DEUTSCHES HERZZENTRUM DER CHARITÉ

MZSB Med. Zentrum Spreebogen Berlin

12. Intensivkurs Stroke Unit Starter

Kardiologie für Neurolog:innen

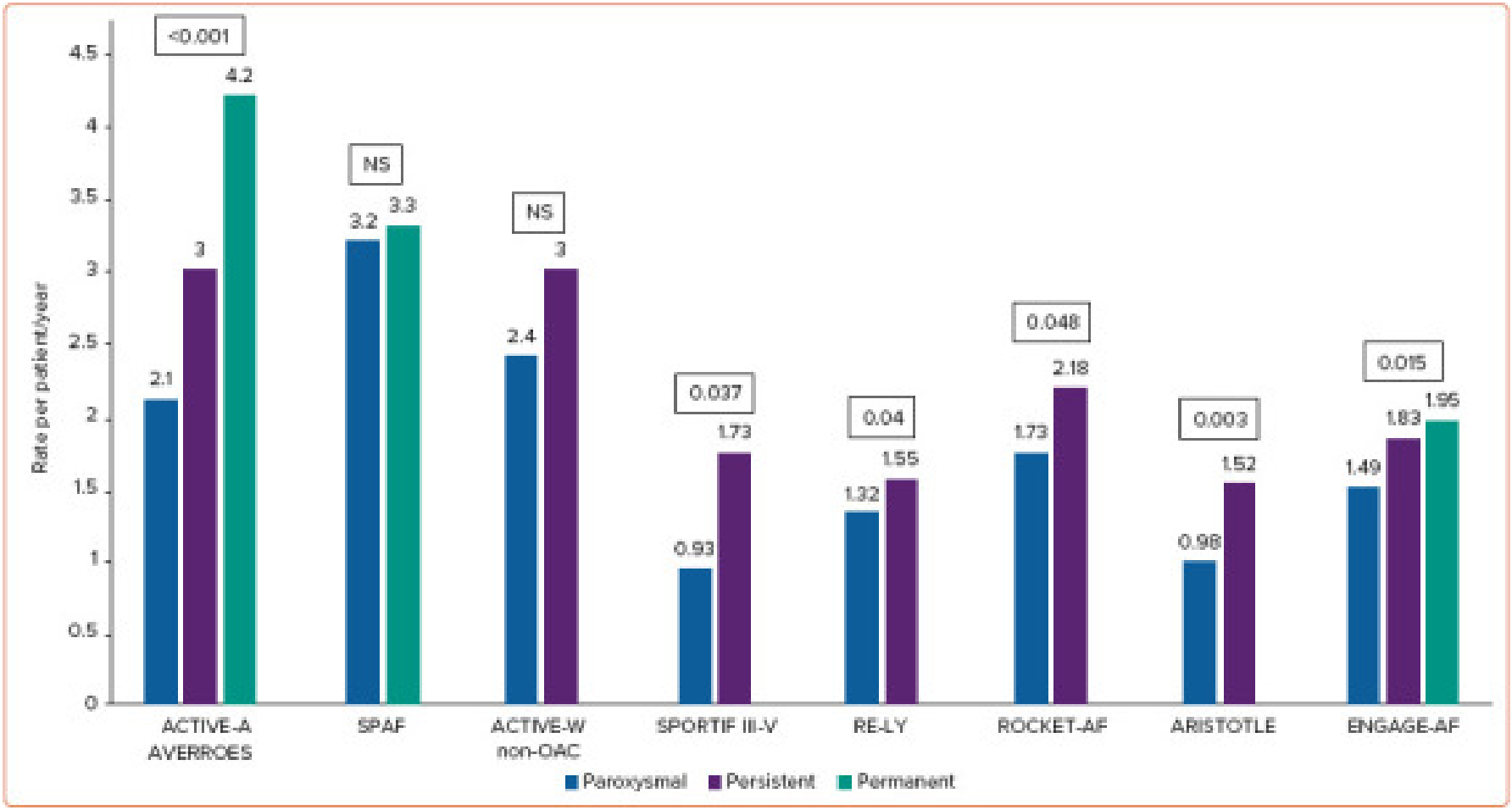
W. Haverkamp

Agenda

- Antikoagulation
- Kardiogenetik
- NOAK-Alternativen
- Neue Medikamente
- Technische Innovationen

Antikoagulation

Schlaganfallrisiko: Formen von Vorhofflimmern



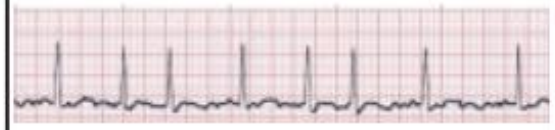
Boto et al. 2021

Vorhofflimmern: Diagnosestellung

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

ECG showing AF
(physician-confirmed)

- Entire conventional 12-lead ECG, or
- An ECG strip with ≥ 30 sec of AF (including wearable-recorded ECGs)



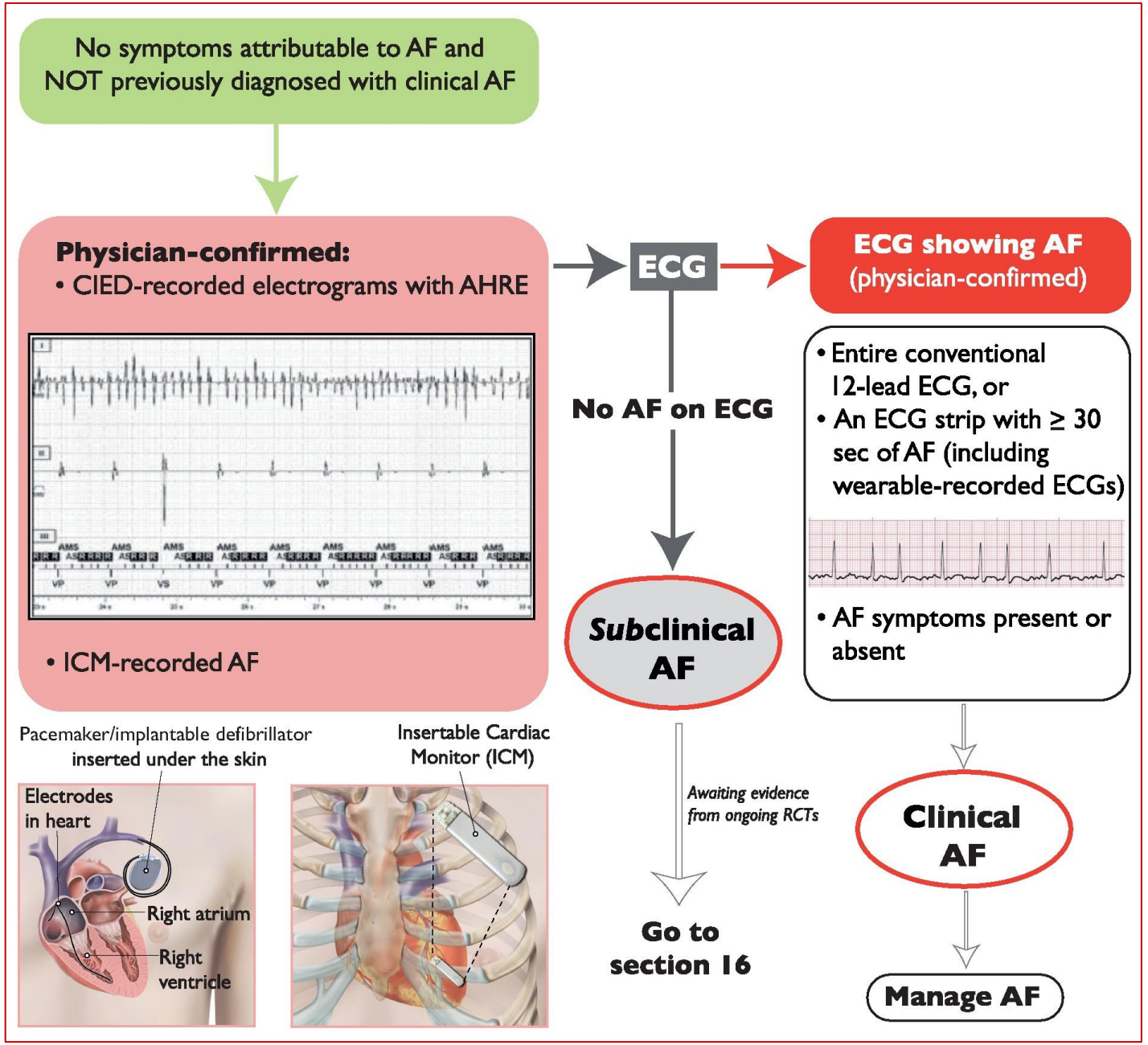
- AF symptoms present or absent

Clinical AF

Manage AF

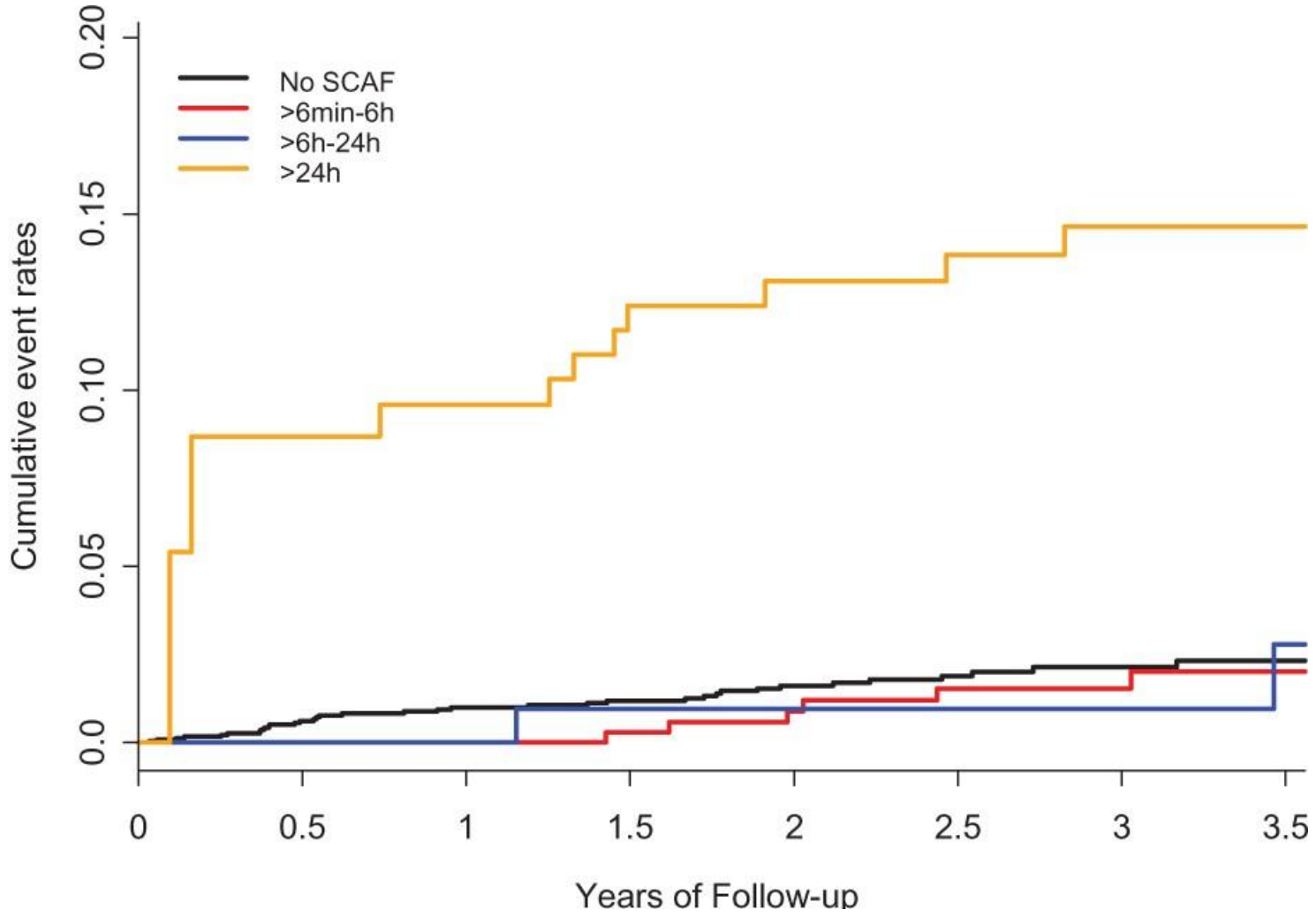
ESC VHF-Leitlinie, Hindricks et al. 2020

