Individualisierte Behandlung von Patienten mit Vorhofflimmern & KHK

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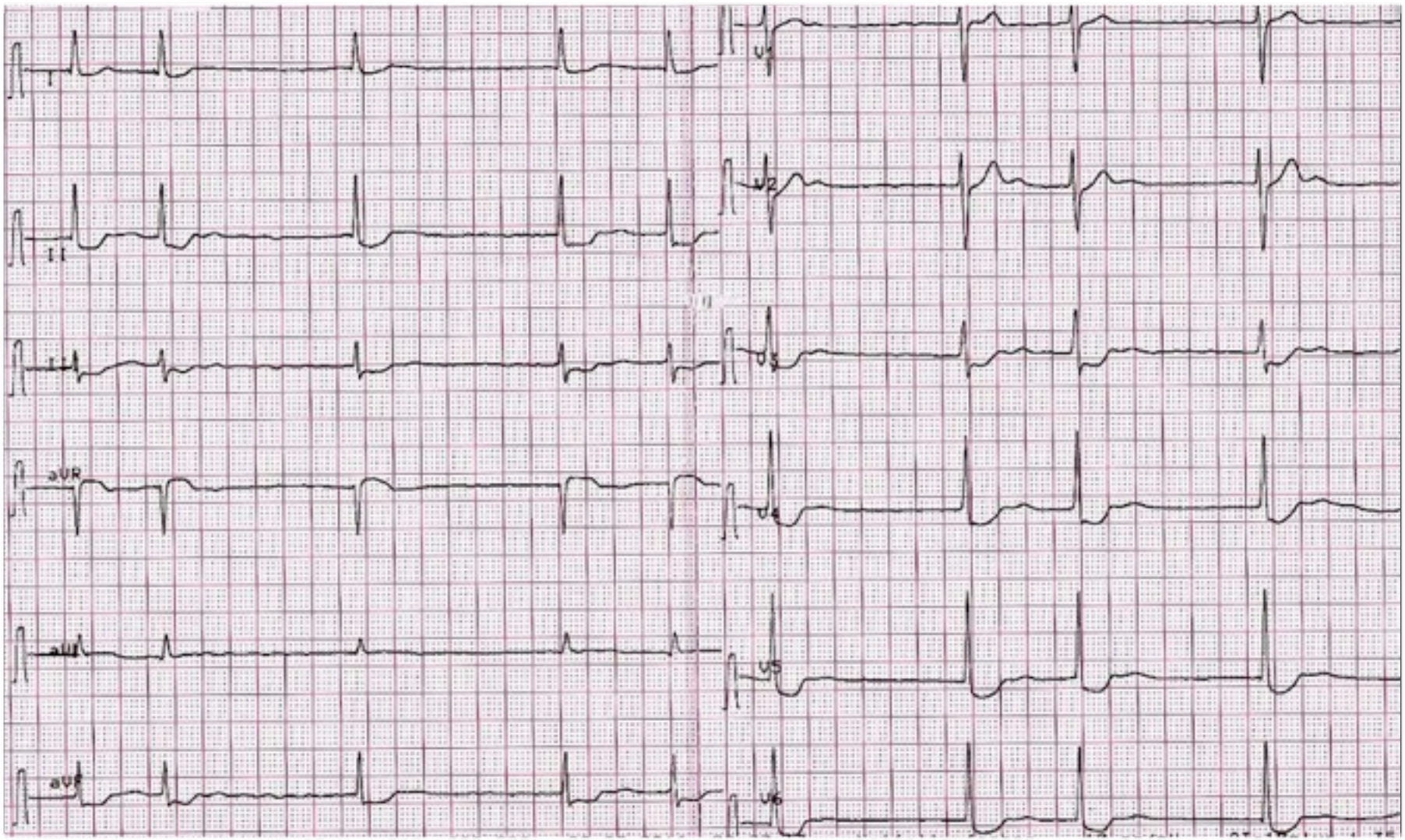
Stainach, 20. Juni 2017


I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

Antikoagulantien - Juni 2017

	Post-OP VTE Proph	Int. VTE Proph.	VTE Therapie	ACS	VH-Flimmern	Klappen-ersatz
VKA*	+	-	+	+	+	+
UFH**	+	-	+	+	-	-
NMH***	+	+	+	+	+	-
Fondaparinux	+	+	+	+	-	-
Dabigatran	+	-	+	-	+	-
Rivaroxaban	+	-	+	+	+	-
Apixaban	+	-	+	-	+	-
Edoxaban	-	-	+	-	+	-

*Vitamin K Antagonist, **unfraktioniertes Heparin, ***niedermolekulares Heparin

Dabigatran - Pradaxa®

Rivaroxaban - Xarelto®

Apixaban - Eliquis®

Edoxaban - Lixiana®

Zulassungsstudien der NOAK bei VHF

Dabigatran	RE-LY NEJM 2009; 361: 1139
Rivaroxaban	ROCKET-AF NEJM 2011; 365: 883
Apixaban	ARISTOTLE NEJM 2011; 365: 883
Edoxaban	ENGAGE-AF NEJM 2013; 369: 2093

„Signifikanzen“ für NOAK vs. Warfarin

Überblick – qualitativ, Gesamtstudie

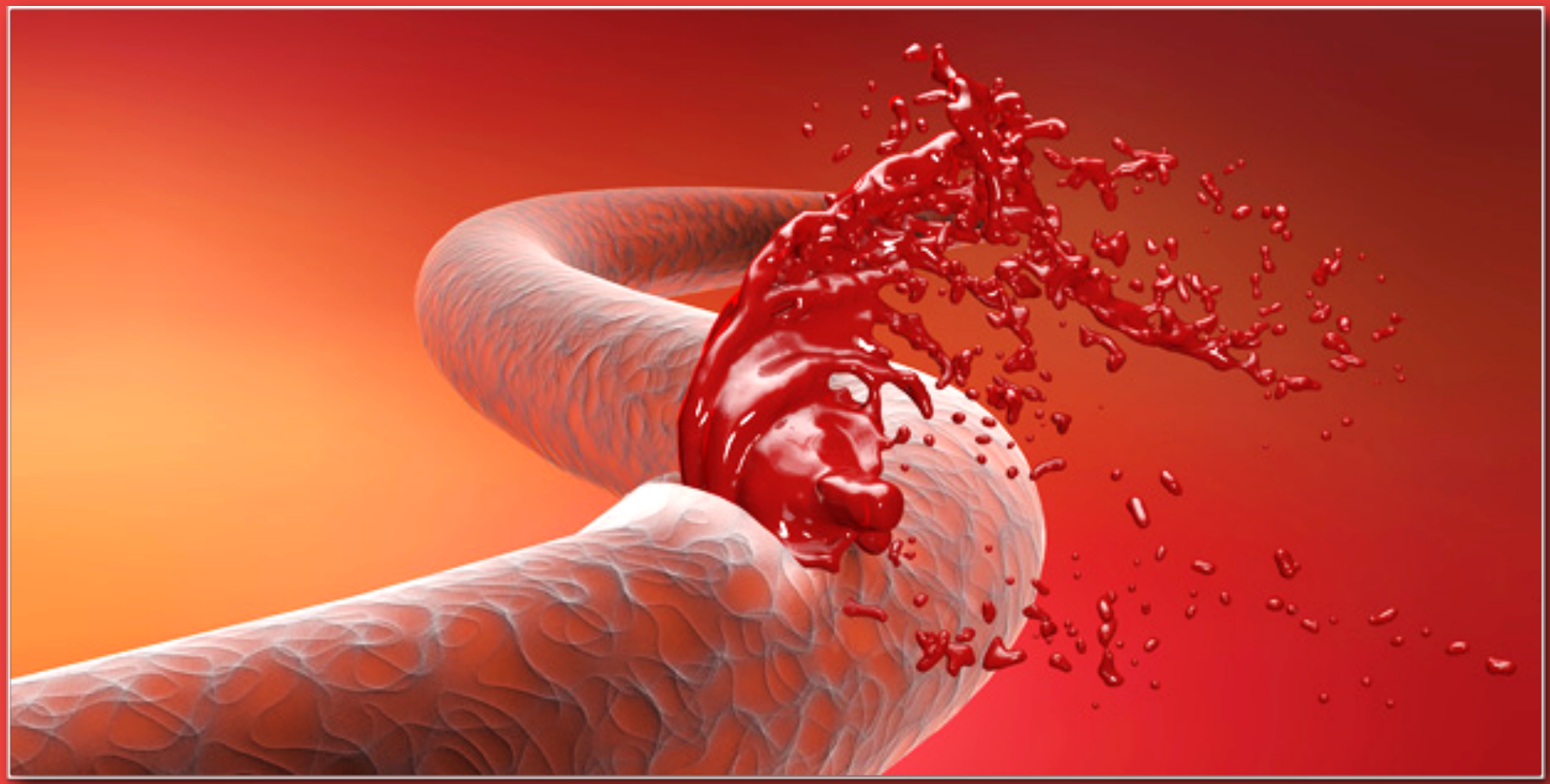
vs. Warfarin	Insult + SSE	ischäm. Insult	schwere Blutungen	Hirn-blutungen
Dabigatran 2 x 110mg	↔	↔	↓	↓
Dabigatran 2 x 150mg	↓	↓	↔	↓
Rivaroxaban 1 x 20mg	↔	↔	↔	↓
Apixaban 2 x 5mg	↓	↔	↓	↓
Edoxaban 1 x 30mg	↔	↑	↓	↓
Edoxaban 1 x 60mg	↔	↔	↓	↓

Spezifische Antidota

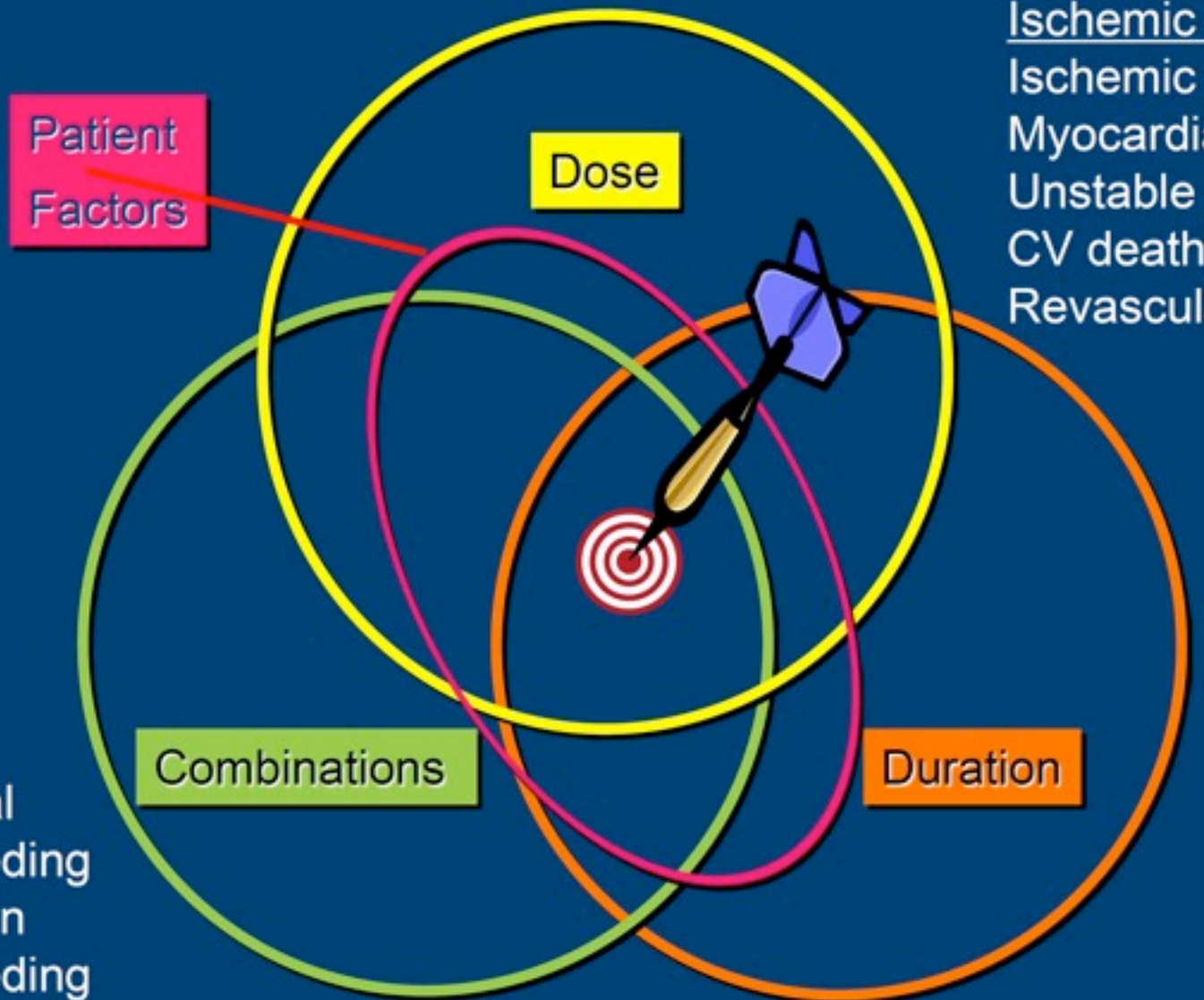
- **Prompter Wirkungseintritt**
- **Vollständige Neutralisierung der NOAK Effekte**
- **Minimales Risiko für prothrombotische Ereignisse**

Höhere Therapiesicherheit

schwerwiegende Blutungskomplikationen



The Sweet Spot for Antithrombotics



Ischemic Events
Ischemic stroke
Myocardial infarction
Unstable angina
CV death
Revascularization

Bleeding
Intracranial
Major bleeding
Transfusion
Minor bleeding

ESC 2012

ICM Internationales Congress Center München

Update on Consensus Statements on Management of Atrial Fibrillation European Heart Rhythm Association

