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HERZ Focus 2025

Was ist neu bei Herzinsuffizienz und Myopathien?
Neue Leitlinie der Kardiomyopathie



PD Dr. Maria Papathanasiou

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Offenlegung von potenziellen Interessenkonflikten gegenüber der Industrie

Vortrags- und Berater-Tätigkeit

Alnylam, Pfizer, Bristol Myers Squibb, Astra-Zeneca, Bayer, Alexion, Prothena, Janssen

Teilnahme an Advisory Boards

Alnylam, Pfizer, Bristol Myers Squibb, Prothena

Teilnahme an klinischen Studien

Alnylam, Cytokinetics

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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)

Authors/Task Force Members: Elena Arbelo *†, (Chairperson) (Spain), Alexandros Protonotarios ‡, (Task Force Co-ordinator) (United Kingdom), Juan R. Gimeno ‡, (Task Force Co-ordinator) (Spain), Eloisa Arbustini (Italy), Roberto Barriales-Villa (Spain), Cristina Basso (Italy), Connie R. Bezzina (Netherlands), Elena Biagini (Italy), Nico A. Blom[1] (Netherlands), Rudolf A. de Boer (Netherlands), Tim De Winter (Belgium), Perry M. Elliott (United Kingdom), Marcus Flather (United Kingdom), Pablo Garcia-Pavia (Spain), Kristina H. Haugaa (Sweden), Jodie Ingles (Australia), Ruxandra Oana Jurcut (Romania), Sabine Klaassen (Germany), Giuseppe Limongelli (Italy), Bart Loeys[2] (Belgium), Jens Mogensen (Denmark), Iacopo Olivotto (Italy), Antonis Pantazis (United Kingdom), Sanjay Sharma (United Kingdom), J. Peter Van Tintelen (Netherlands), James S. Ware (United Kingdom), Juan Pablo Kaski *†, (Chairperson) (United Kingdom), and ESC Scientific Document Group

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Die wichtigsten Punkten aus der Leitlinie

- Neue phänotypische Klassifikation
- Empfehlungen für Kinder und Erwachsene
- Rolle der genetischen Untersuchung
- Risikoeinschätzung des Plötzlichen Herztods (SCD)
- Management der HOCM
- Multidisziplinäre Behandlung

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Guideline Struktur

- Definitionen and Phänotypen der Kardiomyopathien
- Allgemeine diagnostische und therapeutische Ansätze
- Spezifische Kardiomyopathien
- Empfehlungen zu Sport, Schwangerschaft, Operationsrisiko nicht kardialer Eingriffe, Genderunterschiede, Komorbiditäten, COVID-19

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Definition der Kardiomyopathie

Eine Kardiomyopathie ist eine Erkrankung des Herzmuskels, die durch strukturelle und funktionelle Veränderungen des Myokards gekennzeichnet ist, ohne dass eine koronare Herzerkrankung, arterielle Hypertonie, valvuläre Herzerkrankung oder ein angeborener Herzfehler vorliegt.