AHRE:
Atriale Hochfrequenz-episoden (>6 min und >190/min)



ESC VHF-Leitlinie 2020

SCAF-Dauer und Schlaganfallrisiko



van Gelder et al. 2017

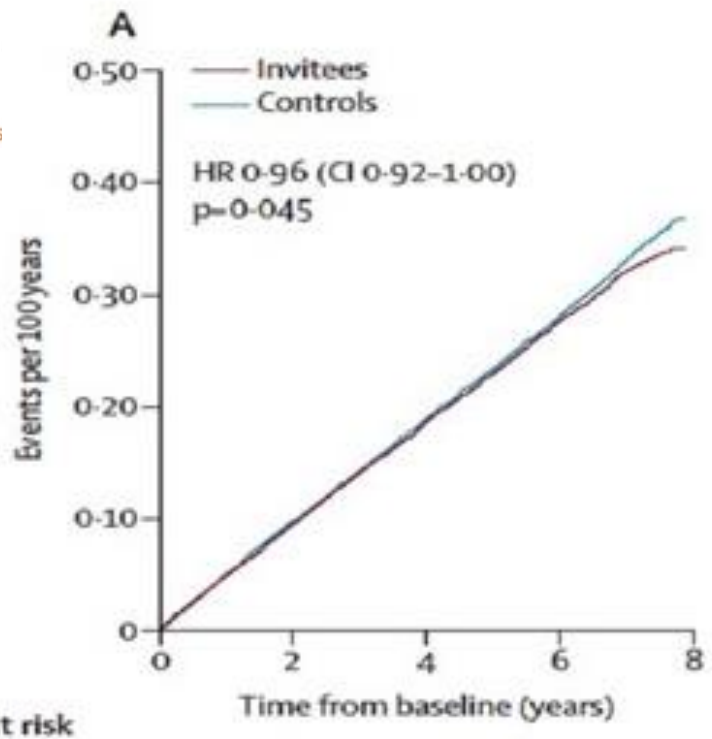
Studien zur Prävention thromboembolisch bedingter Schlaganfälle

Katsanos et al. 2020

STROKESTOP

Twice daily for two weeks

Ischaemic or haemorrhagic stroke, SE, bleeding and all-cause death

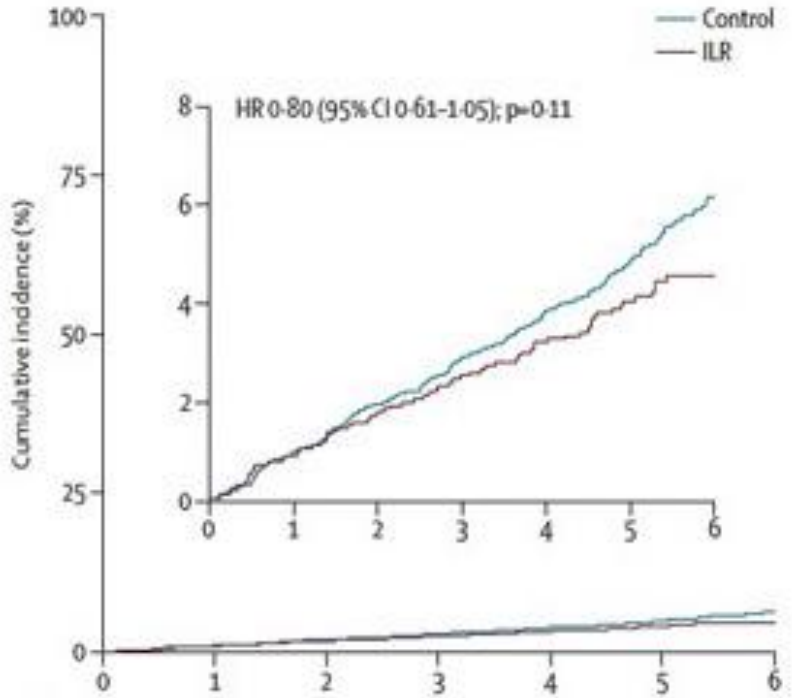


Number at risk					
Invitees	13979	12639	11342	9747	..
Controls	13996	12614	11300	9727	..

Svennberg E et al. *Lancet* 2021

LOOP

Stroke or systemic arterial embolism



Number at risk							
Control	4503	4414	4278	4130	3971	3123	759
ILR	1501	1460	1418	1383	1339	1022	223

Svendsen JH et al. *Lancet* 2021

Smartwatch-EKG: Vorhofflimmern

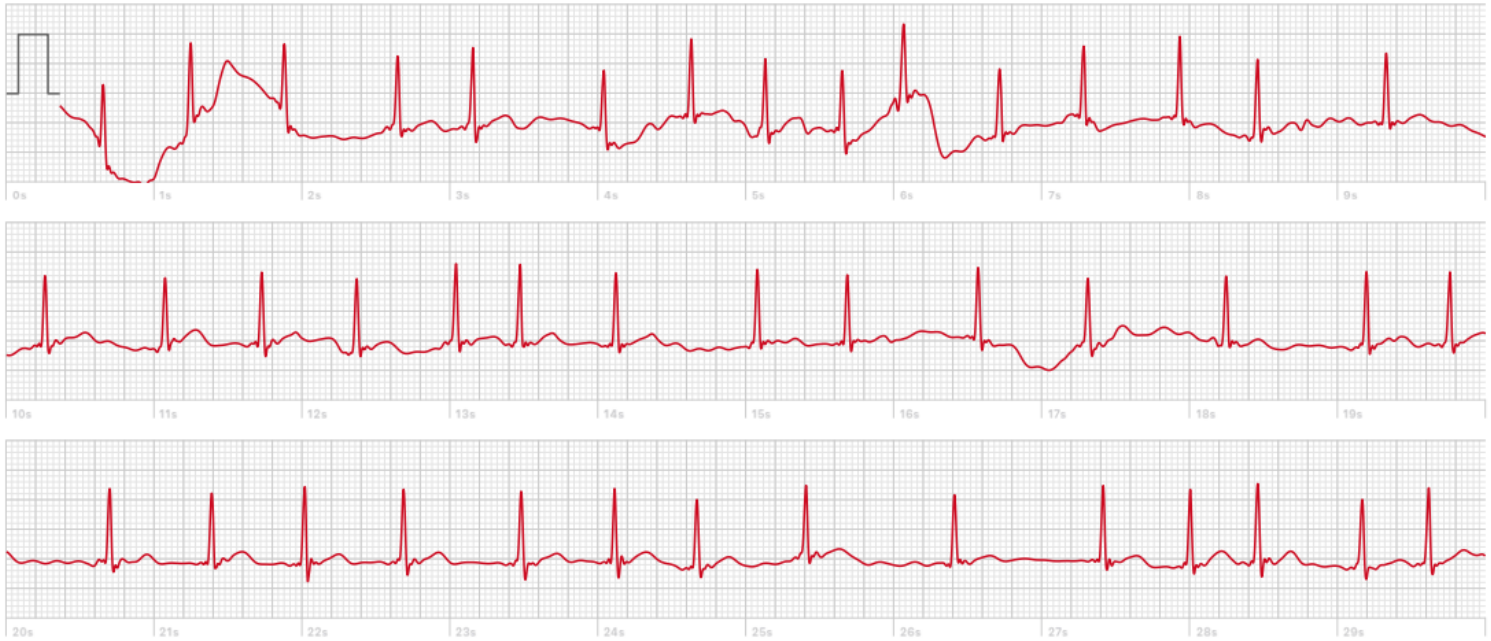
Geburtsdatum: 06.07.1964 (Alter 55)

Aufgezeichnet am 11.06.2020 um 07:16

Vorhofflimmern — ♥ 87 BPM ⌀

Dieses EKG deutet auf Vorhofflimmern hin.

Wenn du dieses Ergebnis nicht erwartet hast, solltest du mit deinem Arzt sprechen.



25 mm/s, 10 mm/mV, Ableitung I, 513 Hz, iOS 13.5, watchOS 6.2.6, Watch4,1 - Die Wellenform ist vergleichbar mit einem Ableitung-I-EKG. Weitere Informationen sind in der Gebrauchsanweisung erhältlich.

EKG-fähige Smartwatches

Apple

Appel Watch Series 6

Fitbit

Sense

Samsung

Galaxy Watch 4

Withings

Scanwatch

$CHADS_2$ -> CHA_2DS_2VASc

CHADS2 Risk	Score
CHF	1
Hypertension	1
Age > 75	1
Diabetes	1
Stroke or TIA	2

CHA2DS2-VASc Risk	Score
CHF or LVEF ≤ 40%	1
Hypertension	1
Age ≥75	2
Diabetes	1
Stroke/TIA/ Thromboembolism	2
Vascular Disease	1
Age 65 - 74	1
Female	1

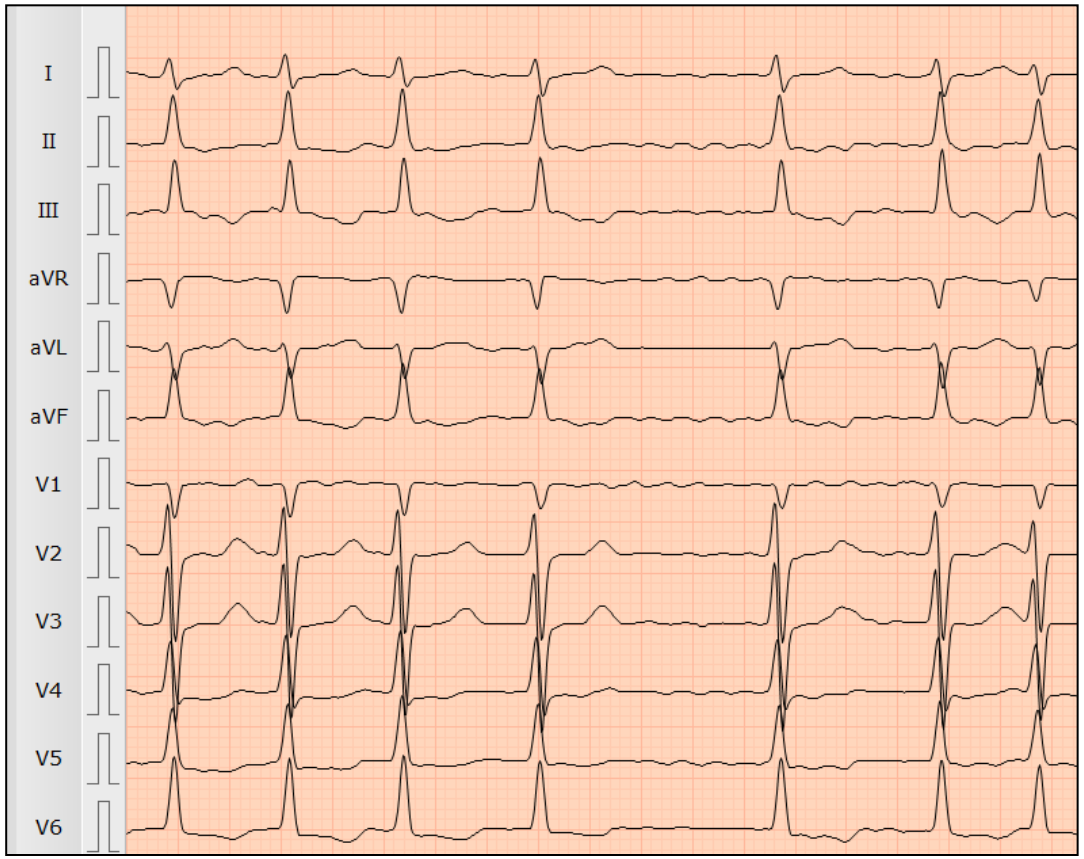
From ESC AF Guidelines
http://escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

CHA2DS2VASc-Score: Diskriminierungsfähigkeit

- **c-Statistik (AUC-ROC)**: 0,6 bis 0,75 (Lip et al. 2012)
- Mäßige bis gute Diskriminierung. Obwohl es nicht perfekt ist, liefert es dennoch wertvolle Informationen für die klinische Entscheidungsfindung, wenn es mit anderen relevanten Faktoren und den Patientenpräferenzen kombiniert wird.