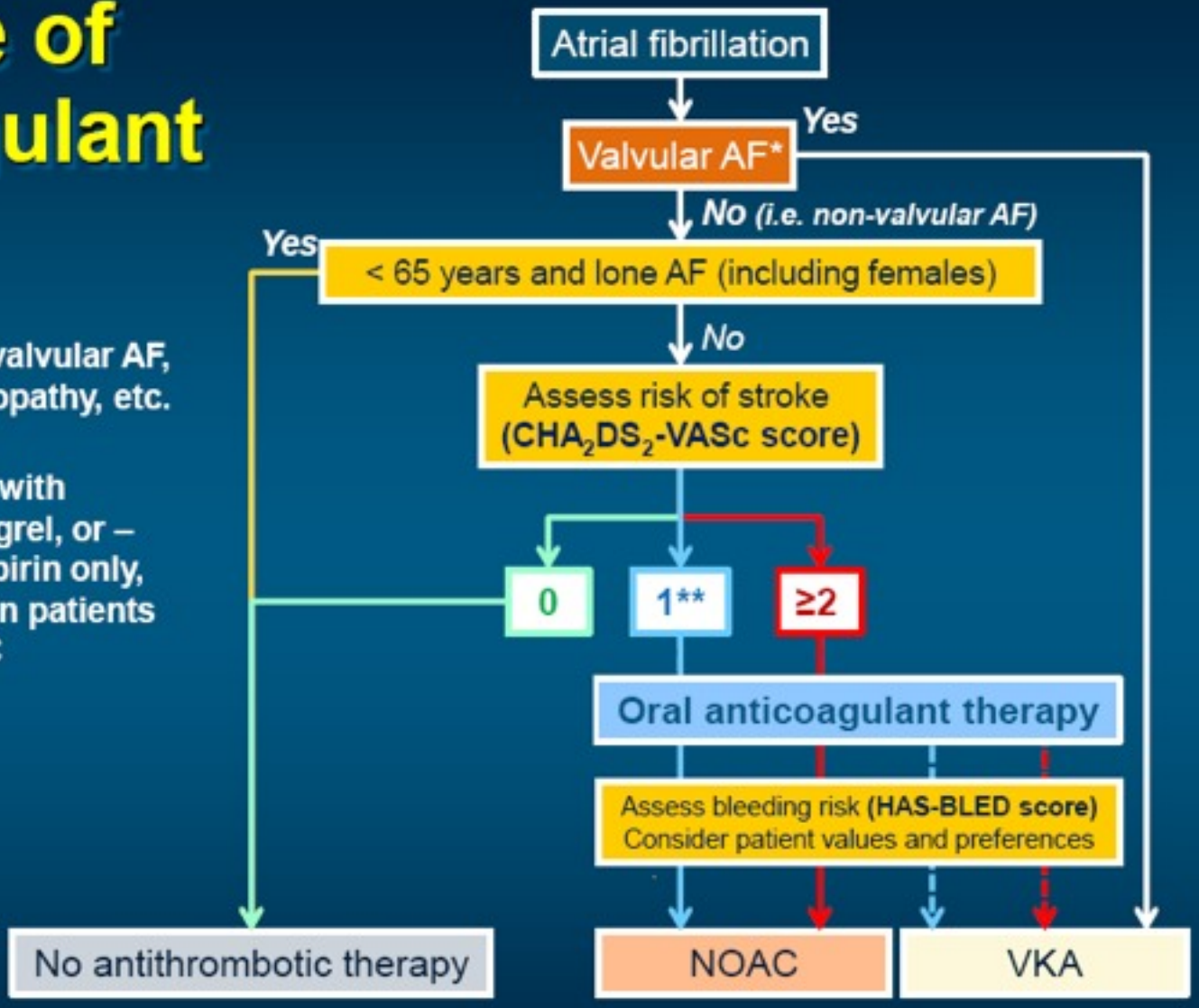
Update of the ESC Guidelines on Medical Therapy 2012

John Camm

St. George's University of London

United Kingdom

Choice of Anticoagulant



* Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs253

ESC 2016 guidelines for prediction of stroke and bleeding risk in atrial fibrillation

Recommendation	Class	Level
The **CHA_2DS_2-VASc score** is recommended for stroke risk prediction in patients with AF	I	A

ESC 2016 guidelines for prediction of stroke and bleeding risk in atrial fibrillation

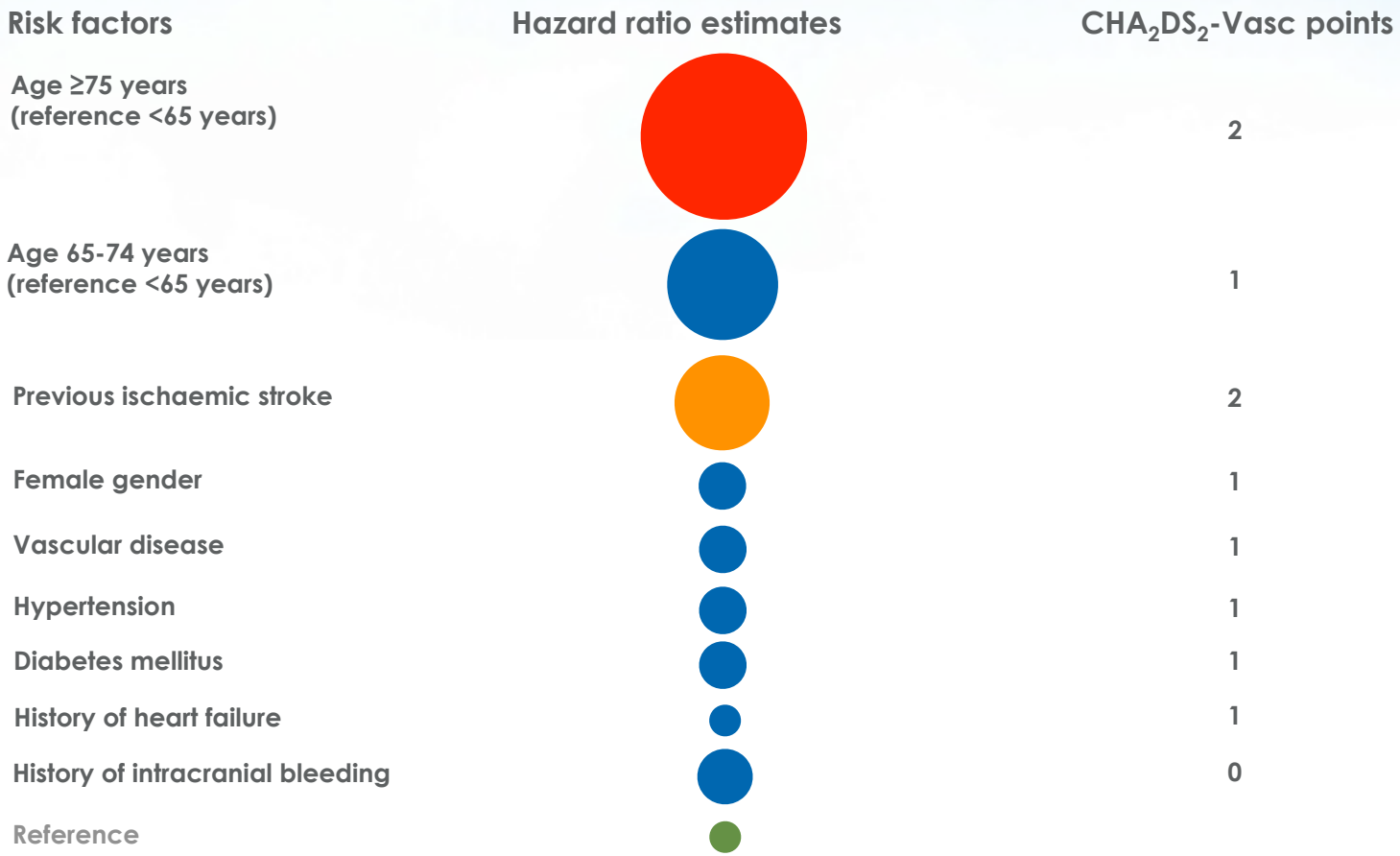
Recommendation	Class	Level
Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding	IIa	B

Which scores do you use regularly to assess thromboembolic and bleeding risk in your patients?

1. CHA_2DS_2-VASc
2. $CHADS_2$
3. HAS-BLED
4. ABC
5. ATRIA
6. ORBIT
7. I do not use any scores

Risiko: Vorhofflimmern

Risk factors for thromboembolic events in AF patients: multivariate hazard ratio estimates



Argulian E et al. Am J Med 2015

European Heart Journal Advance Access published February 4, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw069

REVIEW

Prevention

Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 2

Hans-Christoph Diener[1]*, James Aisenberg[2], Jack Ansell[3], Dan Atar[4], Günter Breithardt[5], John Eikelboom[6], Michael D. Ezekowitz[7,8,9], Christopher B. Granger[10], Jonathan L. Halperin[11], Stefan H. Hohnloser[12], Elaine M. Hylek[13], Paulus Kirchhof[14,15], Deirdre A. Lane[16], Freek W.A. Verheugt[17], Roland Veltkamp[18], and Gregory Y.H. Lip[19,20]

[1]Department of Neurology, University Hospital Essen, Essen, Germany; [2]Icahn School of Medicine at Mount Sinai, New York, USA; [3]Hofstra North Shore/LIJ School of Medicine, Hempstead, USA; [4]Division of Medicine, Oslo University Hospital, Ullevål and University of Oslo, Norway; [5]Division of Rhythmology, Department of Cardiovascular Medicine, Hospital of the University Münster, Münster, Germany; [6]Population Health Research Institute, McMaster University, Hamilton, ON, Canada; [7]Cardiovascular Research Foundation, New York, NY, USA; [8]Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, PA, USA; [9]Lankenau Medical Center, Wynnewood, PA, USA; [10]Department of Medicine, Duke University, Durham, NC, USA; [11]Icahn School of Medicine at Mount Sinai, Mount Sinai Medical Center, New York, NY, USA; [12]Division of Clinical Electrophysiology, Department of Cardiology, J. W. Goethe University, Frankfurt, Germany; [13]Boston Medical Center, Boston University School of Medicine, Boston, MA, USA; [14]Institute of Cardiovascular Sciences, University of Birmingham, SWBH and UHB NHS Trusts, Birmingham, UK; [15]Department of Cardiovascular Medicine, Hospital of the University of Münster, Münster, Germany; [16]University of Birmingham, Institute of Cardiovascular Sciences, City Hospital, Birmingham, UK; [17]Afdeling Cardiologie, Hartcentrum OLVG, Amsterdam, The Netherlands; [18]Imperial College London, London, UK; [19]University of Birmingham, Birmingham, UK; and [20]Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

Patients with a high risk of gastrointestinal bleeding

First choice

For patients with a high risk of gastrointestinal bleeding, apixaban 5 mg twice daily or dabigatran 110 mg twice daily may be used

Second choice

Dabigatran 150 mg twice daily, edoxaban 60 mg once daily, or rivaroxaban 20 mg once daily

Comments

Gastrointestinal bleeding, even in the setting of anticoagulation, does usually not cause death or permanent major disability. Thus, the choice of OAC should be driven mainly by stroke prevention considerations

Patients with renal impairment and on dialysis

First choice

Patients with AF and stage III CKD (creatinine clearance 30–49 mL/min) may be treated with apixaban 5 mg twice daily (apixaban 2.5 mg twice a day if ≥1 additional criteria: age ≥80 years, body weight ≤60 kg, serum creatinine ≥ 1.5 mg/dL (133 mmol/L are present), rivaroxaban 15 mg daily, or edoxaban 30 mg once daily

Second choice

Dabigatran 110 mg twice daily

Not recommended

Dabigatran 150 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily

Non-vitamin K oral anticoagulants and age

First choice

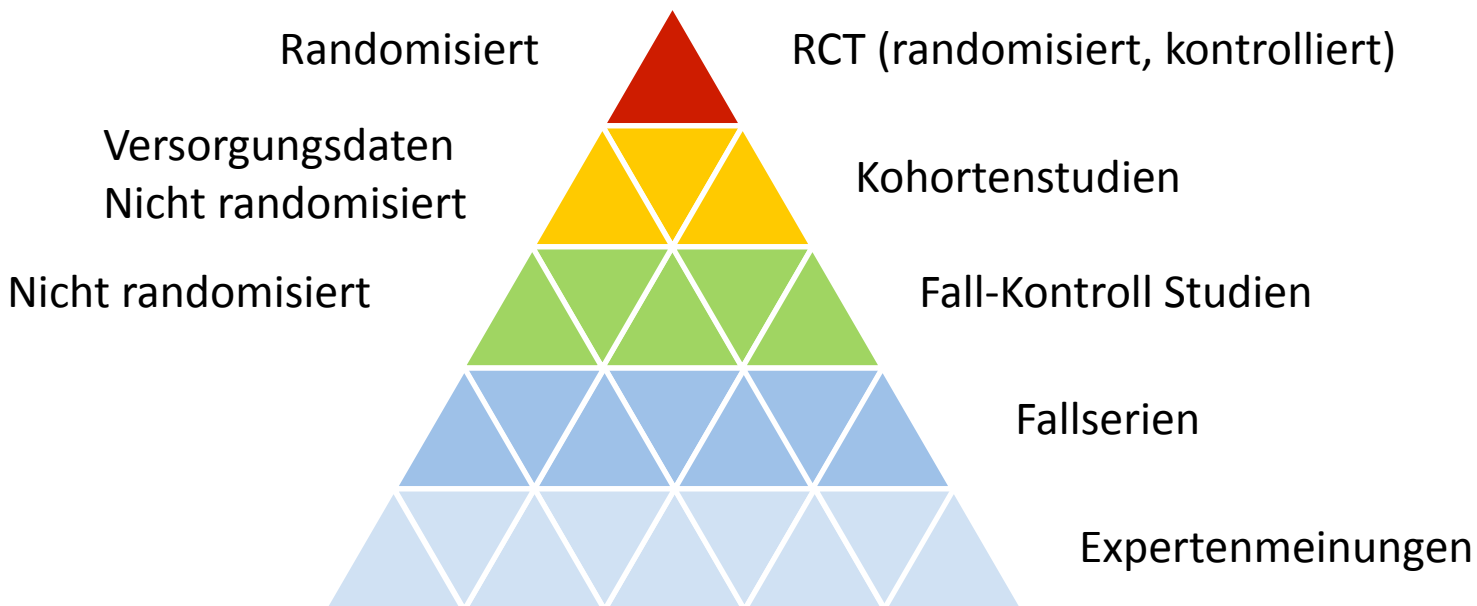
In patients older than 75 years, we suggest apixaban 5 mg twice daily [2.5 mg if ≥2 of the following: age ≥80 years, body weight ≤60 kg, or creatinine ≥1.5 mg/dL (133 mmol/L)]

