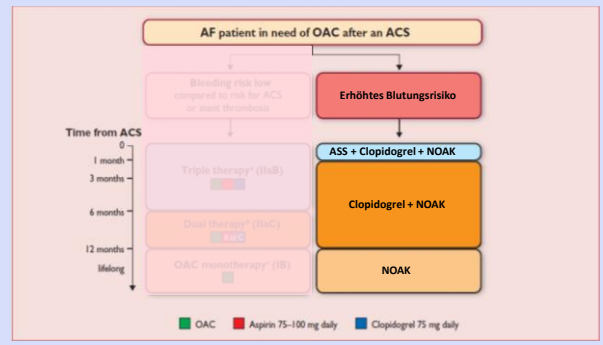
⇨ **Blutungsrisiko bei Antikoagulation**

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

z.B. ASS, Clopidogrel, NSAR

ESC-Guidelines for the management of atrial fibrillation 2010, http://www.escardio.org

TAH & OAK bei PCI und AFib



European Heart Journal. doi:10.1093/eurheartj/ehw210.

LESS IS ALWAYS MORE AND OFTEN *better.*

Klinikum Ernst von Bergmann, Potsdam