0,5: die Diskriminierungsfähigkeit des Modells ist nicht besser ist als Zufall
0,6 - 0,7: mäßige Diskriminierung
0,7 - 0,8: gute Diskriminierung
>0,8: sehr gut bis ausgezeichnete Diskriminierung

Fall: 35-jährige Patienten mit HCM



35-jährige Patientin

- HCM (Septumdicke 20 mm)*
- Z. n. PVI bei paroxysmalem Vorhofflimmern
- Subjektiv noch gelegentlich Arrhythmieepisoden
- CHA_2DS_2-Vasc: 0

*diagnostisch: ≥ 15 mm

ANTIKOAGULATION?

Fall: 35-jährige Patienten mit HCM

die sich vom 07.09.2020 bis zum 11.09.20 in unserer stationären Behandlung befand.

Diagnose/n:

Hirninfarkt durch nicht näher bezeichneten Verschluß oder Stenose cerebraler Arterien
- kardioembolischer Genese bei

Paroxysmales Vorhofflimmern seit Jahren bekannt
- Ablation vor 3 Jahren
- NOAK Therapie von der Patientin entgegen der Empfehlung nicht eingenommen

HCM und Vorhofflimmern

AHA/ACC CLINICAL PRACTICE GUIDELINE

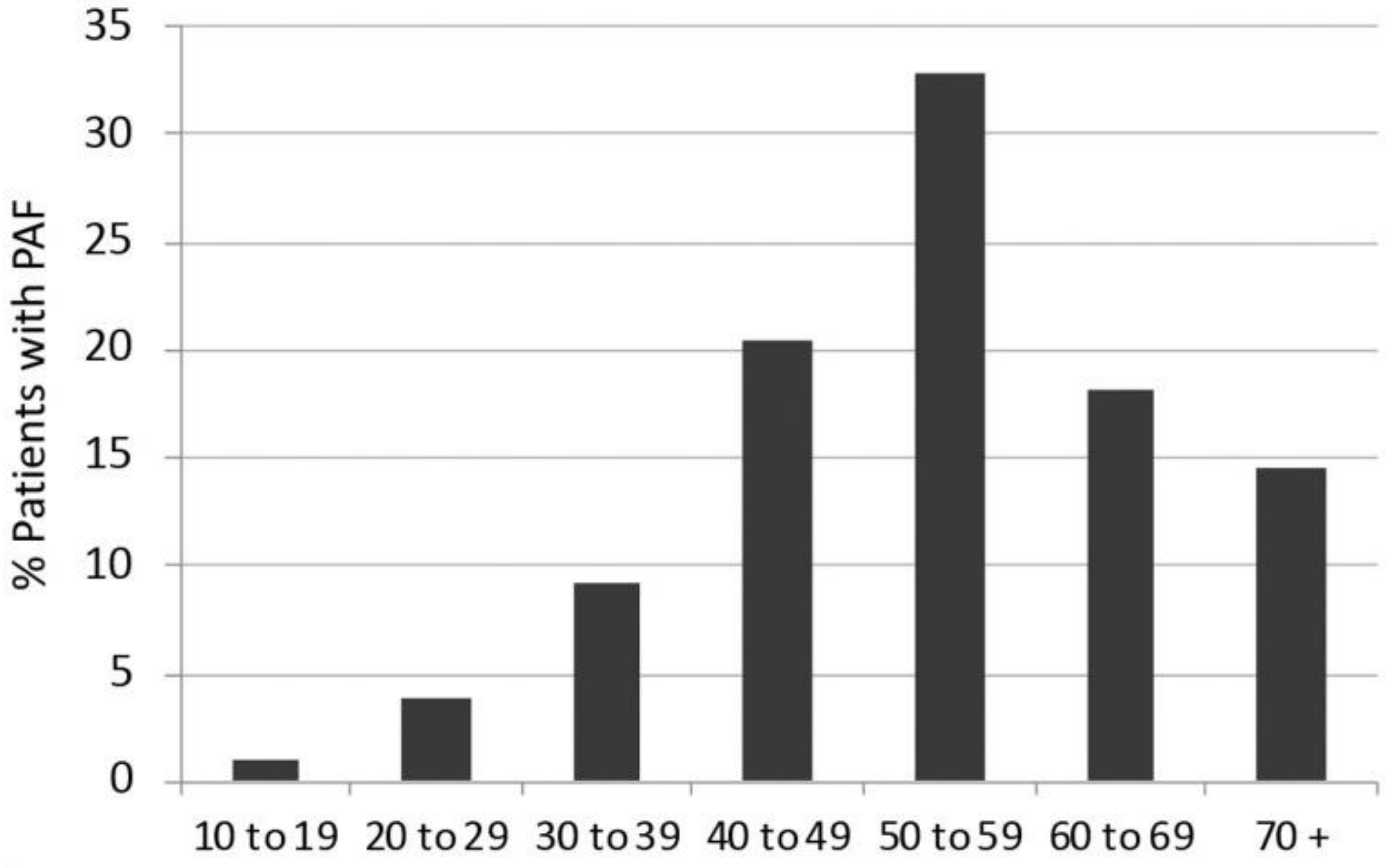
2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Patients with HCM and persistent or paroxysmal atrial fibrillation have a sufficiently increased risk of stroke such that oral anticoagulation with direct oral anticoagulants (or alternatively warfarin) should be considered the default treatment option independent of the CHA_2DS_2VASc score. As rapid atrial fibrillation is often poorly tolerated in patients with HCM, maintenance of sinus rhythm and rate control are key pursuits in successful treatment.

Ommen et al. 2020

VHF bei HCM: Manifestationsalter

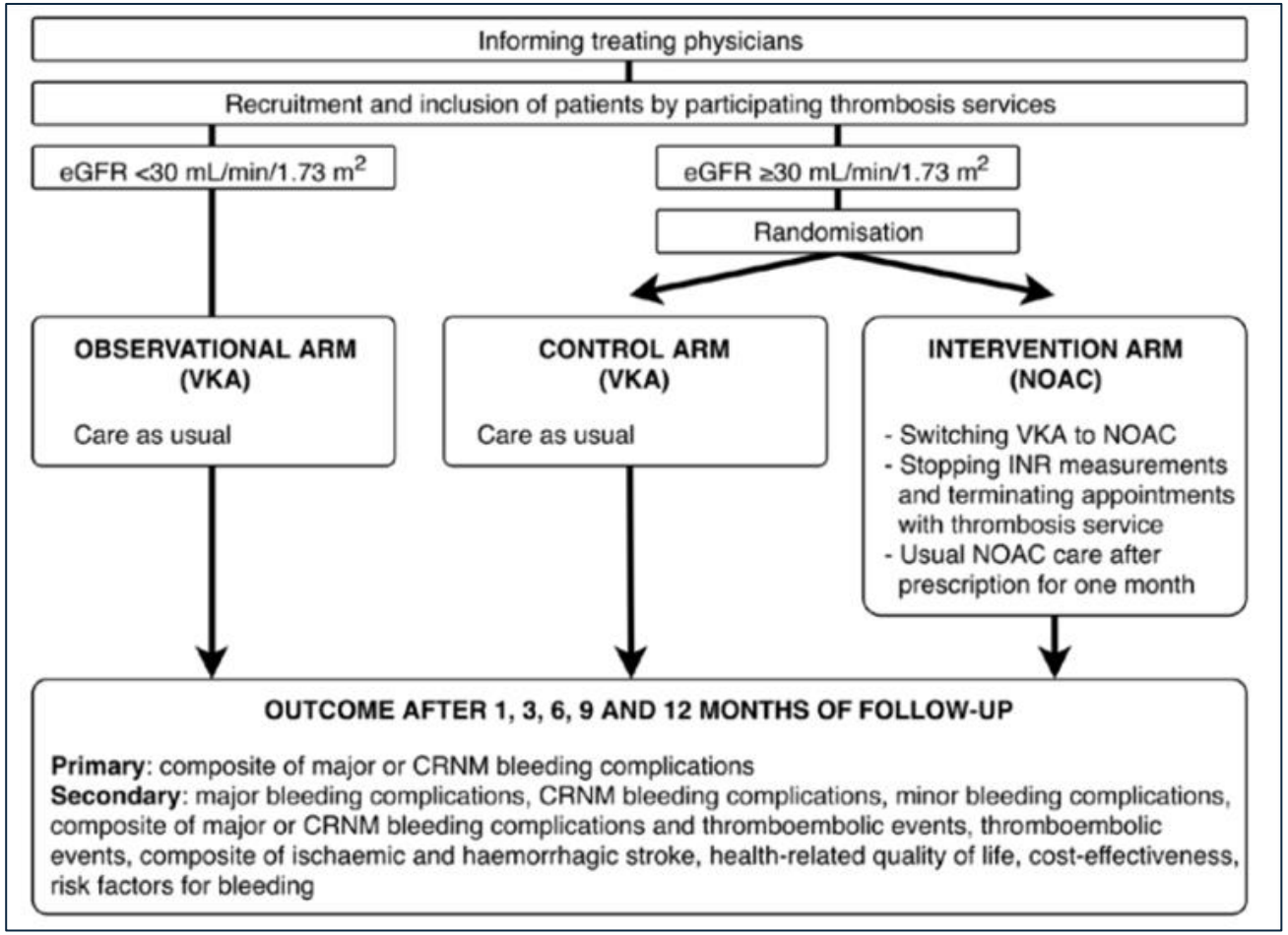


Rowin et al. 2022

NOAK-Alternativen?

ESC 2023
European Society of Cardiology

FRAIL-AF



Rekrutierung 2018 - 2022

Joosten et al. 2021

FRAIL-AF

Baseline characteristics

Characteristic	Continue with VKA (n=661)	Switch to NOAC (n=662)
Age in years*	83 (5)	83 (5)
Female sex†	239 (36)	274 (41)
Groningen Frailty Indicator score‡	4 (3-6)	4 (3-6)
CHA_2DS_2-VASc score‡	4 (3-5)	4 (3-5)
Heart failure†	150 (23)	129 (20)
Hypertension†	336 (51)	365 (55)
Diabetes mellitus†	140 (21)	140 (21)
eGFR in mL/min/1.73m^2*	63 (16)	63 (16)

Joosten et al. 2021

FRAIL-AF

Intervention arm

NOAC type	Number (%)
Dabigatran	57 (8.6)
Rivaroxaban	332 (50.2)
Apixaban	115 (17.4)
Edoxaban	109 (16.5)
Missing information on the prescribed NOAC	3 (0.5)
Continued with VKA-therapy	22 (3.3)
Withdrew consent	24 (3.6)

NOAC dose	Number (%)
Off-label dose reduction	44 (6.6)

Joosten et al. 2021

ESC 2023
European Society of Cardiology

FRAIL-AF

1,330 patients aged ≥75 years, with a Groningen Frailty Indicator score ≥3, who were managed with VKAs at a participating Dutch thrombosis centre were randomised to continue on a VKA or to switch to a NOAC, with the choice of agent at the physician's discretion.