Second choice

Dabigatran 110 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily

Vergleich der Resultate von RE-LY, ROCKET AF und ARISTOTLE

Versorgunsdaten - Evidenz



REAL-WORLD-DATEN: Mayo Clinic Analyse

ORIGINAL RESEARCH

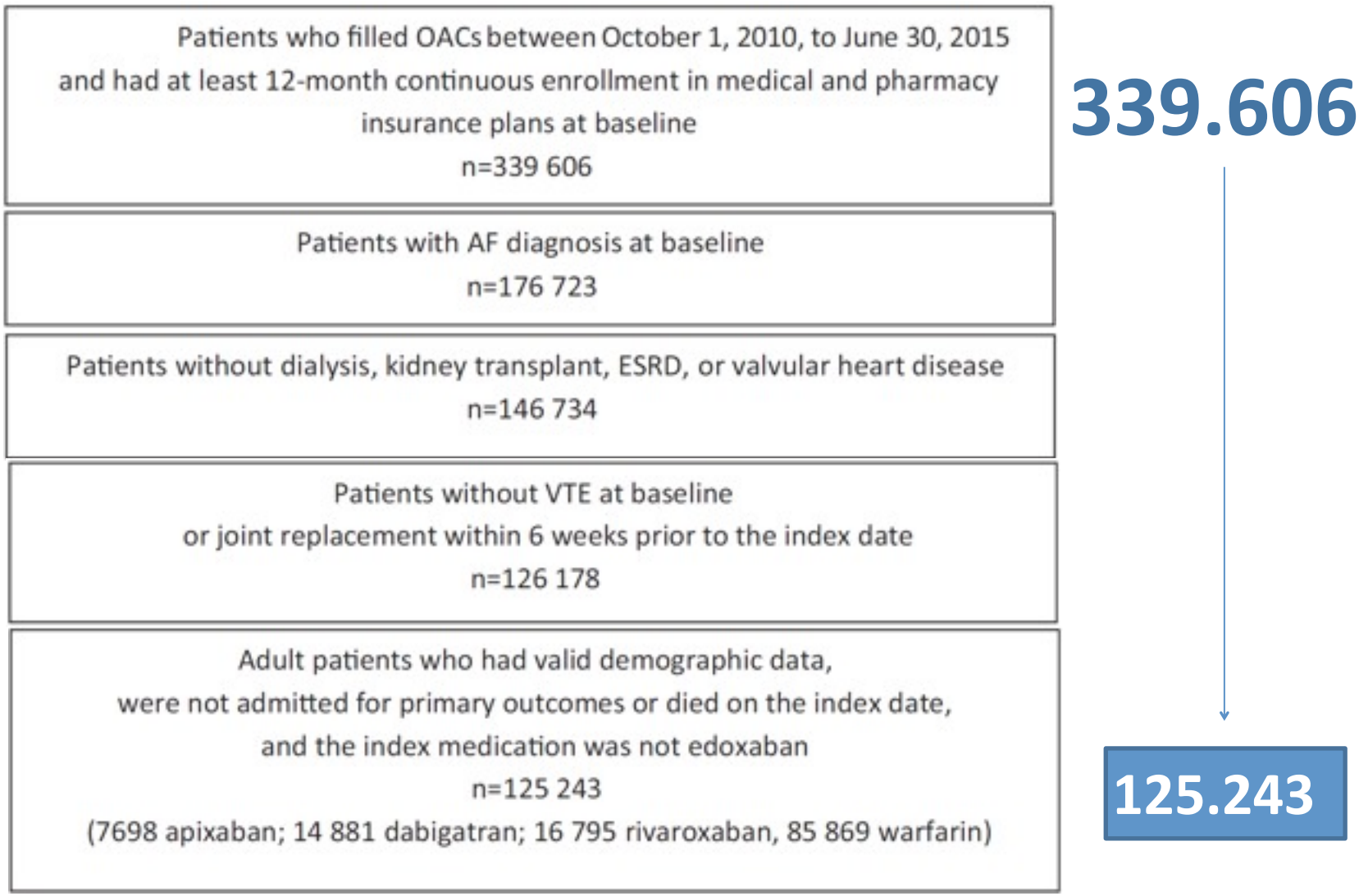
American Heart Association | American Stroke Association

Effectiveness and Safety of Dabigatran, Rivaroxaban, and Apixaban Versus Warfarin in Nonvalvular Atrial Fibrillation

Xiaoxi Yao, PhD; Neena S. Abraham, MD, MSCE; Lindsey R. Sangaralingham, MPH; M. Fernanda Bellolio, MD, MS; Robert D. McBane, MD; Nilay D. Shah, PhD; Peter A. Noseworthy, MD