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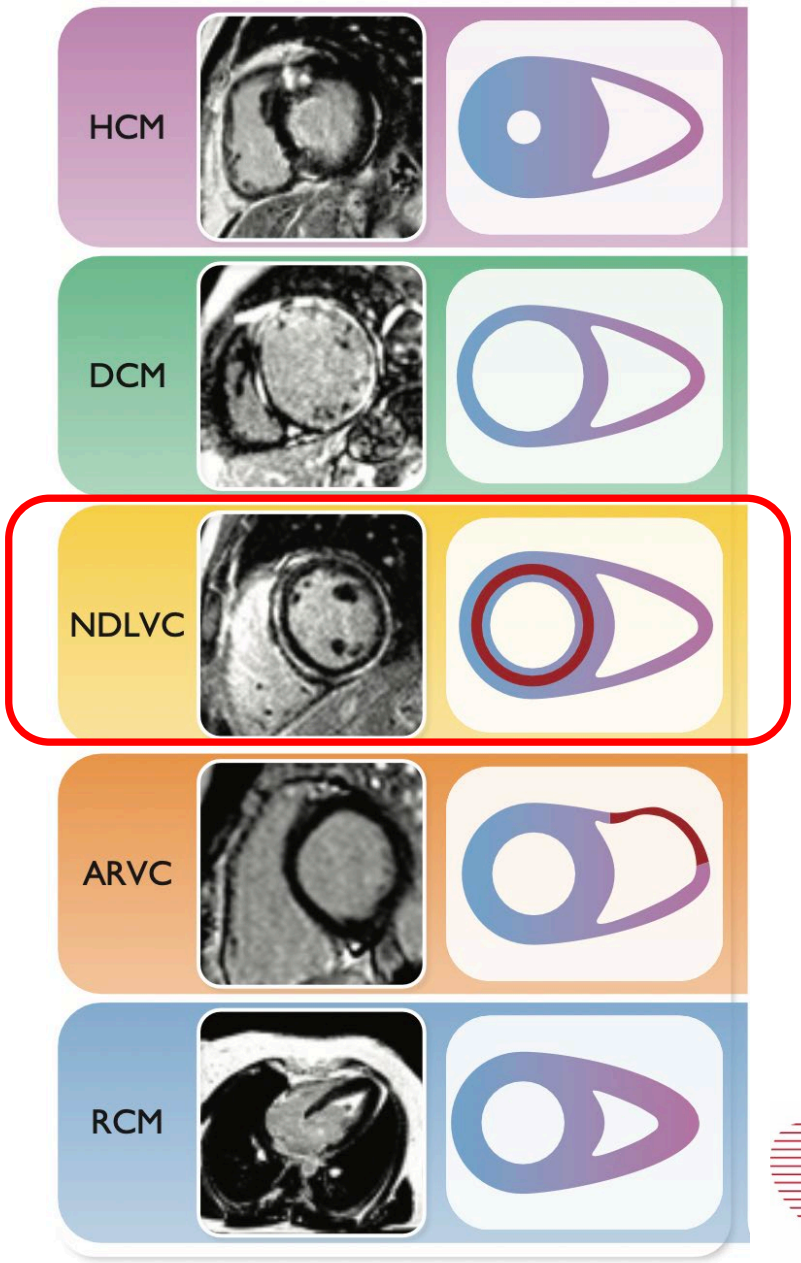
Neue phänotypische Klassifikation der Kardiomyopathien



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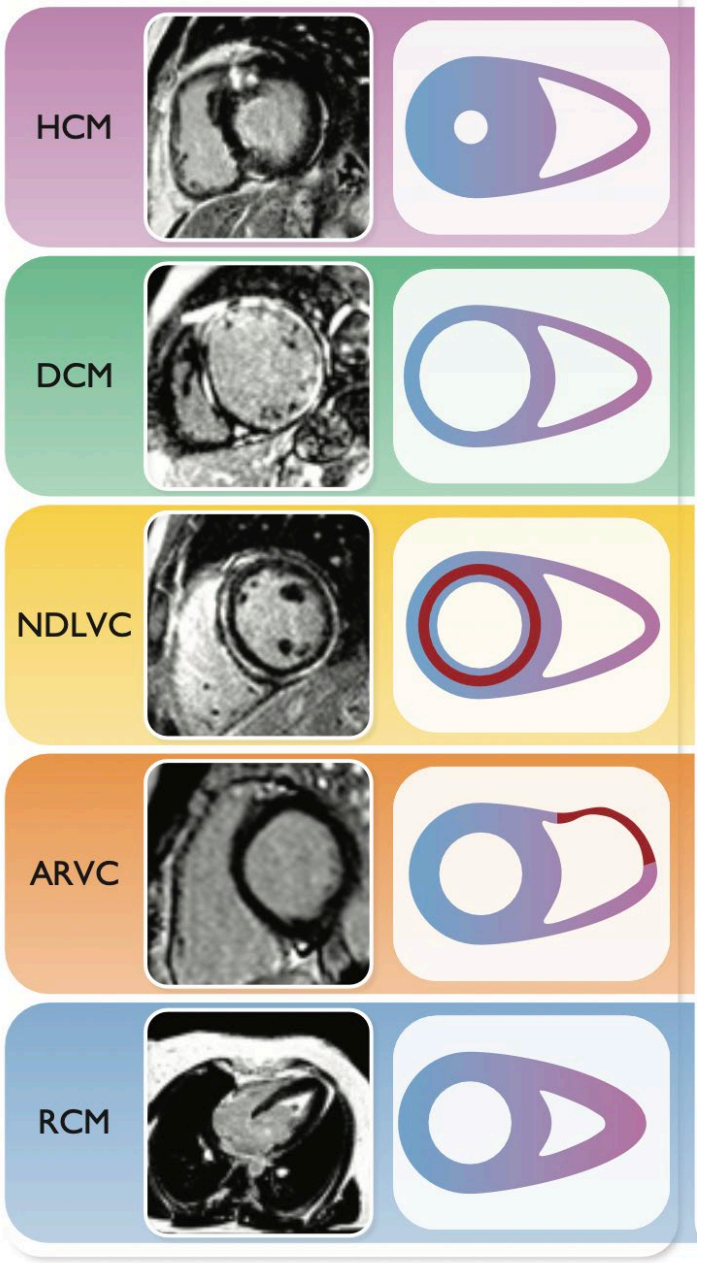
Neue phänotypische Klassifikation der Kardiomyopathien