HR for the primary outcome of **major or clinically relevant non-major bleeding** was **1.69** (95% CI 1.23 to 2.32) for switching to a NOAC relative to continuing a VKA.

HR for thromboembolic events was **1.26** (95% CI 0.60 to 2.61).

No difference in overall **mortality**.

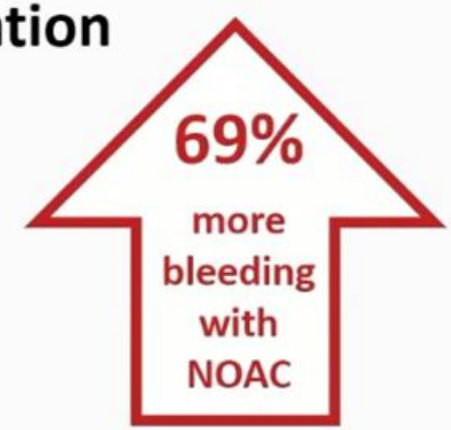
Joosten et al. 2023

FRAIL-AF

Conclusions

- **FRAIL-AF is a unique study as it is the first randomised NOAC trial that exclusively included frail older patients**

- **Switching from a VKA to a NOAC should not be considered without a clear indication in frail older patients with AF**



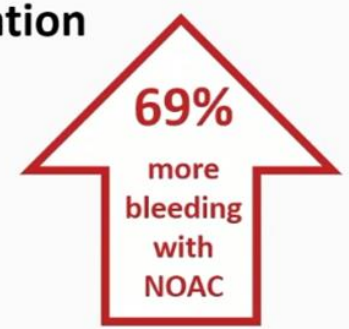
Joosten et al. 2021

FRAIL-AF

Conclusions

- FRAIL-AF is a unique study as it is th… …omised NOAC trial that exclusively included frail old… …s
- Switching from a VKA to… should not be consid… …out a clear indication in frail older pati… …AF

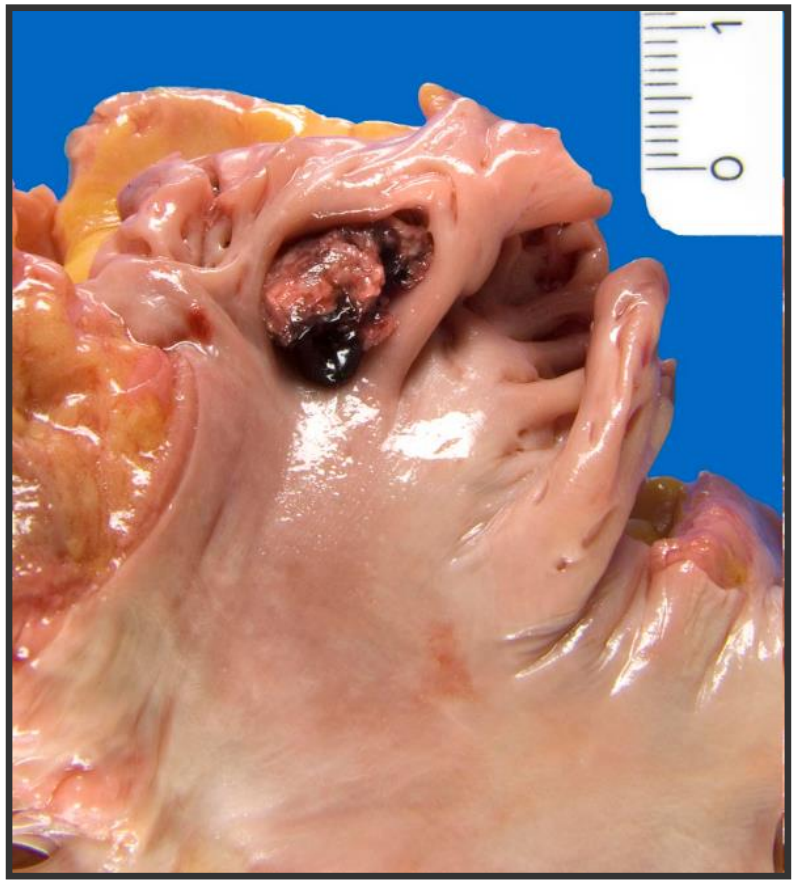
FALSCH!

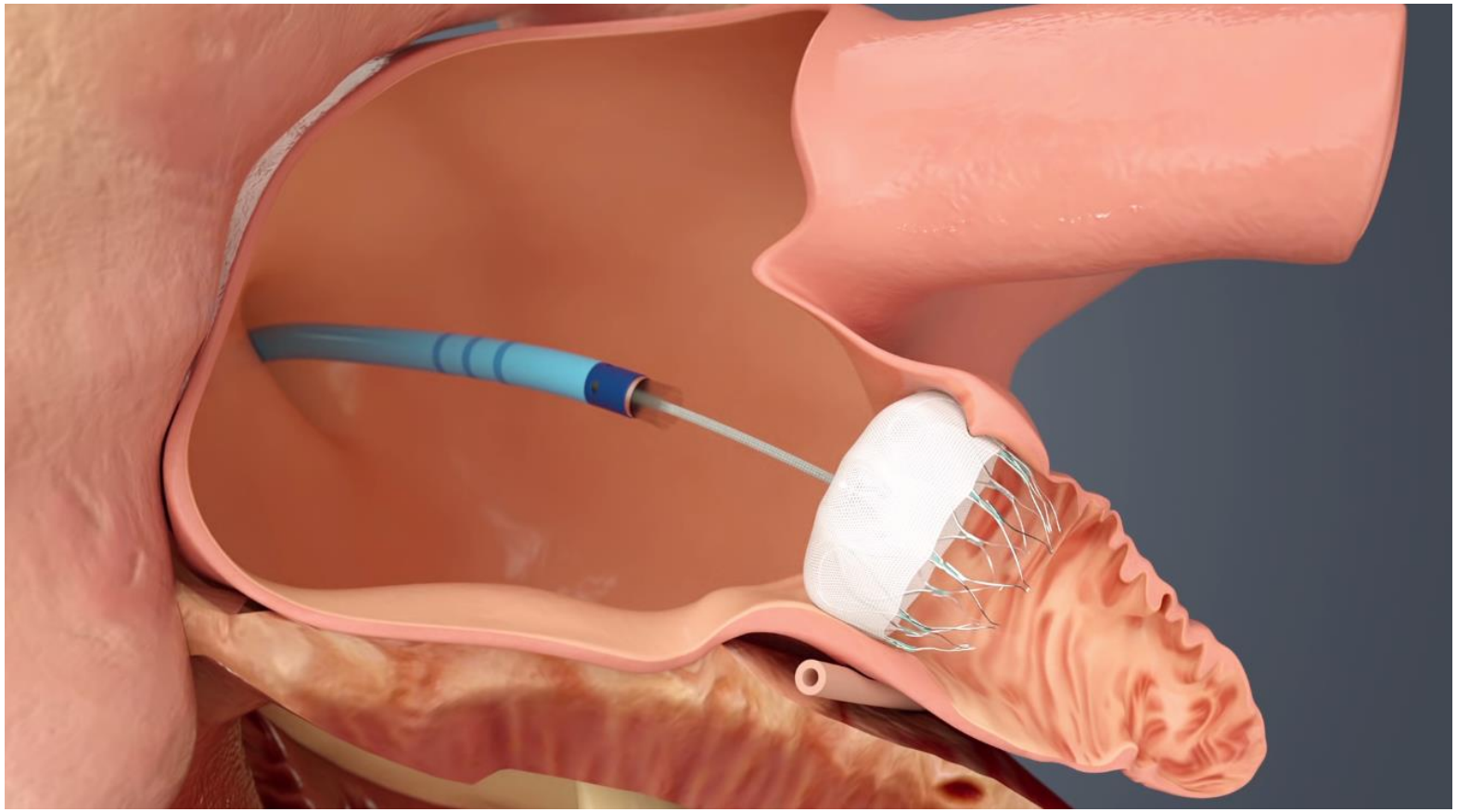


Die richtige Dosis und sorgfältige Kontrollen sind notwendig!

Joosten et al. 2021

Thrombus im linken Vorhofohr/LAA-Verschluss





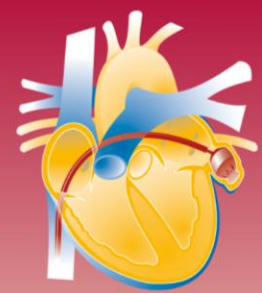
DZHK-STUDIE CLOSURE-AF-DZHK16

Login | Impressum und Datenschutz

CLOSURE-AF
DZHK TRIAL 16

Suche ...

Hintergrund und Ziele | Teilnahme | Dokumente | Publikationen | Kontakt



CLOSURE-AF Studie

Perkutaner Verschluss des linken Vorhofohres bei Patienten mit Vorhofflimmern und hohem Schlaganfall- und Blutungsrisiko im Vergleich zur medikamentösen Standardtherapie: eine prospektive, randomisierte klinische Studie

CLOSURE-AF-DZHK16

EudraCT-Nr.: 2017-000058-21

ClinicalTrials.gov Identifier: NCT03463317

Hotline

Bei Rückfragen zur CLOSURE-AF Studie können Sie jederzeit unsere Hotline unter der Telefonnummer **+49 (0)451 500 – 44516** kontaktieren.

Kurzinformation

Die CLOSURE-AF Studie ist eine prospektive, randomisierte, multizentrische Studie. Sie vergleicht den perkutanen Verschluss des linken Vorhofohres mit einer medikamentösen Standardtherapie bei Patienten mit Vorhofflimmern und hohem Schlaganfall- und Blutungsrisiko.

Geplant ist die Durchführung an mehr als 60 spezialisierten Zentren in Deutschland. Insgesamt sollen ca. 1.000 Patienten teilnehmen.

Sponsor der Studie ist die Charité–Universitätsmedizin Berlin.

Die Studie wird in Höhe von 7,4 Mio. Euro durch das Deutsche Zentrum für Herz-Kreislauf-Forschung e. V. (DZHK) gefördert.