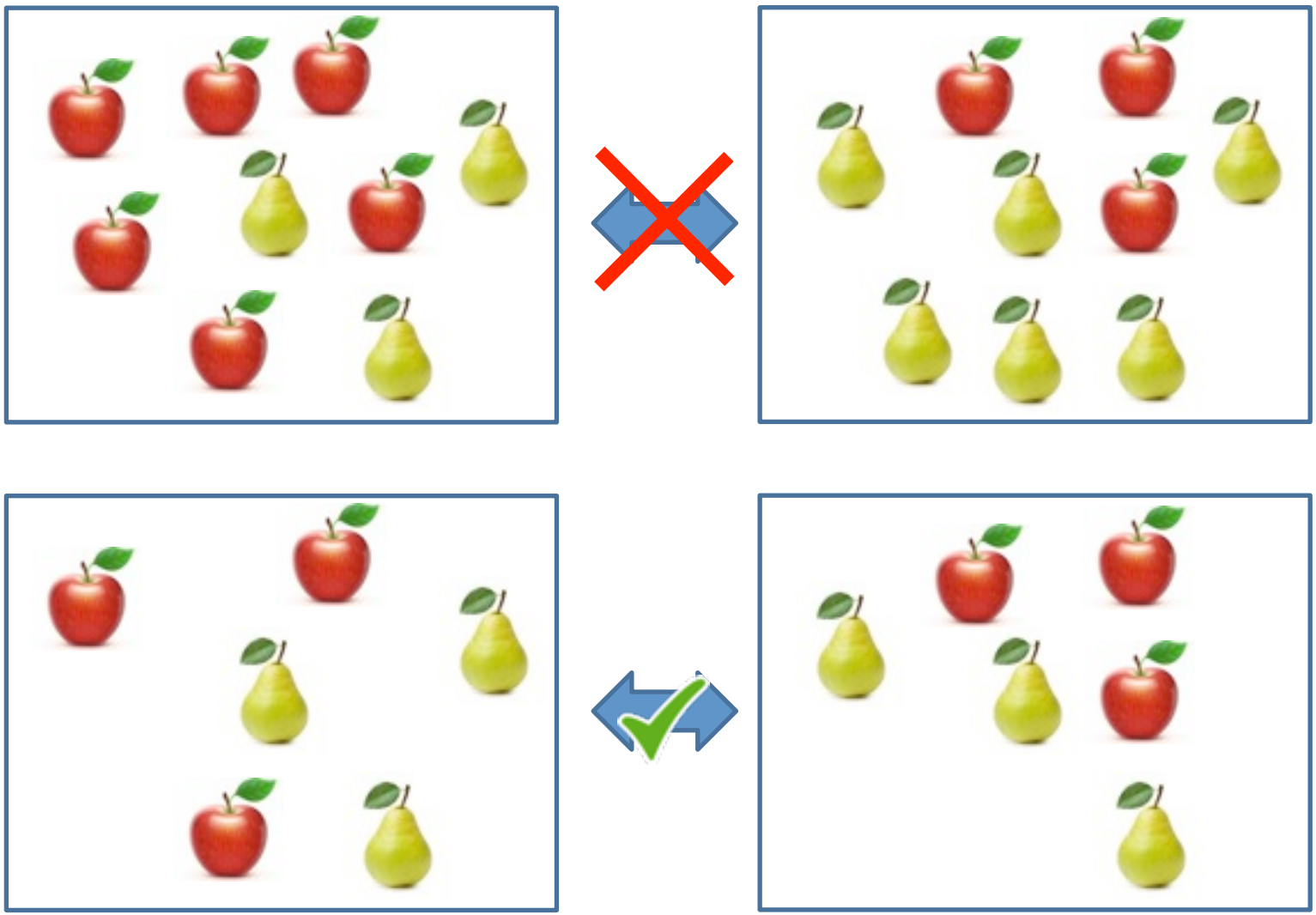
Bristol-Myers Squibb Pfizer

Studienpopulation



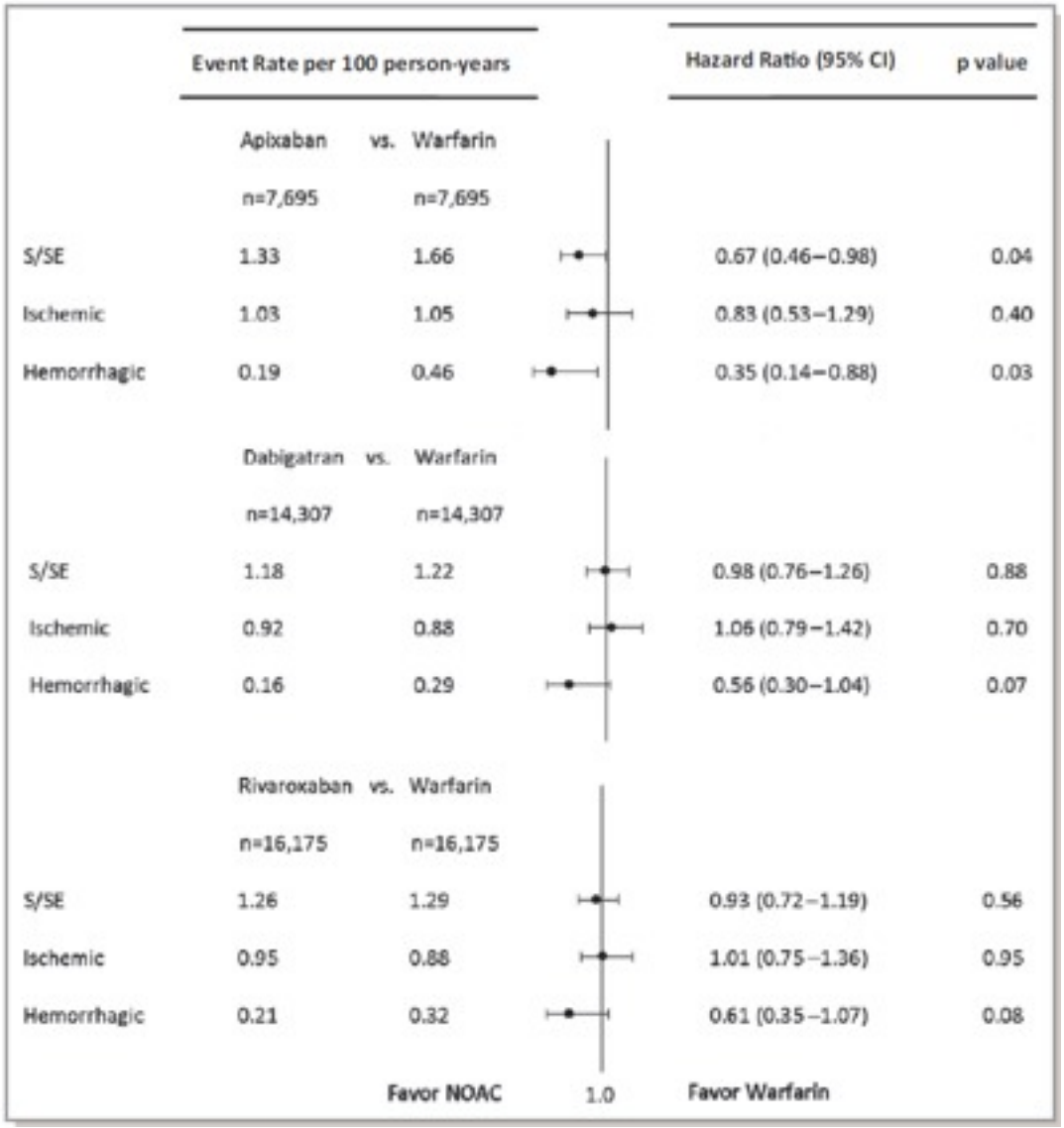
Bristol-Myers Squibb Pfizer

Propensity Score Matching: Prinzip



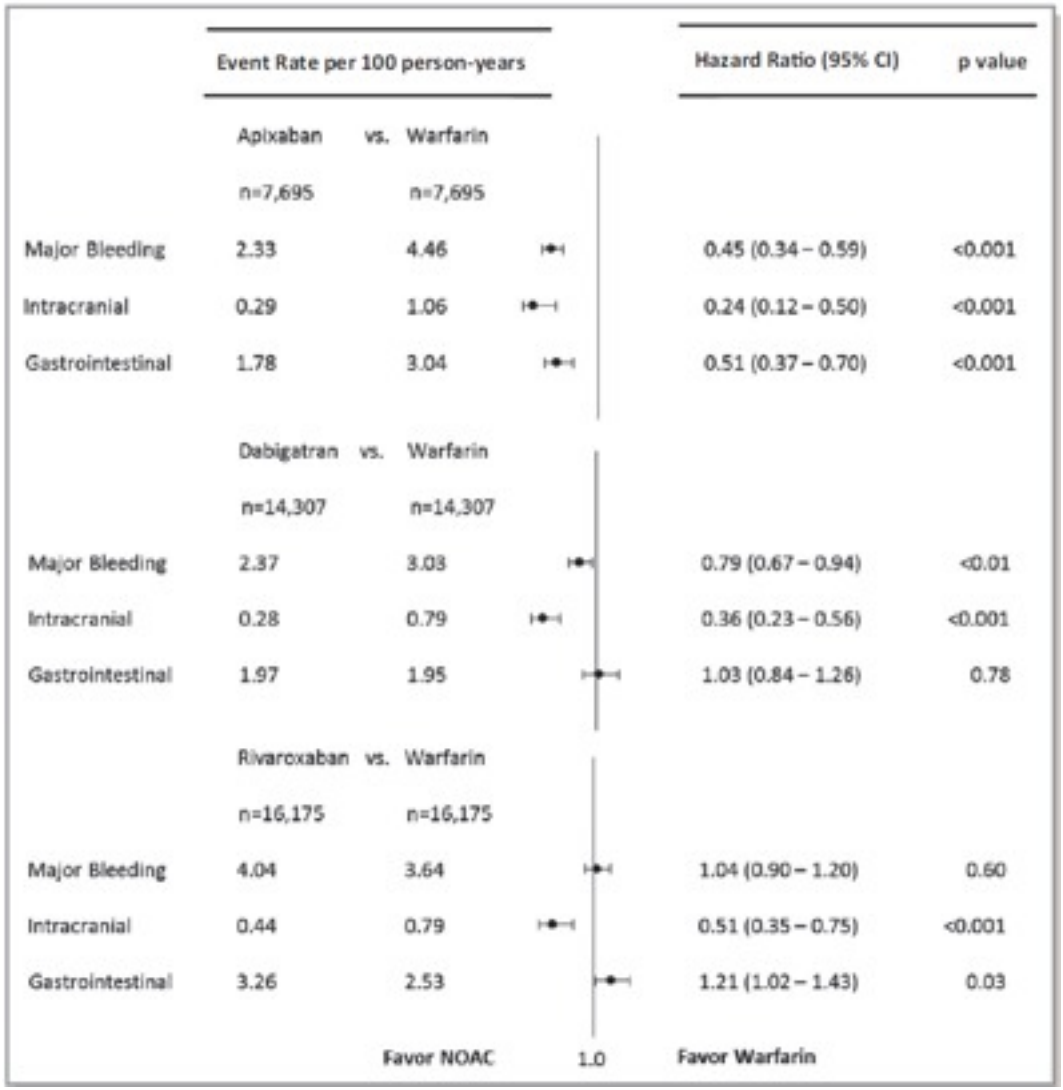
Bristol-Myers Squibb Pfizer

Ergebnisse: Schlaganfall



Bristol-Myers Squibb Pfizer

Ergebnisse: Schwere Blutung

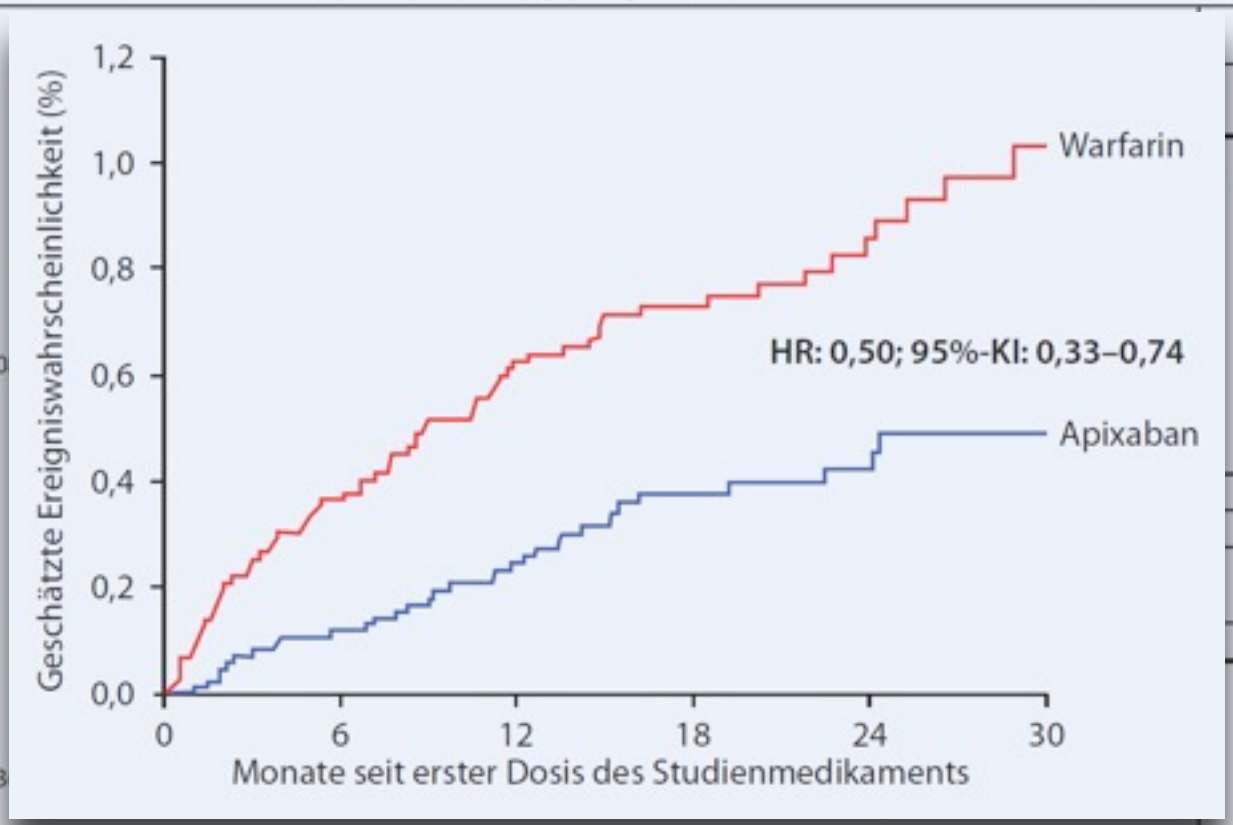


Bristol-Myers Squibb Pfizer

Mortalität

nach antikoagulanzienassoziierten schweren Blutungen

Studie/Subgruppe	NOAK Ereignisse	NOAK Summe	VKA±NMH Ereignisse	VKA±NMH Summe	Gewichtung	Odds Ratio MW [SEM, 95%-KI]
ARISTOTLE						
ENGAGE-AF						
J-ROCKET						
RE-LY						
ROCKET-AF						
Zwischensumme (95%-KI)						
Gesamtzahl Ereignisse						
Heterogenität: I^2=0%						
Test auf Gesamteffekt: Z=5,0						
AMPLIFY						
EINSTEIN-DVT						
EINSTEIN-PE						
Hokusai-VTE						
RE-COVER						
RE-MEDY						
Zwischensumme (95%-KI)						
Gesamtzahl Ereignisse						
Heterogenität: I^2=0%						
Test auf Gesamteffekt: Z=2,3						

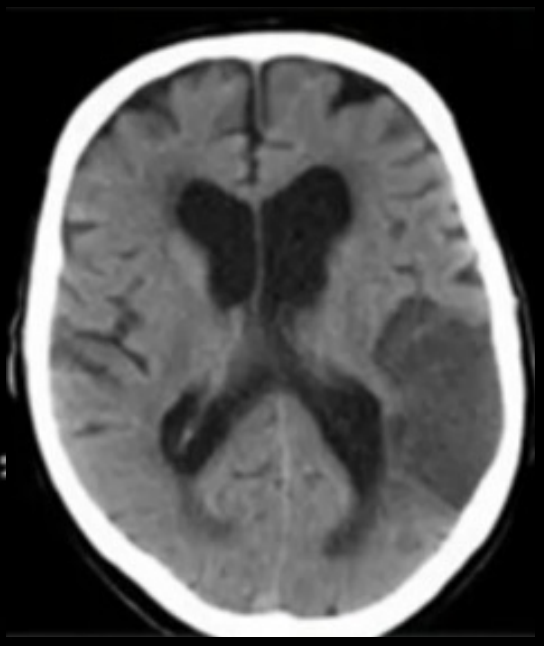


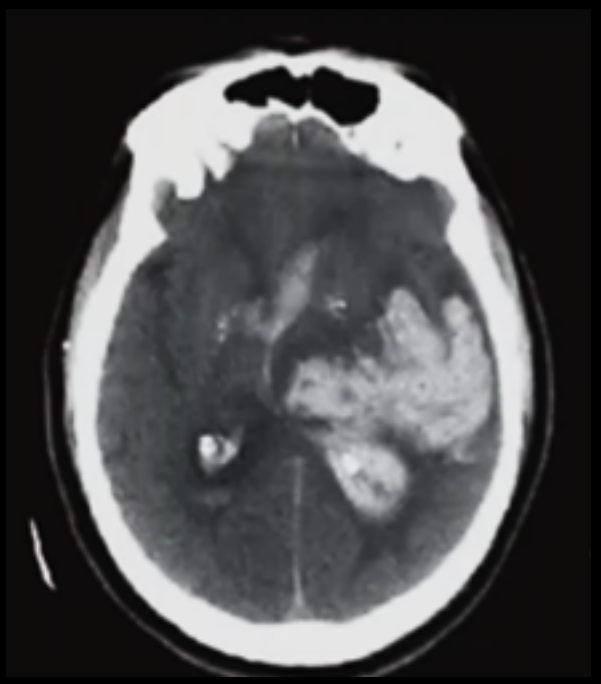
Test auf Subgruppendifferenzen: p=0,38; I^2=0%

0,01 0,1 1 10 100

Favorisiert NOAK Favorisiert VKA±NMH

Heart 101:1204–1211





Akuter Thoraxschmerz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Geburtsdatum:
Geschlecht:
KH Schwa
Patientenname:
Patientennummer:
Blutdruck:
Tel.:
Aufnahmedatum: 18.03.2016 14:25:42
P: PQ: QRS: 98ms QT: 428ms QTc: 407ms QTrel: 104% Herzfrequenz: 54/min
I
II
III
aVR
aVL
aVF
Filter: MND


Notfall-Name: Unbekannt 18.03.2016 14:25:42
Geburtsdatum:
Geschlecht:
KH Schw
Patientenname:
Patientennummer:
Blutdruck:
Tel.:
Aufnahmedatum: 18.03.2016 14:25:42
P: PQ: QRS: 98ms QT: 428ms QTc: 407ms QTrel: 104% Herzfrequenz: 54/min
V1
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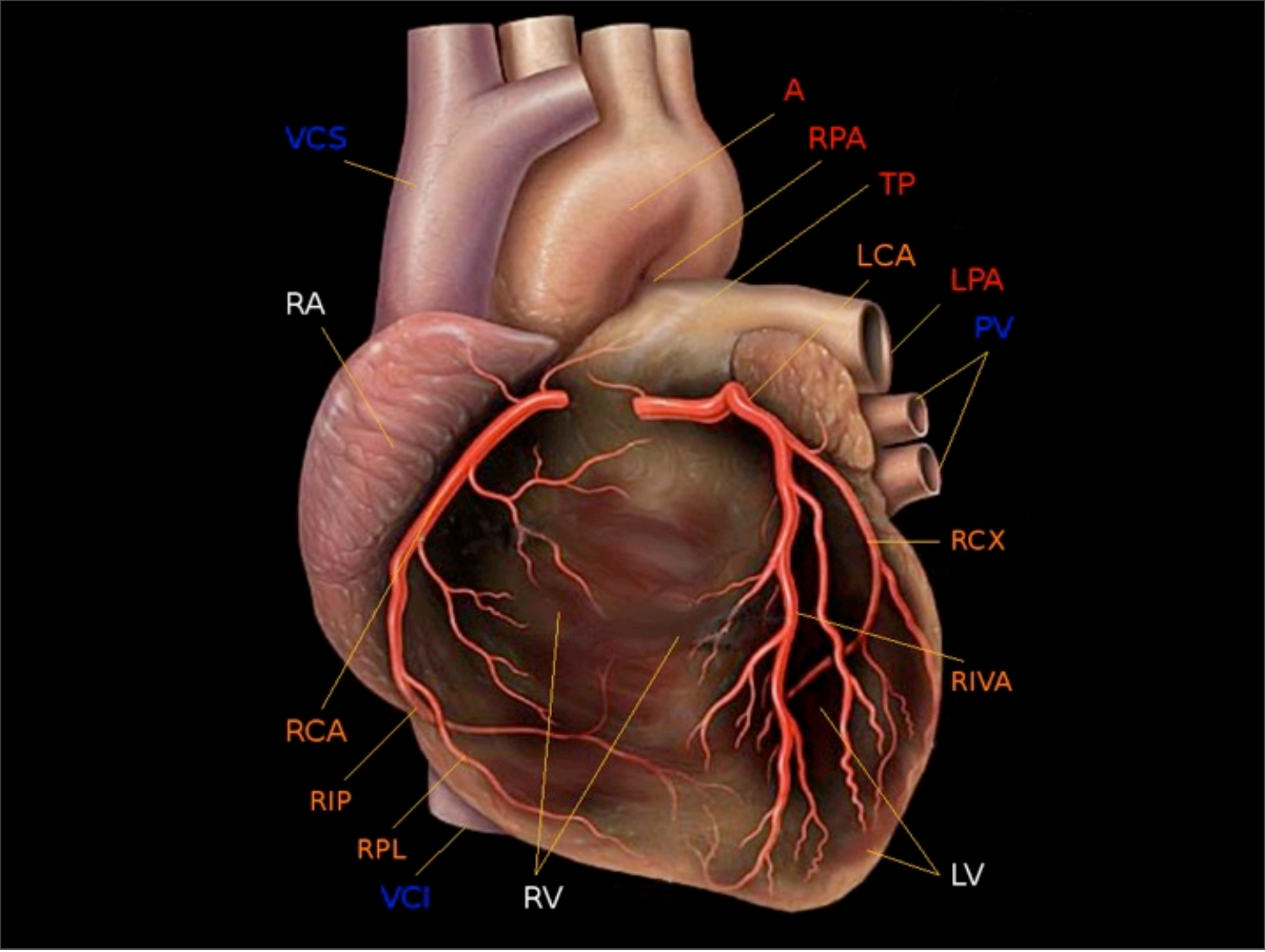
A
VCS
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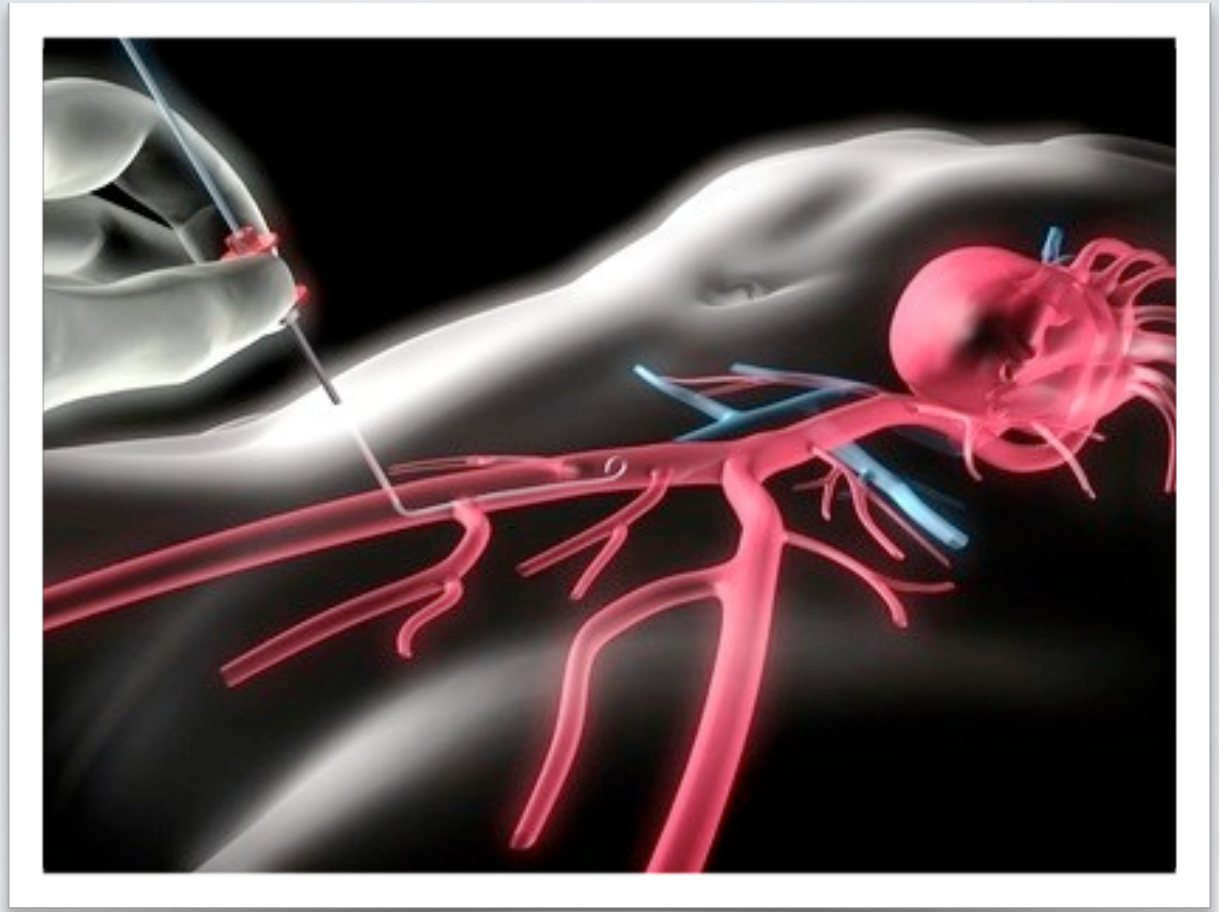
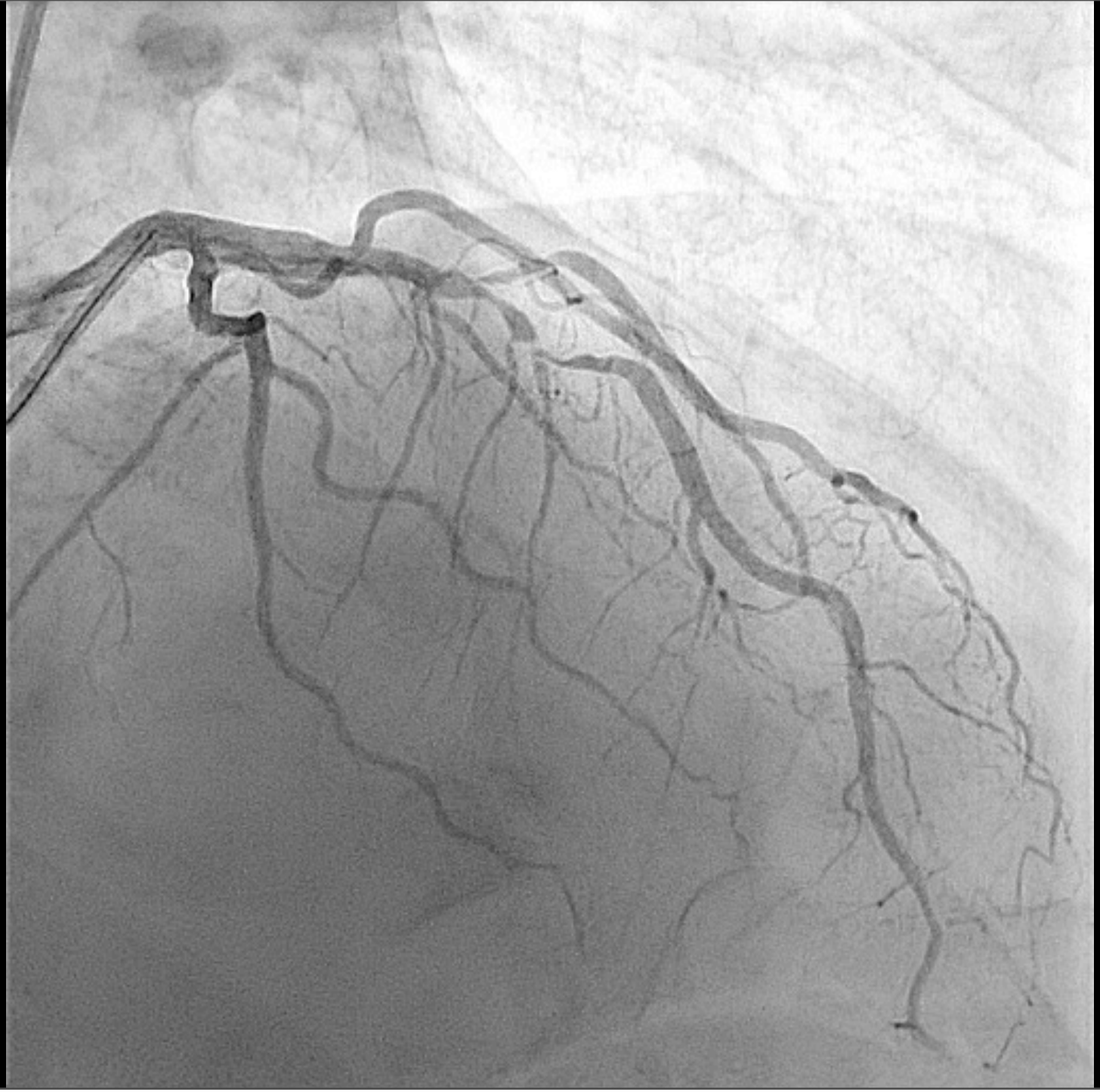
LCA
LPA
RA
PV
RCX
RIVA
RCA
RIP
RPL
VCI
RV
LV