Probanden-Informationsplattform

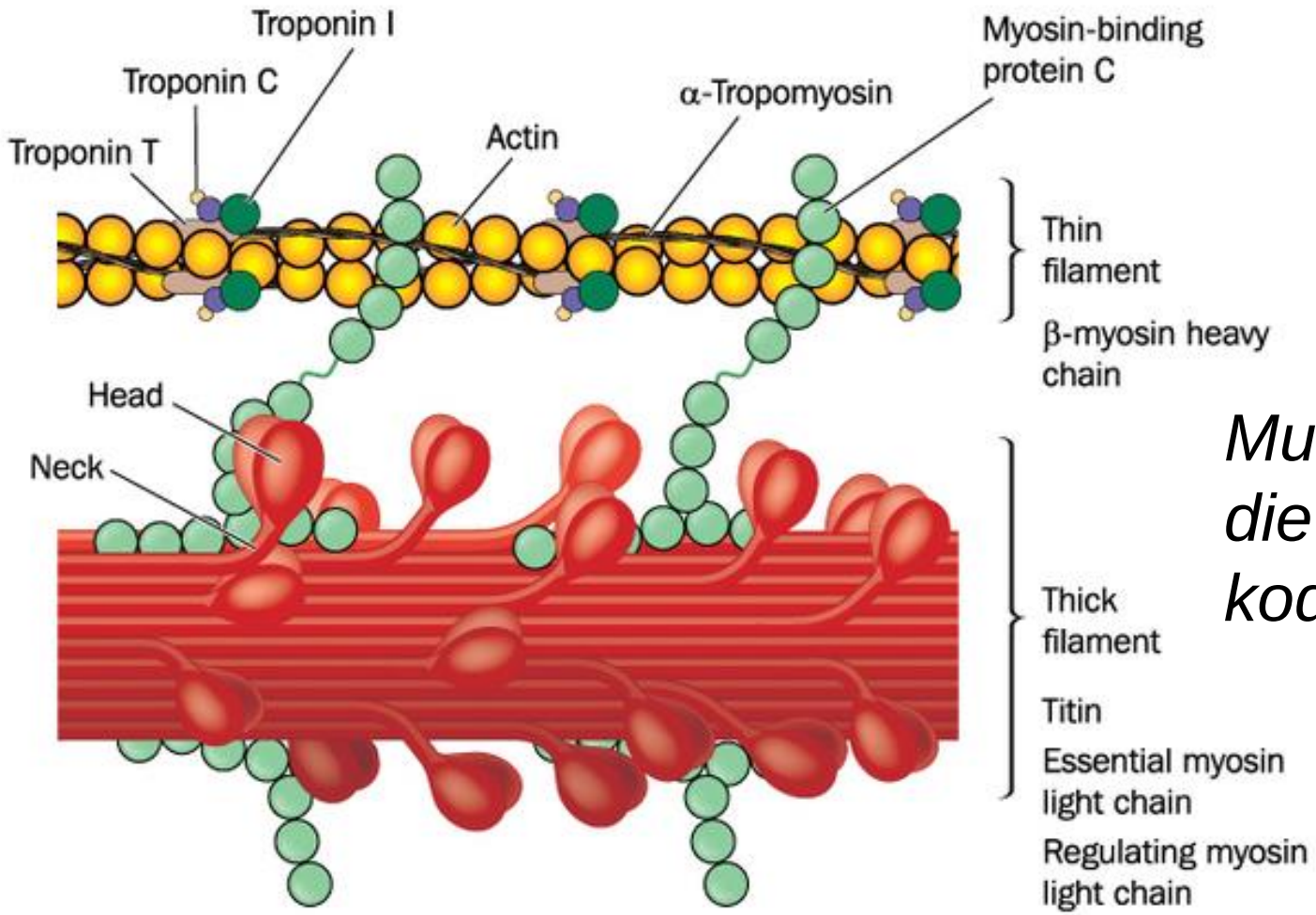
Login | Impressum und Datenschutz

DZG DEUTSCHE ZENTREN DER GESUNDHEITSFORSCHUNG

Gefördert vom Bundesministerium für Bildung und Forschung und den zehn Sitzländern

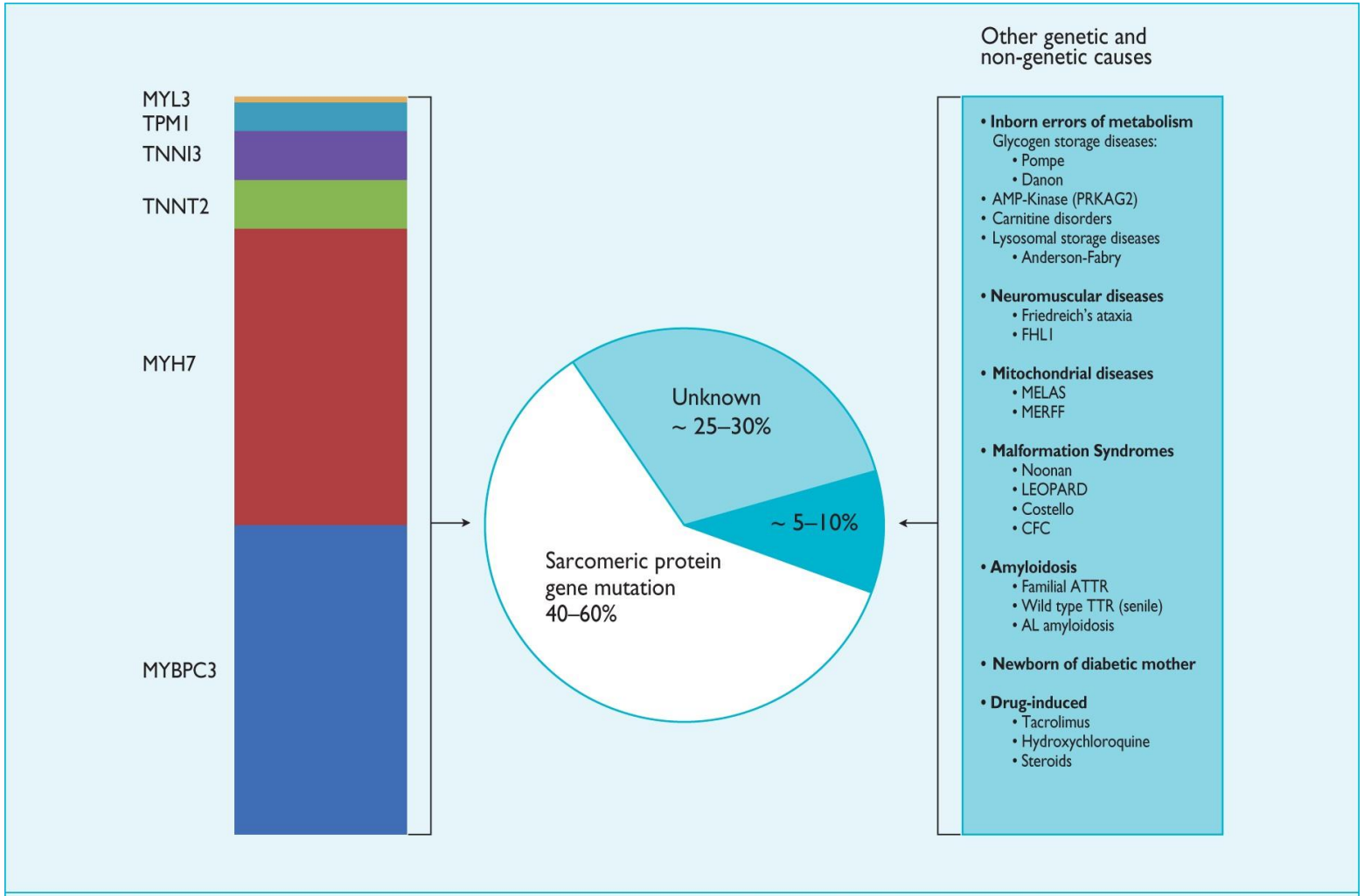
Kardiogenetik

HCM: Genetik



*Mutationen in Genen, die für **Sarkomerproteine** kodieren (in 60-70%)*

Ätiologie der hypertrophen Kardiomyopathie



The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes. AL = amyloid light chain; ATTR=amyloidosis, transthyretin type.
CFC = cardiofaciocutaneous; FHL-1=Four and a half LIM domains protein 1; LEOPARD = lentigines, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth, and sensorineural deafness; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERFF = myoclonic epilepsy with ragged red fibres; MYL3 = myosin light chain 3; MYBPC3 = myosin-binding protein C, cardiac-type; MYH7 = myosin, heavy chain 7; TNNI3 = troponin I, cardiac; TNNT2 = troponin T, cardiac: TPM1 = tropomyosin 1 alpha chain; TTR = transthyretin.

ESC
European Society
of Cardiology

2014

Table 5 Impact of genetic testing for the proband

Disease	Diagnostic	Prognostic	Therapeutic
Arrhythmia syndromes			
Long QT syndrome	+++	+++	+++
CPVT	+++	+	+
Brugada syndrome	+	+	+
Progressive cardiac conduction disease	+	+	+
Short QT syndrome	+	+	+
Sinus node disease	–	+	–
Atrial fibrillation	–	+	–
Early repolarization syndrome	–	–	–
Cardiomyopathies			
Hypertrophic cardiomyopathy	+++	++	++
Dilated cardiomyopathy	++	+++	++
Arrhythmogenic cardiomyopathy	+++	++	++
Left ventricular non-compaction	+	+	–
Restrictive cardiomyopathy	+	+	+
Congenital heart disease			
Syndromic CHD	+++	+	–
Non-syndromic CHD	+	–	–
Familial CHD	++	–	–

ESC European Society of Cardiology
Europace (2022) **24**, 1307–1367
https://doi.org/10.1093/europace/euac030

POSITION PAPER

European Heart Rhythm Association (EHRA)/ Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases

Wilde et al. 2022

+++: is recommended/is indicated or useful.
++: can be recommended/can be useful.
+: may be considered/may be useful.
–: is not recommended/is not indicated nor useful.

Wilde et al. 2022

In Deutschland dürften über 300.000 Patienten von einer mit strukturellen Herzveränderungen einhergehenden Kardiomyopathie betroffen sein.

ESC
European Society of Cardiology

European Heart Journal (2023) **00**, 1–124
https://doi.org/10.1093/eurheartj/ehad194

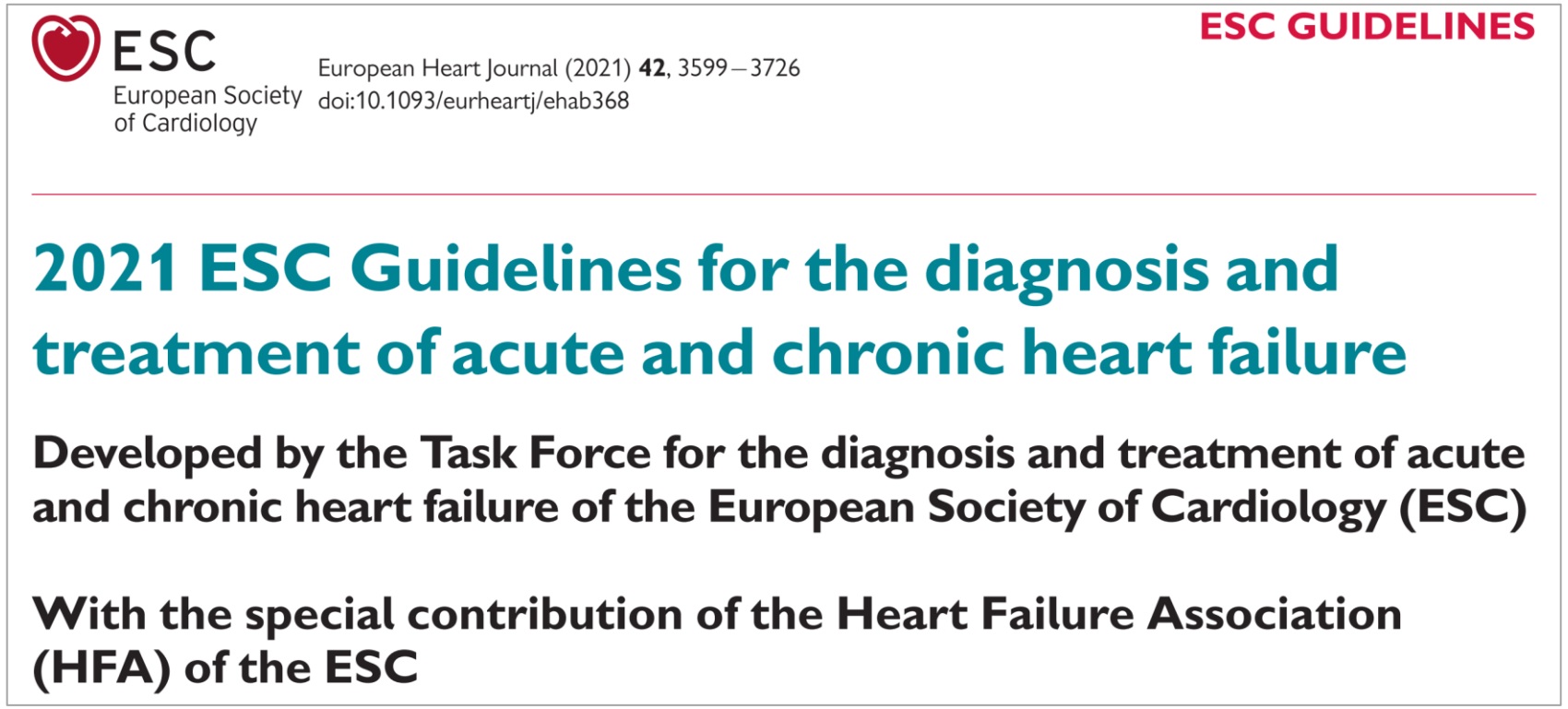
ESC GUIDELINES

2023 ESC Guidelines for the management of cardiomyopathies

Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

Neue Medikamente

2021 ESC-Leitlinie CHF*

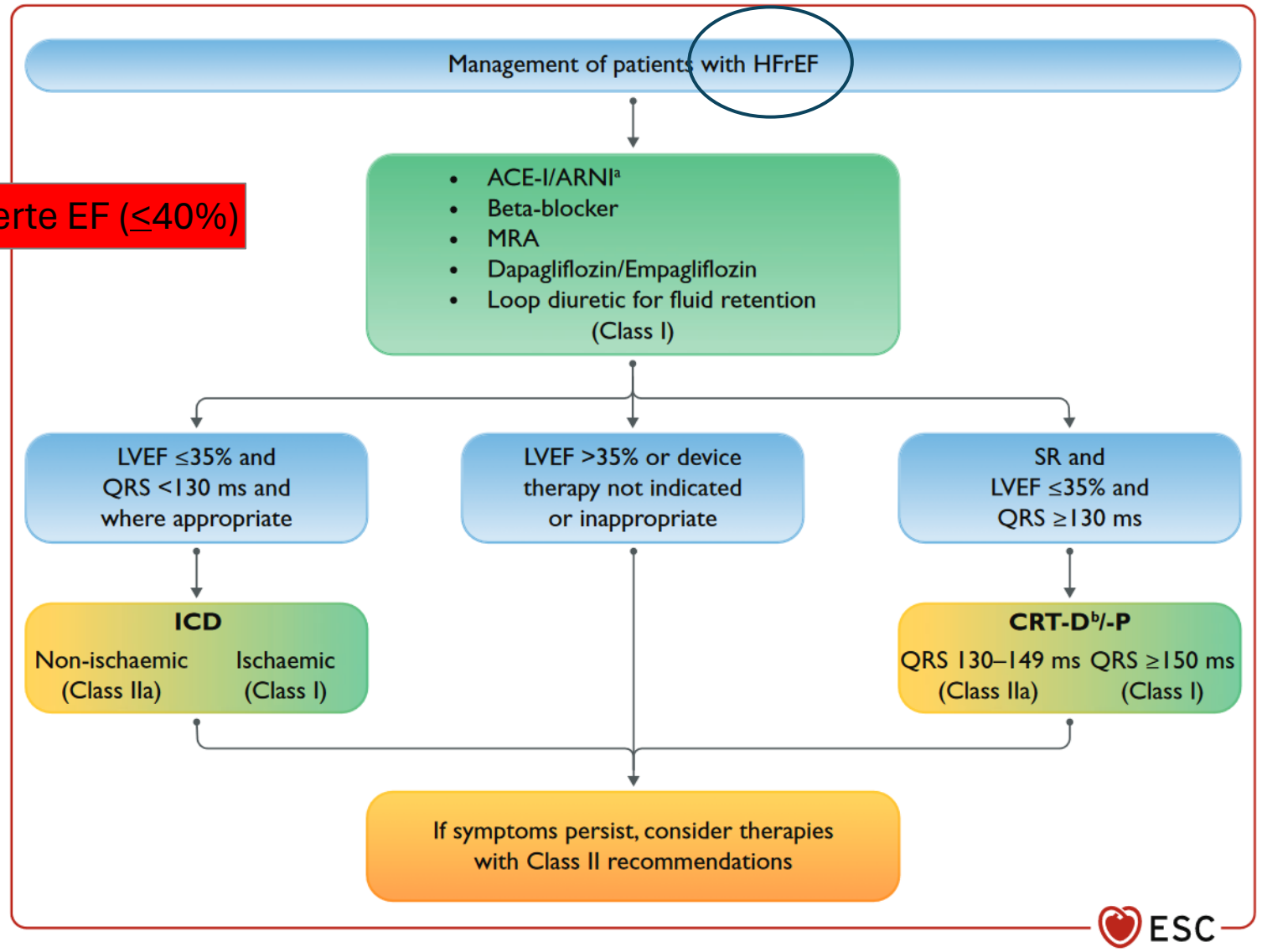


*CHF: Chronische Herzinsuffizienz

McDonagh et al. 2021

HFrEF: Management laut ESC-Leitlinie 2021

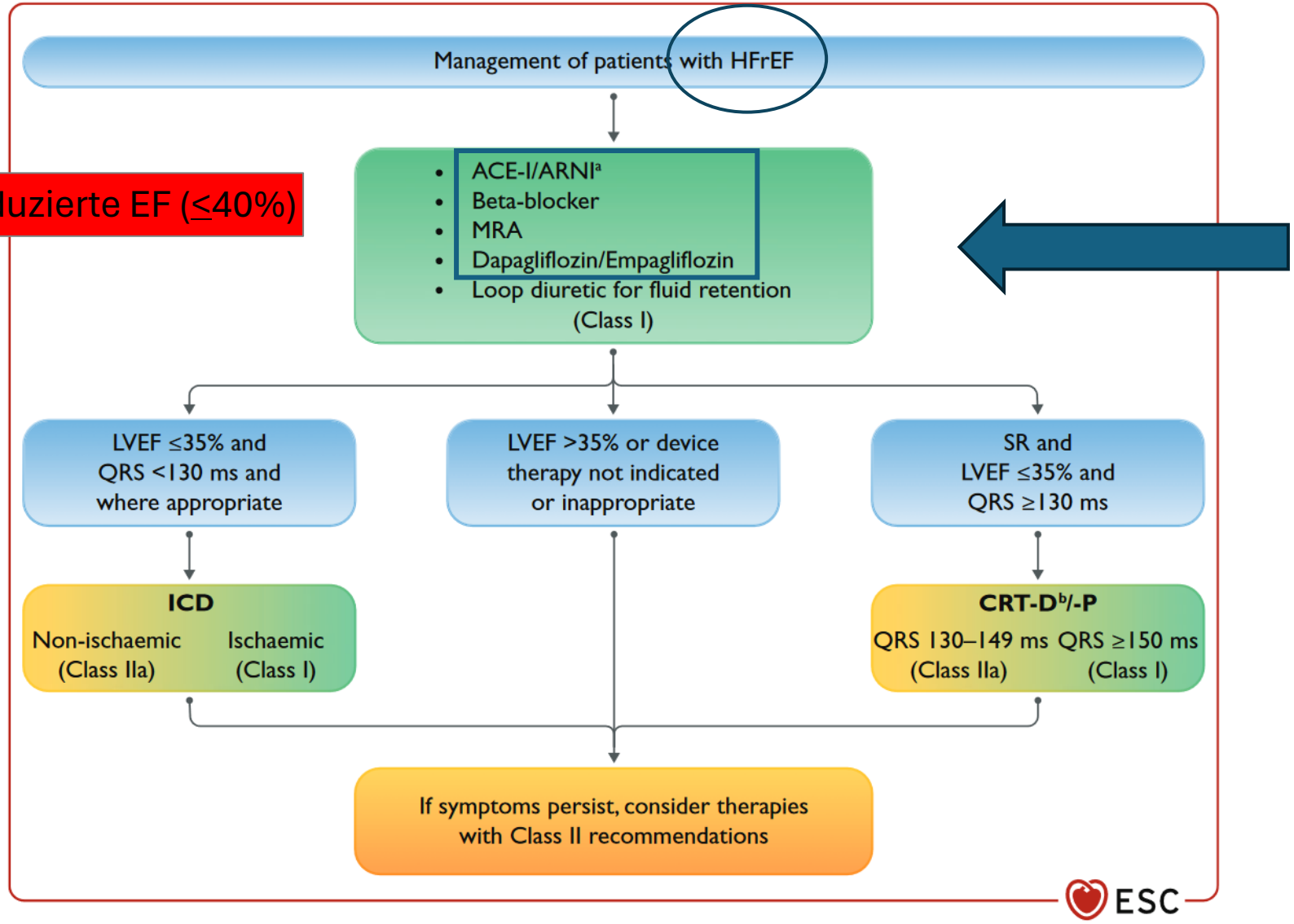
rEF: reduzierte EF (≤40%)



McDonagh et al. 2021

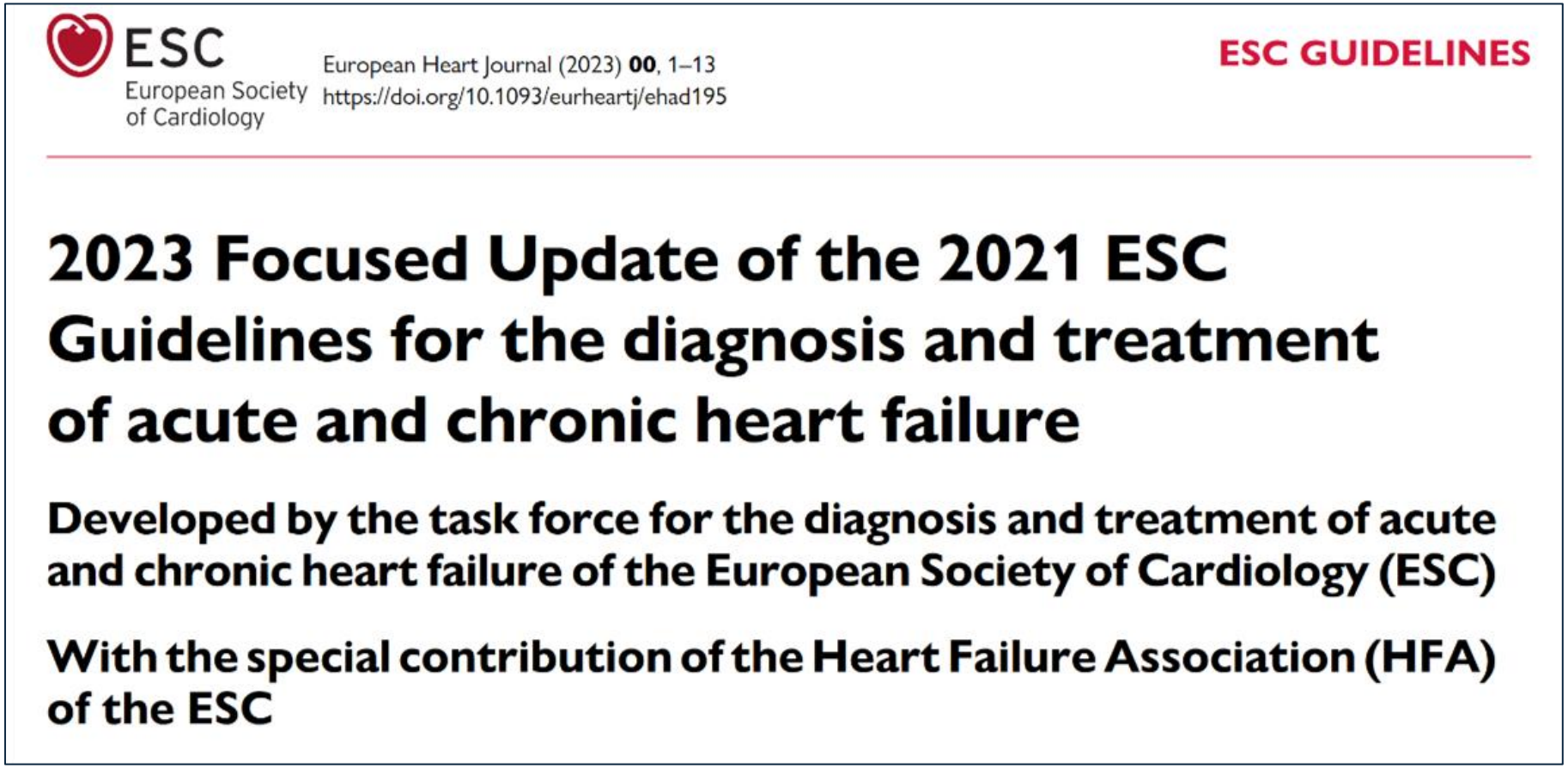
HFrEF: Management laut ESC-Leitlinie 2021

rEF: reduzierte EF (≤40%)