VORHOFFLIMMERN & ACS & STENT

- **Patientin**
- **71 Jahre**
- **Hypertonie**
- **Z.n. Magenblutung**
- **Chronisches Vorhofflimmern**
- **NSTEMI ACS**
- **GFR 68 ml/min**

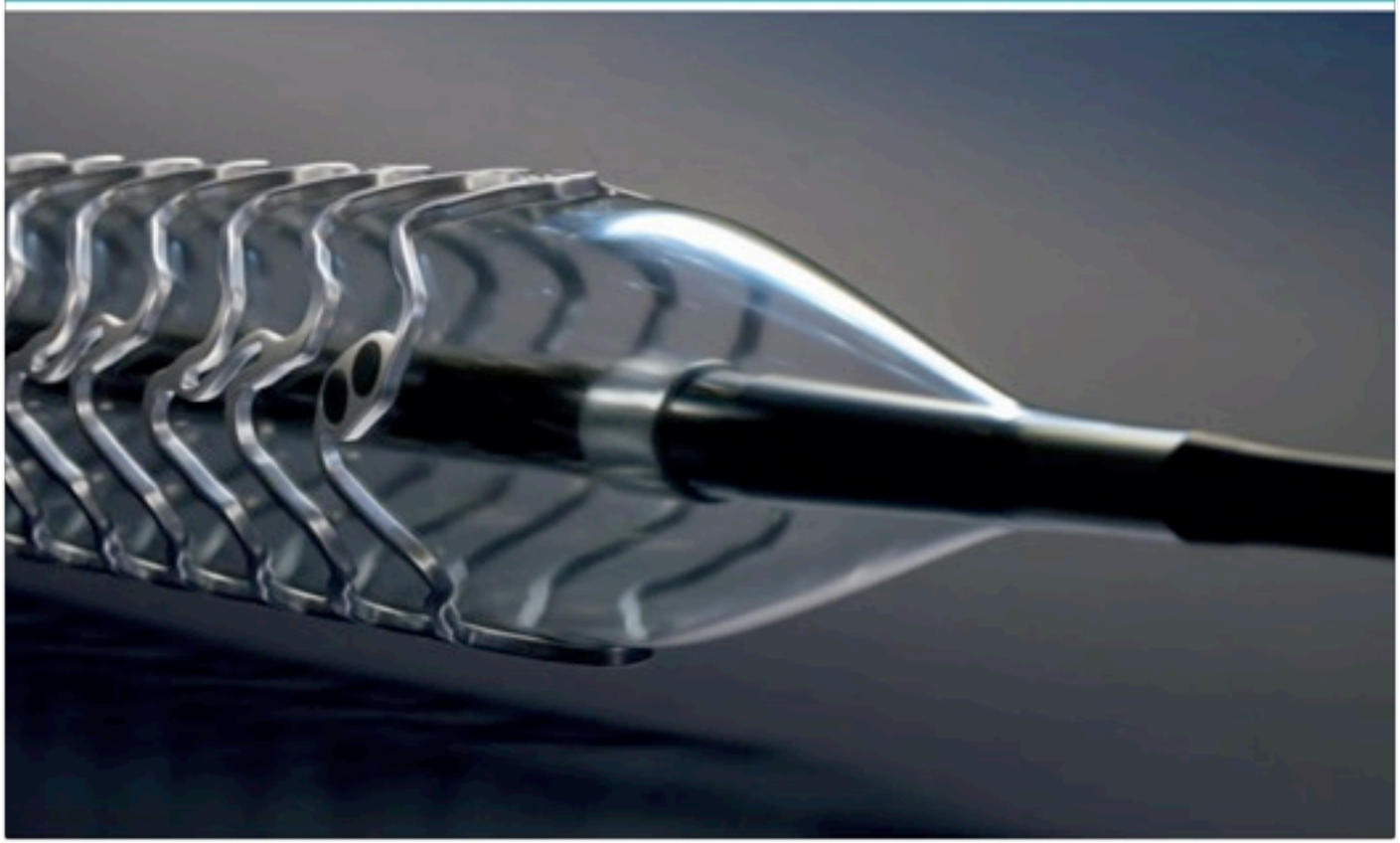




Magmaris

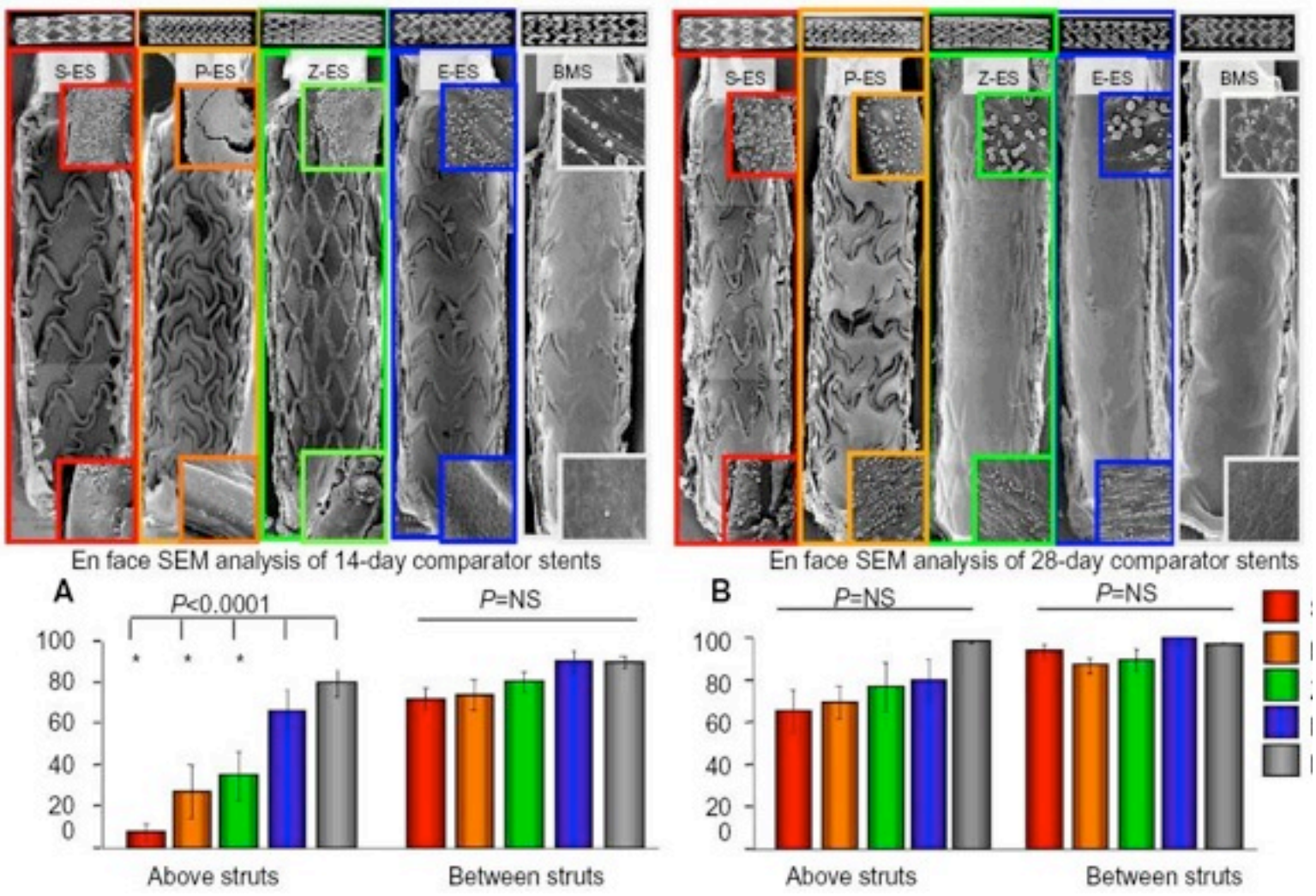
Resorbierbarer Magnesium Scaffold

Indiziert für de novo Läsionen in Herzkranzgefäßen[1]



VORHOFFLIMMERN & ACS & STENT

DES on Endothelialisation - “stent-coverage”



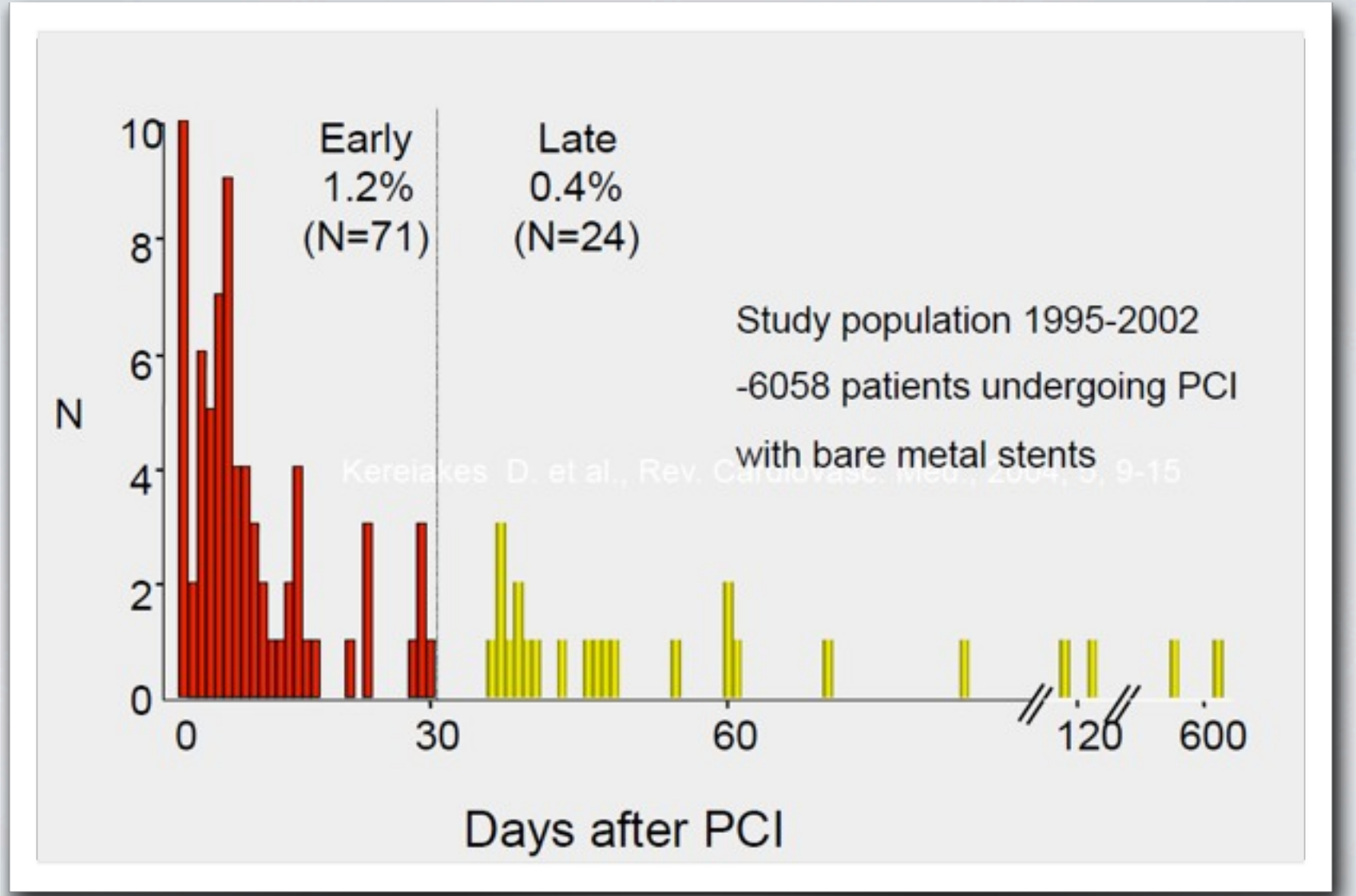
“At pathology, CoCr-EES revealed less inflammation and greater strut coverage when compared to 1st Gen DES, while maintaining similar efficacy in reducing neointimal growth. Specifically, in small vessel disease, CoCr-EES have been shown to be less thrombogenic compared to 1st Gen DES.”

Stent Thrombose

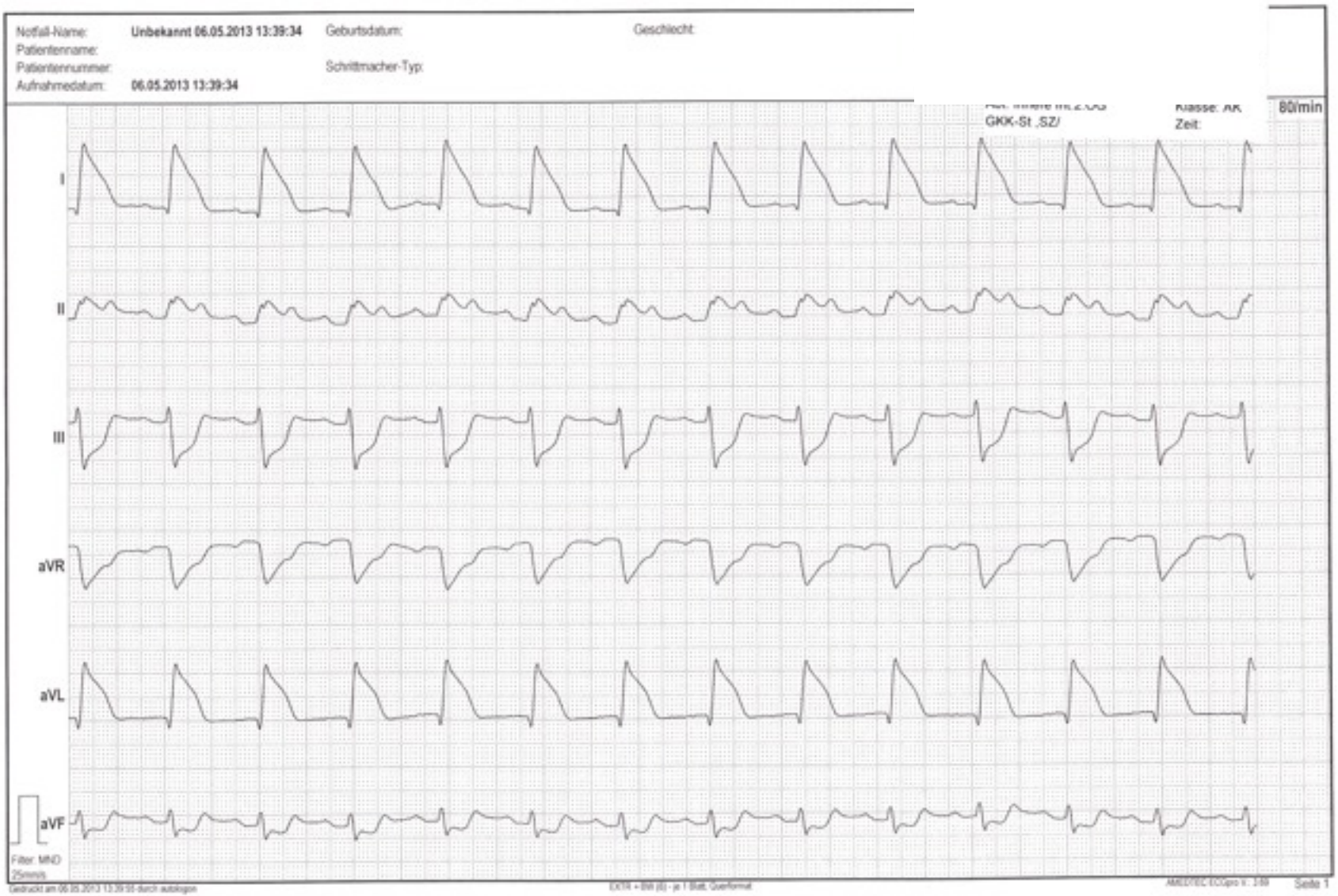
Frühe ≤ 1 Mo	Späte > 1 Mo ≤ 1Jahr	Sehr späte > 1Jahr

Tag 0	bis Tag 1	Akute Stentthrombose
>Tag 1	bis 1 Monat	Subakute Stentthrombose (SAT)
>1 Monat	to 1 Jahr	Späte Stentthrombose (LST)
(VLST)	> 1 year	Sehr späte Stentthrombose (VLST)

Stent Thrombose



Wenaweser P et al. Eur Heart J 2005;26:1180-7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Geburtsdatum:
Geschlecht:
Schrittmacher-Typ:
GKK-St ,SZ/
Klasse: AK
Zeit:
80/min
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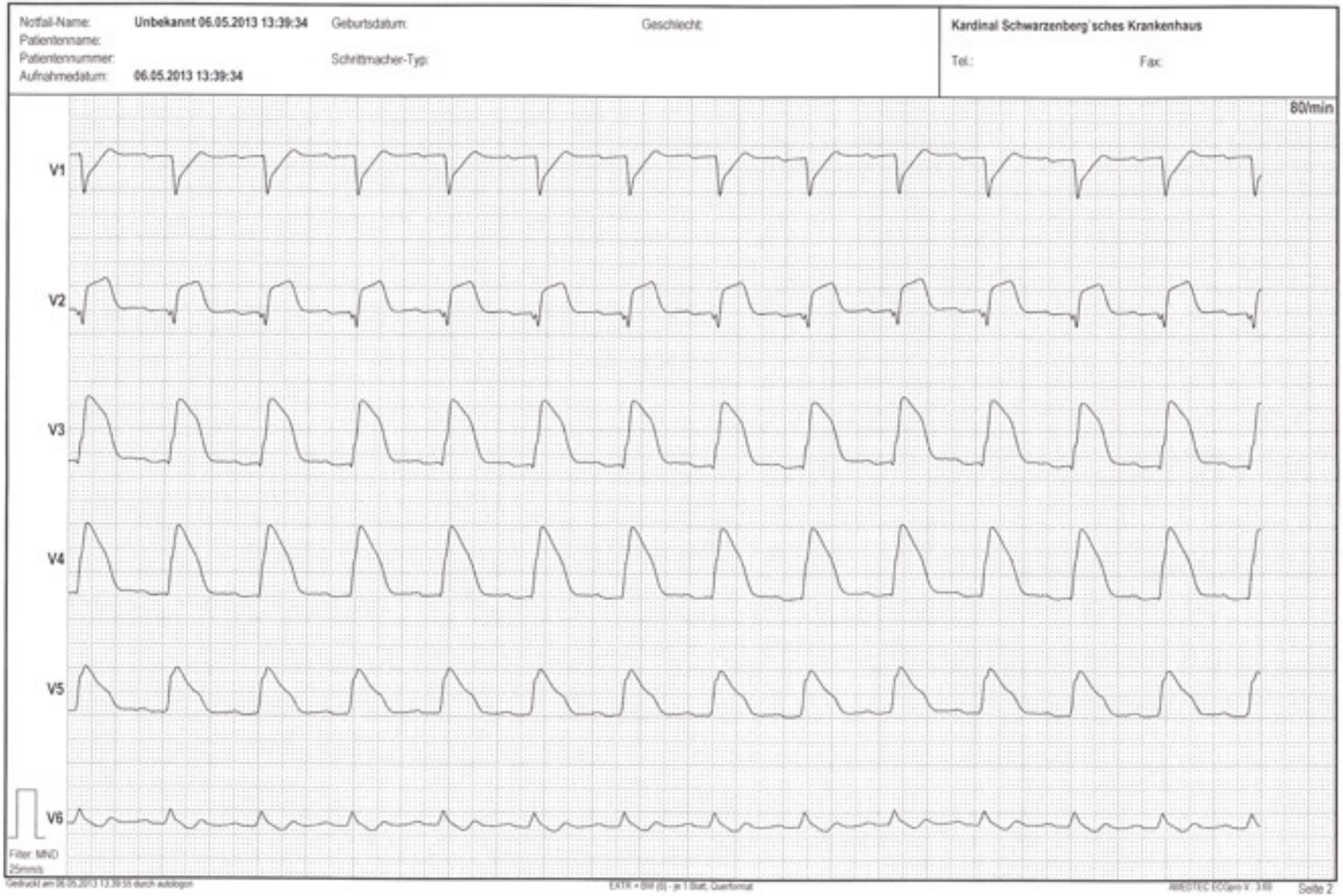
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Kardinal Schwarzenberg'sches Krankenhaus
Tel.:
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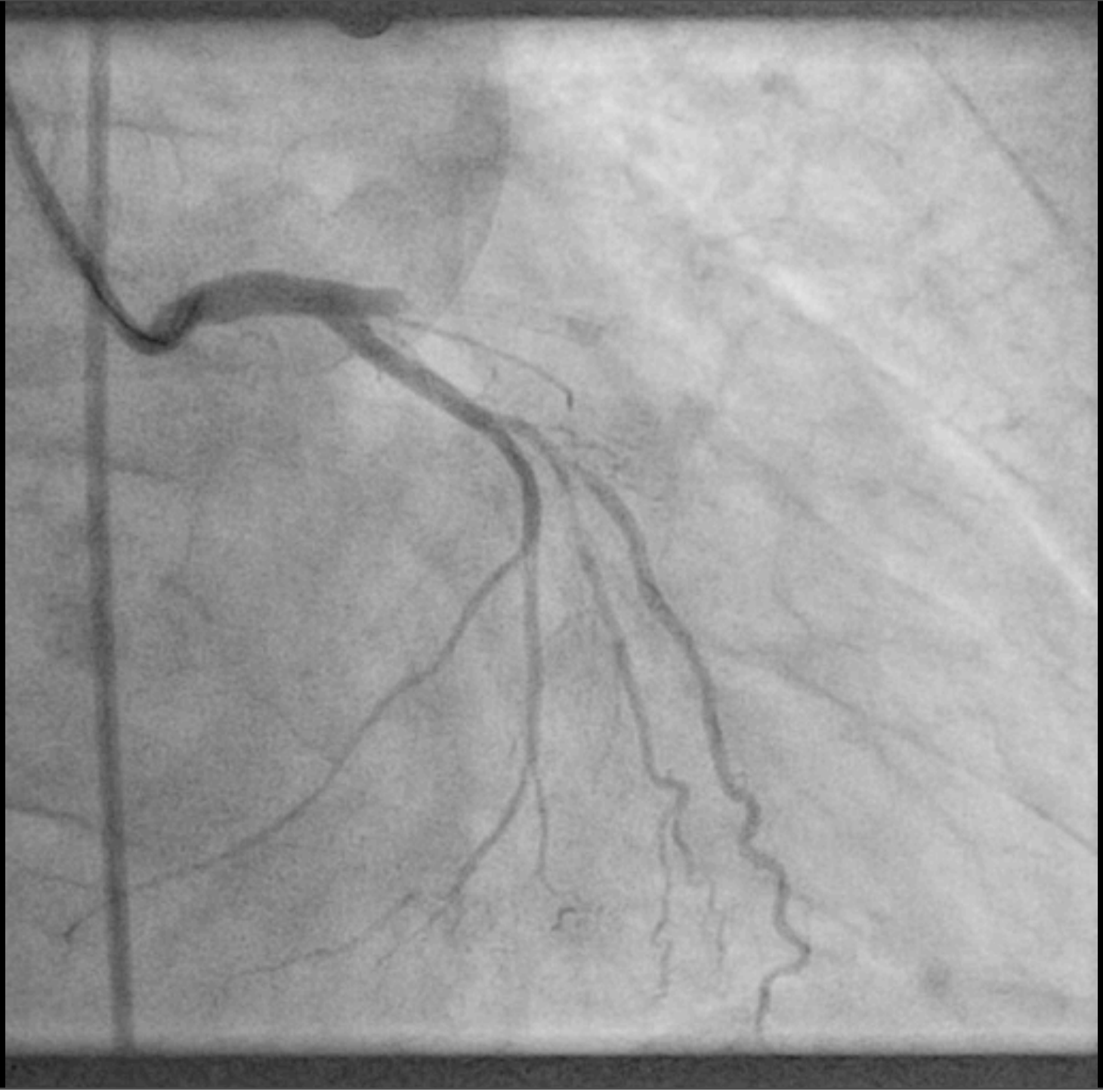
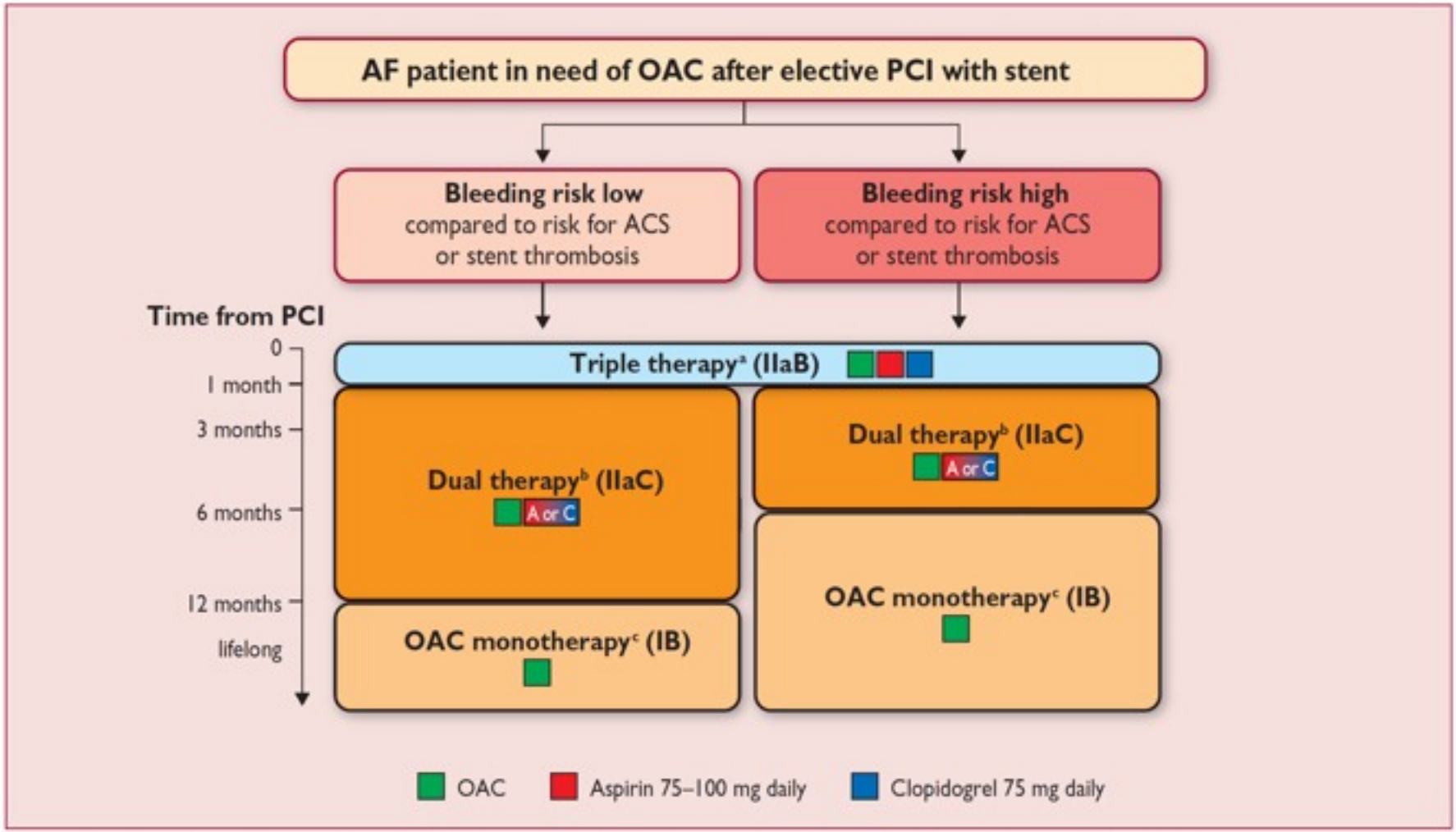