McDonagh et al. 2021

Leitlinie Update-Herzinsuffizienz 2023



ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–13
https://doi.org/10.1093/eurheartj/ehad195

ESC GUIDELINES

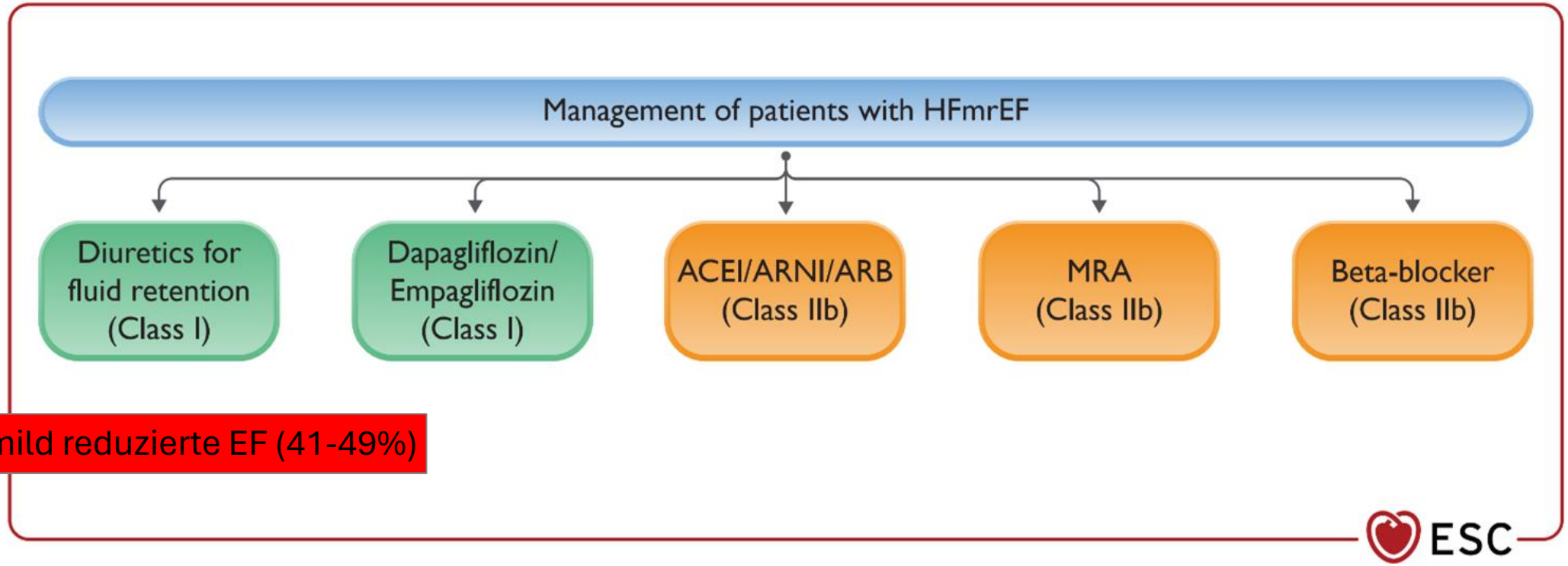
2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

McDonagh et al. 2021

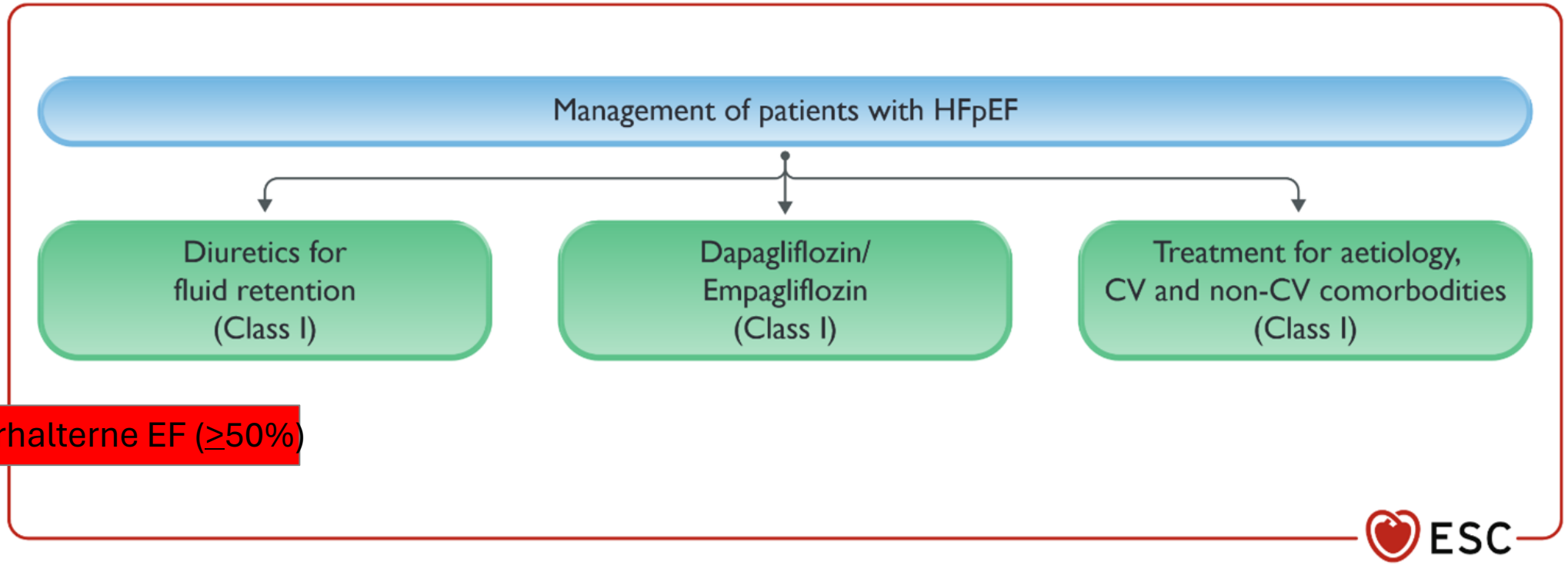
HFmrEF: Management laut Update 2023



mrEF: mild reduzierte EF (41-49%)

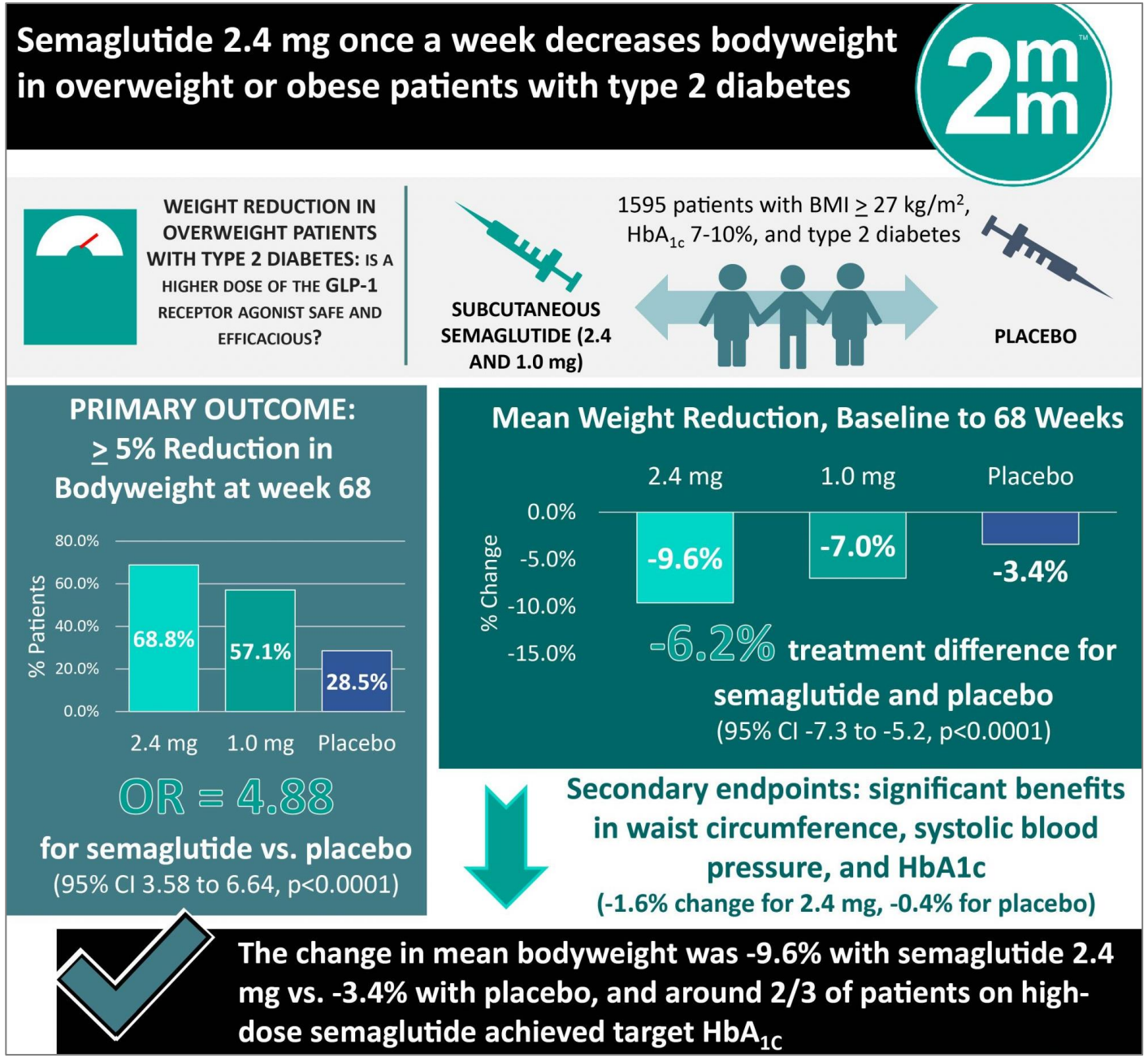
McDonagh et al. 2021

HFpEF: Management laut Update 2023



mrEF: erhalterne EF (≥50%)

McDonagh et al. 2021



Semaglutid

Davies et al. 2021

The SELECT Trial

Semaglutide and Cardiovascular outcomes in obesity without diabetes

Lincoff et al, New England Journal of medicine, 2023

Question

Can Semaglutide reduce Cardiovascular risk associated with overweight and obesity without diabetes?