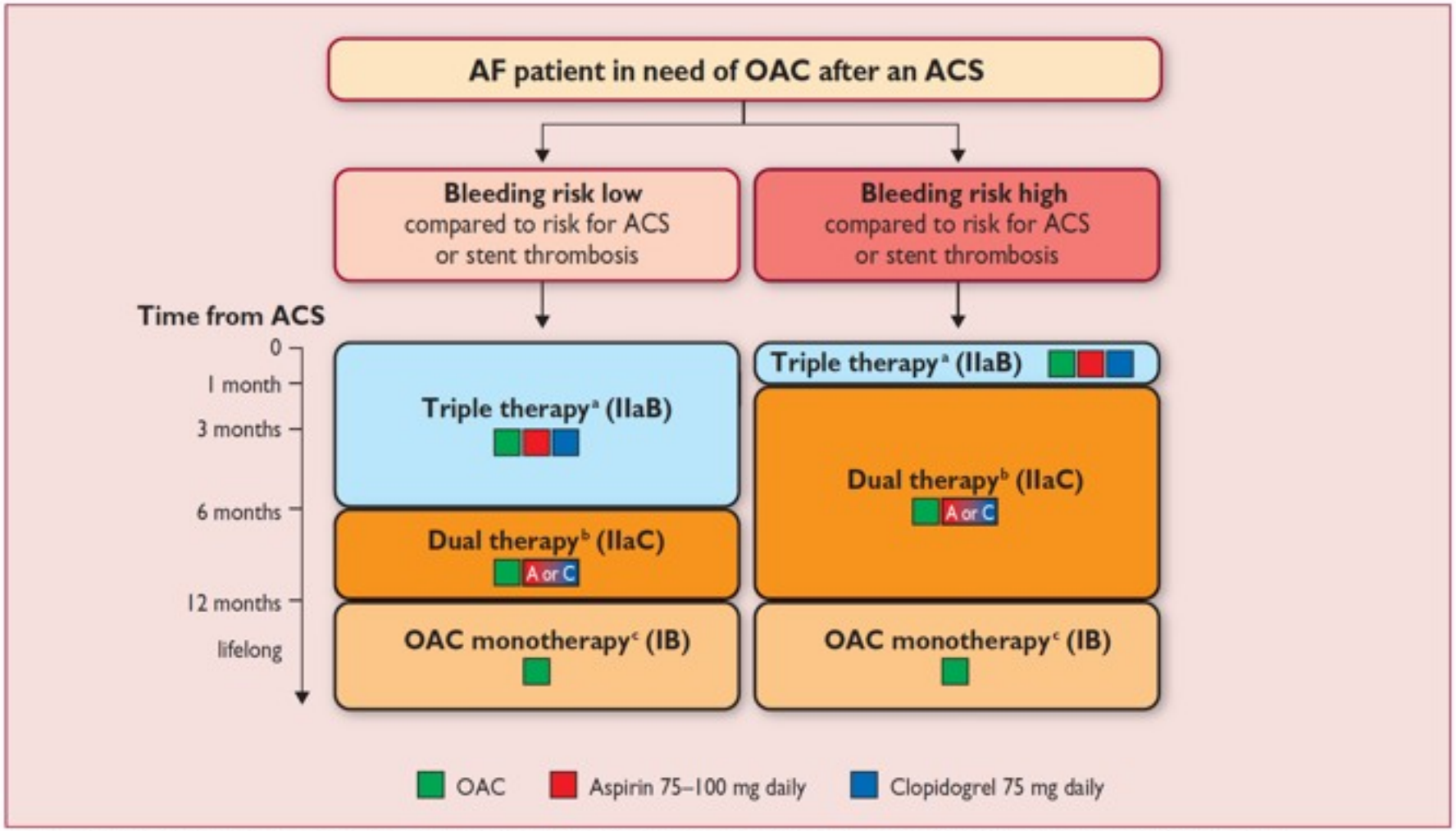
ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients.

[b]OAC plus single antiplatelet.

[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Figure 13 Antithrombotic therapy after elective percutaneous intervention in atrial fibrillation patients requiring anticoagulation.



ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.

[b]OAC plus single antiplatelet.

[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Figure 12 Antithrombotic therapy after an acute coronary syndrome in atrial fibrillation patients requiring anticoagulation.

VORHOFFLIMMERN & ACS & STENT

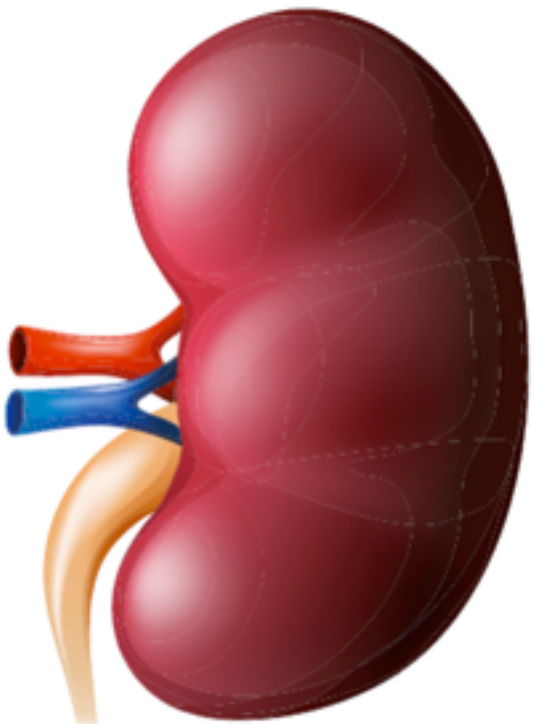
- **Patientin**
- **71 Jahre**
- **Hypertonie**
- **Z.n. Magenblutung**
- **Chronisches Vorhofflimmern**
- **NSTEMI ACS**
- **GFR 68 ml/min**

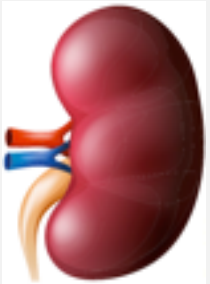
VORHOFFLIMMERN & ACS & STENT

VORHOFFLIMMERN & ACS & STENT

- **Woche 1-4**
  - ASS 100 mg 0/1/0
  - Clopidogrel 75 mg 1/0/0
  - Eliquis 2.5 mg 1/0/1
- **Monat 2-12**
  - Clopidogrel 75 mg 1/0/0
  - Eliquis 2.5 mg 1/0/1
- **Nach einem Jahr**
  - Eliquis 5 mg 1/0/1

DOAK: Niereninsuffizienz





DOAK: Niereninsuffizienz

Thrombose- und Blutungsrisiko allgemein höher

DOAK werden renal ausgeschieden

- Pradaxa® ⟶ 80%
- Eliquis®, Xarelto®, Lixiana® ⟶ 25 - 35%

KI (GFR, ml.Min)

- Pradaxa®: < 30
- Xarelto®: < 15
- Eliquis®: < 15
- Lixiana®: < 15

Pradaxa®: Welche Dosis soll verwendet werden?

Vorhofflimmern

2 x 110 mg/Tag ist **empfohlen**

- Patienten > 80 Jahre
- Verapamil (Isoptin ®) als Begleitmedikation

2 x 110 mg/Tag ist **zu erwägen**

- Patienten zwischen 75 und 80 Jahren mit erhöhtem Blutungs- und niedrigem Thromboembolierisiko
- Patienten mit hohem Blutungsrisiko und beeinträchtigter Nierenfunktion (CrCl 30-50 ml/Min)
- Patienten mit Gastritis, Ösophagitis oder gastro-ösophagealem Reflux

Fachinformation PRADAXA® in der aktuellen Fassung

Xarelto®: Welche Dosis soll verwendet werden?

Vorhofflimmern

- 20 mg/Tag (Standarddosis)
- 15 mg/Tag (Kreatininclearance 15-49 ml/Min)

Fachinformation XARELTO® in der aktuellen Fassung

Eliquis®: Welche Dosis soll verwendet werden?

Vorhofflimmern

- 2 x 5 mg/Tag (Standarddosis)

- 2 x 2,5 mg/Tag:
  - Kreatininclearance 15-29 ml/Min oder
  - mindestens 2 von folgenden Kriterien
    - < 60 kg und/oder
    - > 80 Jahre
    - > 1,5 mg/dl Serumkreatinin

Fachinformation ELIQUIS® in der aktuellen Fassung

Lixiana®: Welche Dosis soll verwendet werden?

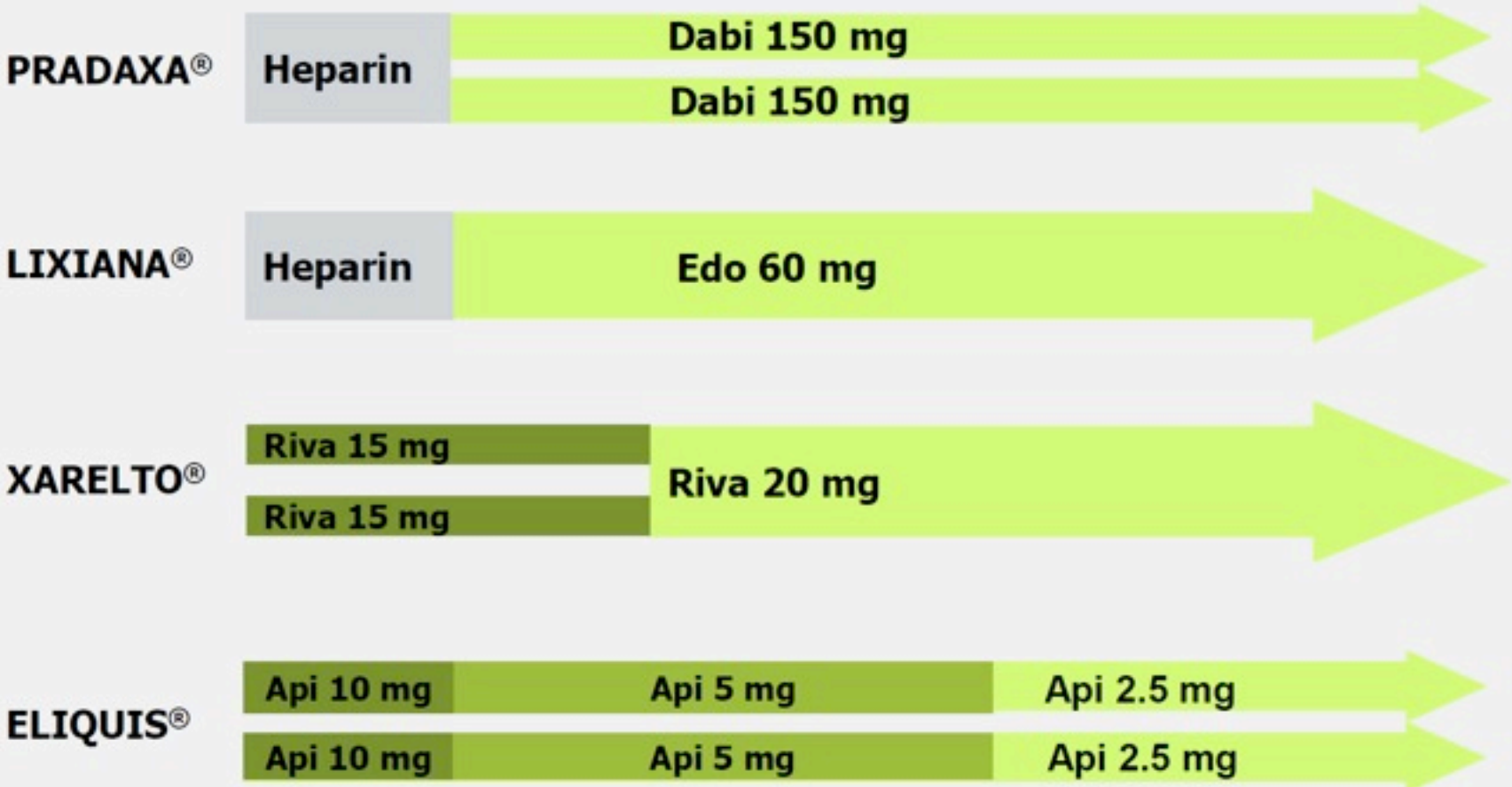
Vorhofflimmern

- 60 mg/Tag (Standarddosis)

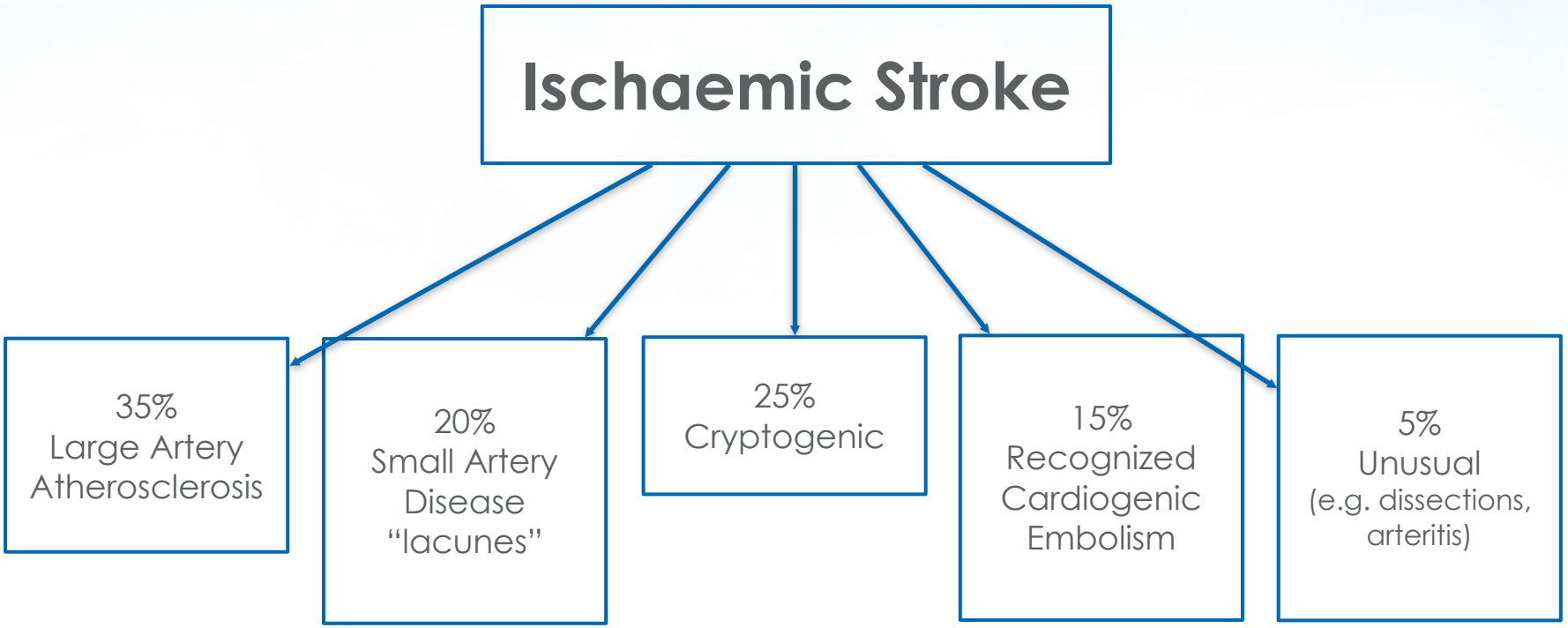
- 30 mg/Tag:
  - Kreatininclearance 15-50 ml/Min und/oder
  - < 60 kg und/oder
  - Komedikation mit Cyclosporin, Dronedaron, Erythromycin, Ketoconazol