Methods

multi-center, double blind, randomized, placebo controlled, event driven superiority trial, 804 clinical sites in 41 countries

Inclusion Criteria

- Age≥ 45
- BMI≥ 27
- Established Cardiovascular disease

Exclusion Criteria

- History of Diabetes
- HbA1c≥ 6.5%
- On Glucose lowering medication or GLP-1 Agonist within the previous 90 days
- NYHA class IV heart failure
- ESRD or on Dialysis

Semaglutide 8803 **1:1** Placebo 8801

Duration 34.2±13.7 months
Follow up 39.8±9.4 months

Primary End Point

Death from cardiovascular causes, non-fatal MI, non-fatal stroke

6.5% vs 8% (HR~0.8 P-value<0.001)

Secondary End Point

Death from cardiovascular causes

2.5% vs 3% (HR~0.85 P-value<0.07)

Death from heart failure

HR~0.82

Death from any cause

HR~0.81

Mean Change in Body Weight

-9.39% vs -0.88%

Adverese events leading to permanent discontinuation of trial product

16.6% vs 8.2% (P-Value<0.001)

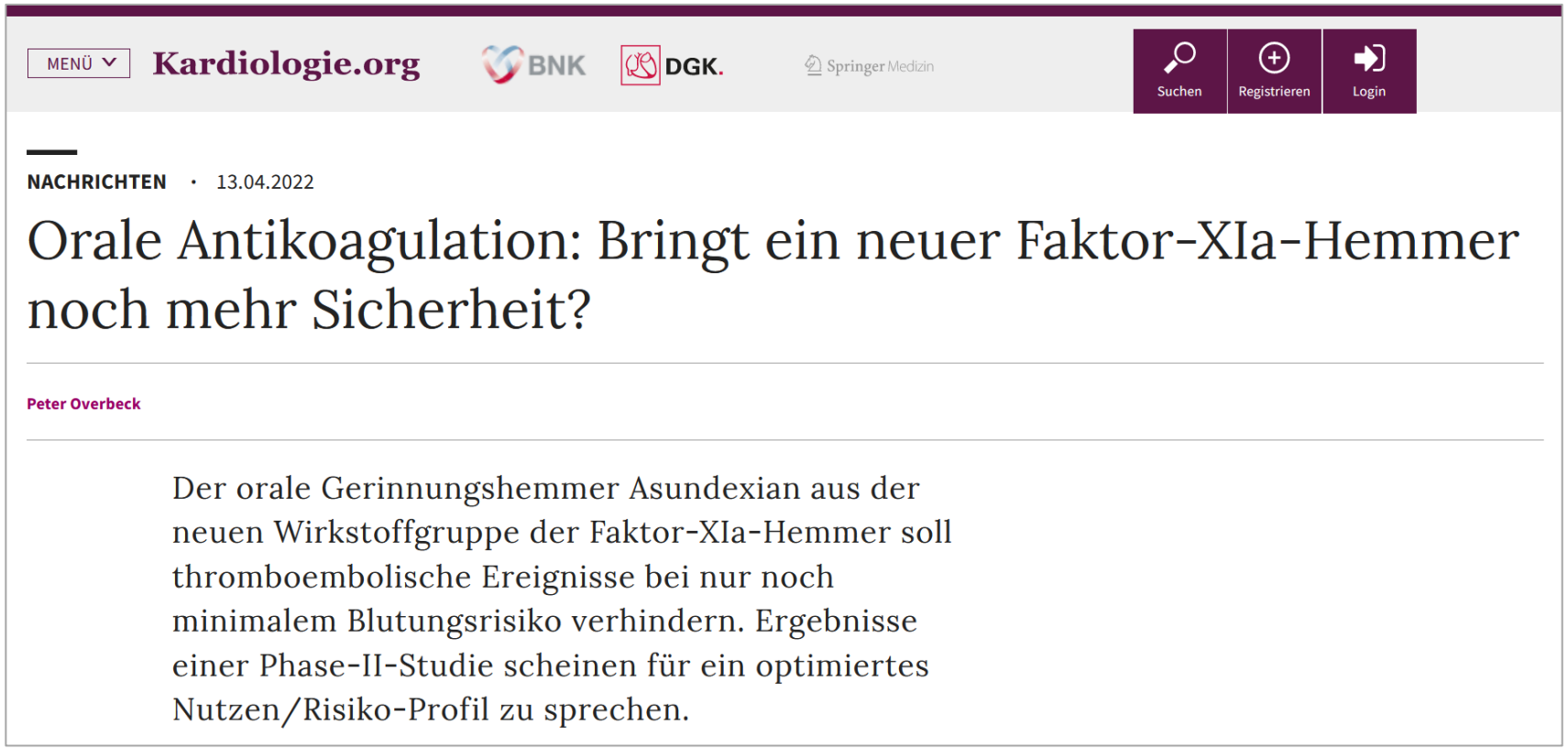
Conclusion

Weekly subcutaneous Semaglutide 2.4 mg was superior to placebo in reducing the incidence of death in cardiovascular causes, nonfatal MI, or nonfatal stroke at a mean follow up 39.8 months in patients with preexisting cardiovascular disease and overweight or obesity but without diabetes. The incidence of adverse events was lower among patients who received semaglutide.

Is Wegovy really a gamechanger for heart health? A consultant cardiologist gives his verdict

Published: September 1, 2023 12.18pm CEST

Faktor XIa-Inhibition



MENÜ Kardiologie.org BNK DGK. Springer Medizin Suchen Registrieren Login

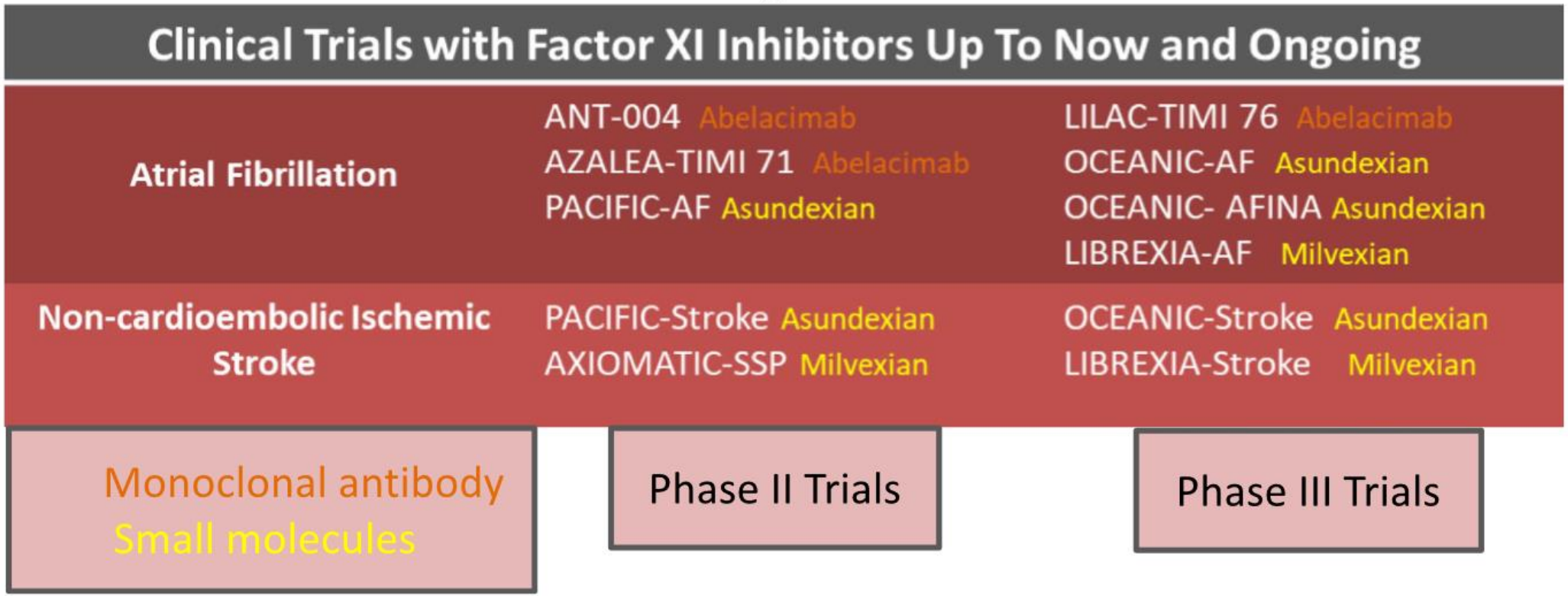
NACHRICHTEN · 13.04.2022

Orale Antikoagulation: Bringt ein neuer Faktor-XIa-Hemmer noch mehr Sicherheit?

Peter Overbeck

Der orale Gerinnungshemmer Asundexian aus der neuen Wirkstoffgruppe der Faktor-XIa-Hemmer soll thromboembolische Ereignisse bei nur noch minimalem Blutungsrisiko verhindern. Ergebnisse einer Phase-II-Studie scheinen für ein optimiertes Nutzen/Risiko-Profil zu sprechen.

Clinical Trials and Sites of Action of Factor XI/XII Inhibitors and Other Anticoagulants



Prisco et al. 2024

Faktor-XIa-Hemmer

Rückschlag für Asundexian

Die Firma Bayer hat eine Phase-III-Studie mit dem noch nicht zugelassenen Faktor-XIa-Hemmer Asundexian wegen unterlegener Wirksamkeit gegenüber dem bekannten Faktor-Xa-Hemmer Apixaban abgebrochen. Eine andere Phase-III-Studie wird aber fortgesetzt.

Sven Siebenand

20.11.2023 15:30 Uhr

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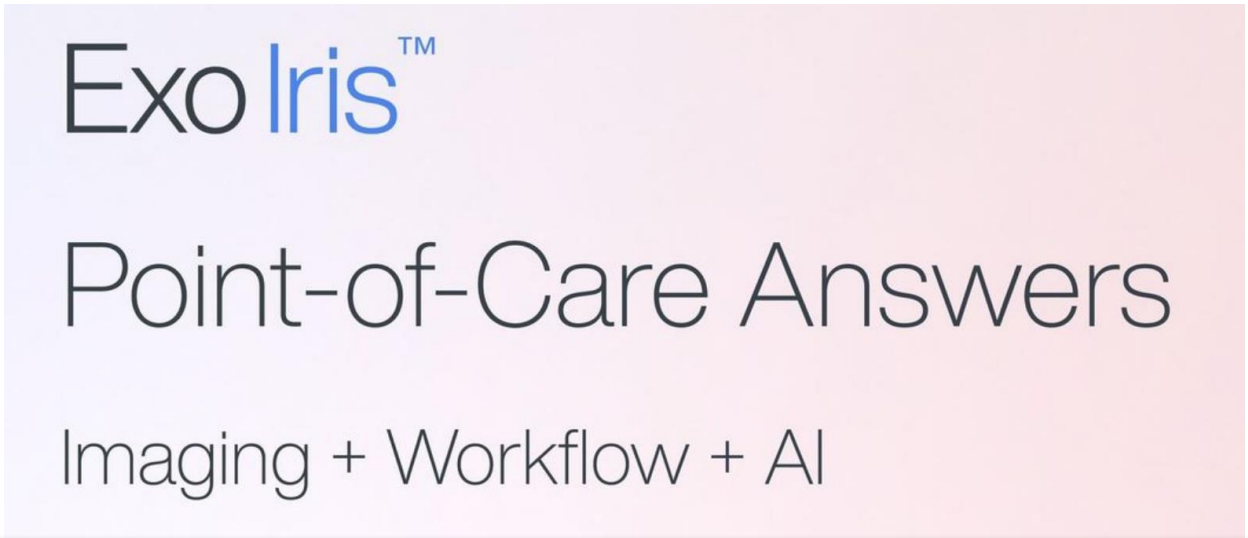

The Iris system is now available for purchase in the U.S. at a starting price of $3,500. Its cart-based competitors, meanwhile, can retail for anywhere between $5,000 and $200,000.