Fachinformation LIXIANA® in der aktuellen Fassung

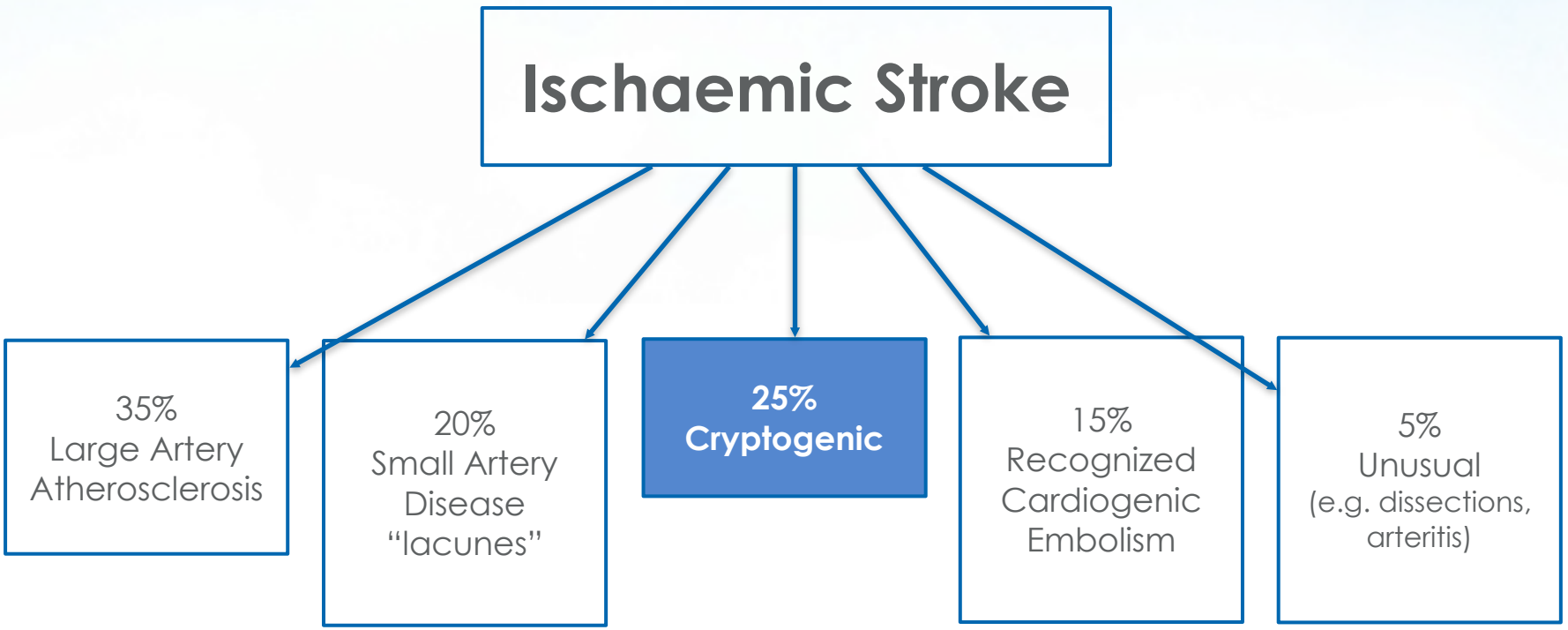
Behandlung der VTE



Distribution of ischaemic stroke subtypes



Distribution of ischaemic stroke subtypes



What is ESUS?

A Case for a New Clinical Construct

Panel 2: Criteria for diagnosis of embolic stroke of undetermined source*

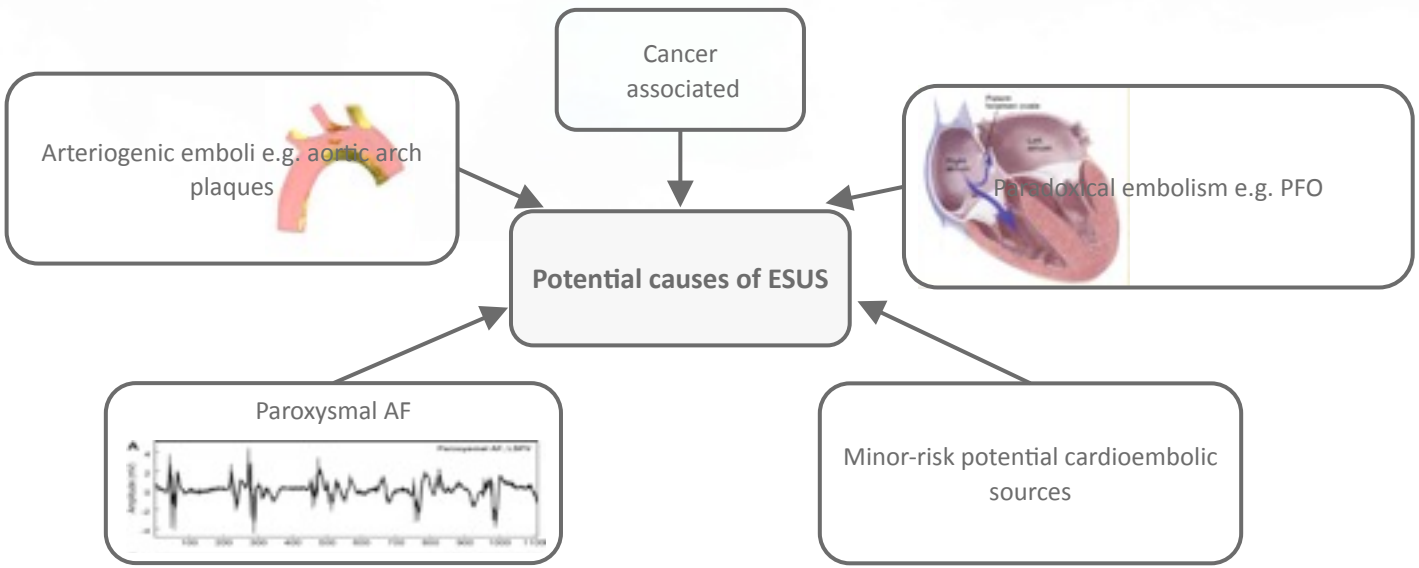
- Stroke detected by CT or MRI that is not lacunar†
- Absence of extracranial or intracranial atherosclerosis causing ≥50% luminal stenosis in arteries supplying the area of ischaemia
- No major-risk cardioembolic source of embolism‡
- No other specific cause of stroke identified (eg, arteritis, dissection, migraine/vasospasm, drug misuse)

*Requires minimum diagnostic assessment (panel 3). †Lacunar defined as a subcortical infarct smaller than or equal to 1·5 cm (≤2·0 cm on MRI diffusion images) in largest dimension, including on MRI diffusion-weighted images, and in the distribution of the small, penetrating cerebral arteries; visualisation by CT usually needs delayed imaging greater than 24–48 h after stroke onset. ‡Permanent or paroxysmal atrial fibrillation, sustained atrial flutter, intracardiac thrombus, prosthetic cardiac valve, atrial myxoma or other cardiac tumours, mitral stenosis, recent (<4 weeks) myocardial infarction, left ventricular ejection fraction less than 30%, valvular vegetations, or infective endocarditis.

Hart RG *et al*, *Lancet Neurol* 2014;13:429–438

ESUS

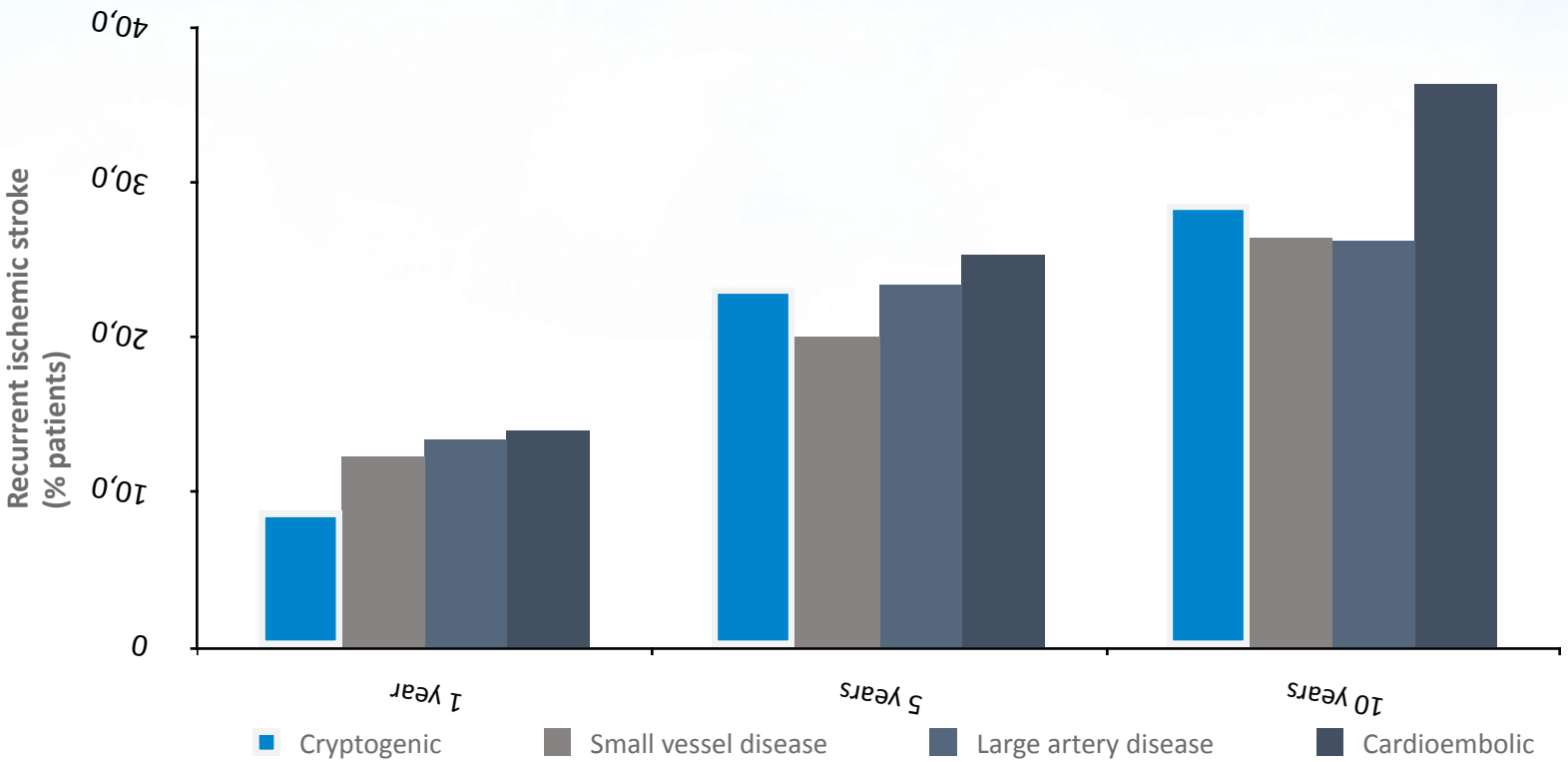
embolic stroke of unknown source



1. Hart RG *et al*, *Lancet Neurol* 2014;13:429–438; 2. The ESPRIT Study Group *Lancet* 2006;367:1665–1673;
3. CAPRIE Steering Committee. *Lancet* 1996;348:1329–1339;

ESUS

embolic stroke of unknown source



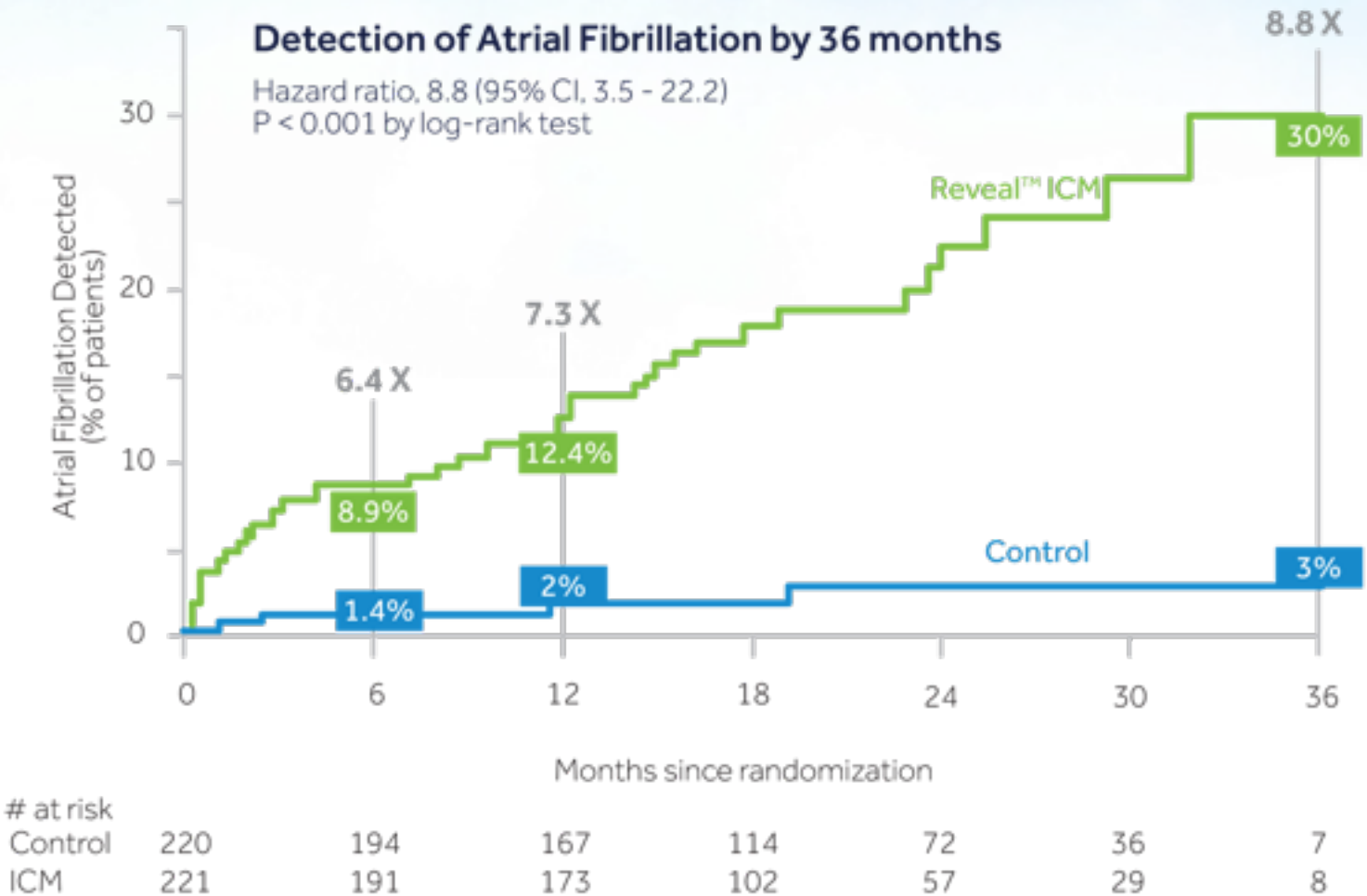
Li L *et al*, *Lancet Neurol* 2015;14:903–913

the more you look

the more you find

CRYSTAL AF study

AF detection after cryptogenic stroke



Sanna T et al. N Engl J Med 2014

CRYSTAL AF study

AF detection after cryptogenic stroke

Sanna T et al. N Engl J Med 2014