Nicht mehr als KMP klassifiziert

- Left ventricular non-compaction
- Takotsubo-Syndrom
- Kanalopathien

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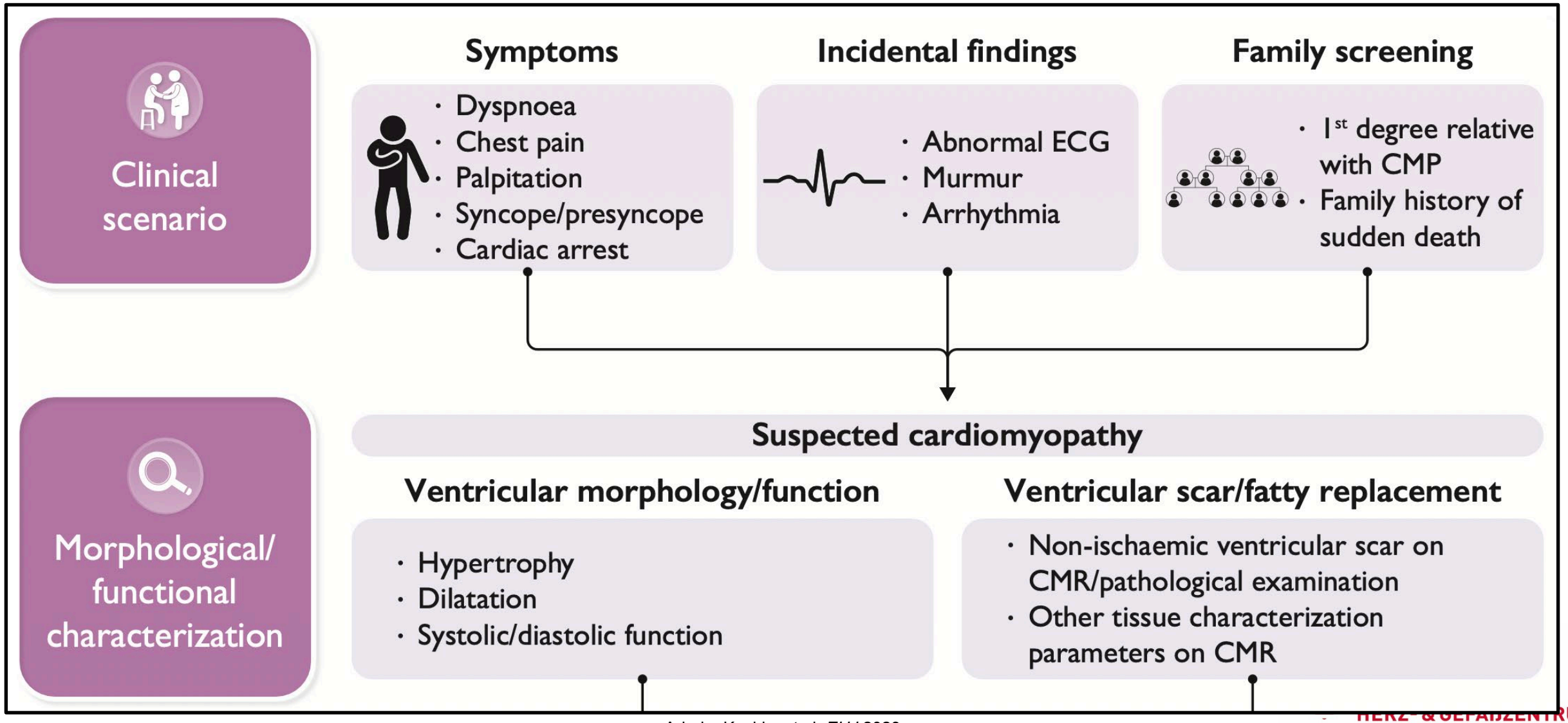
Patientenpfad und Diagnostik bei V.a. Kardiomyopathie



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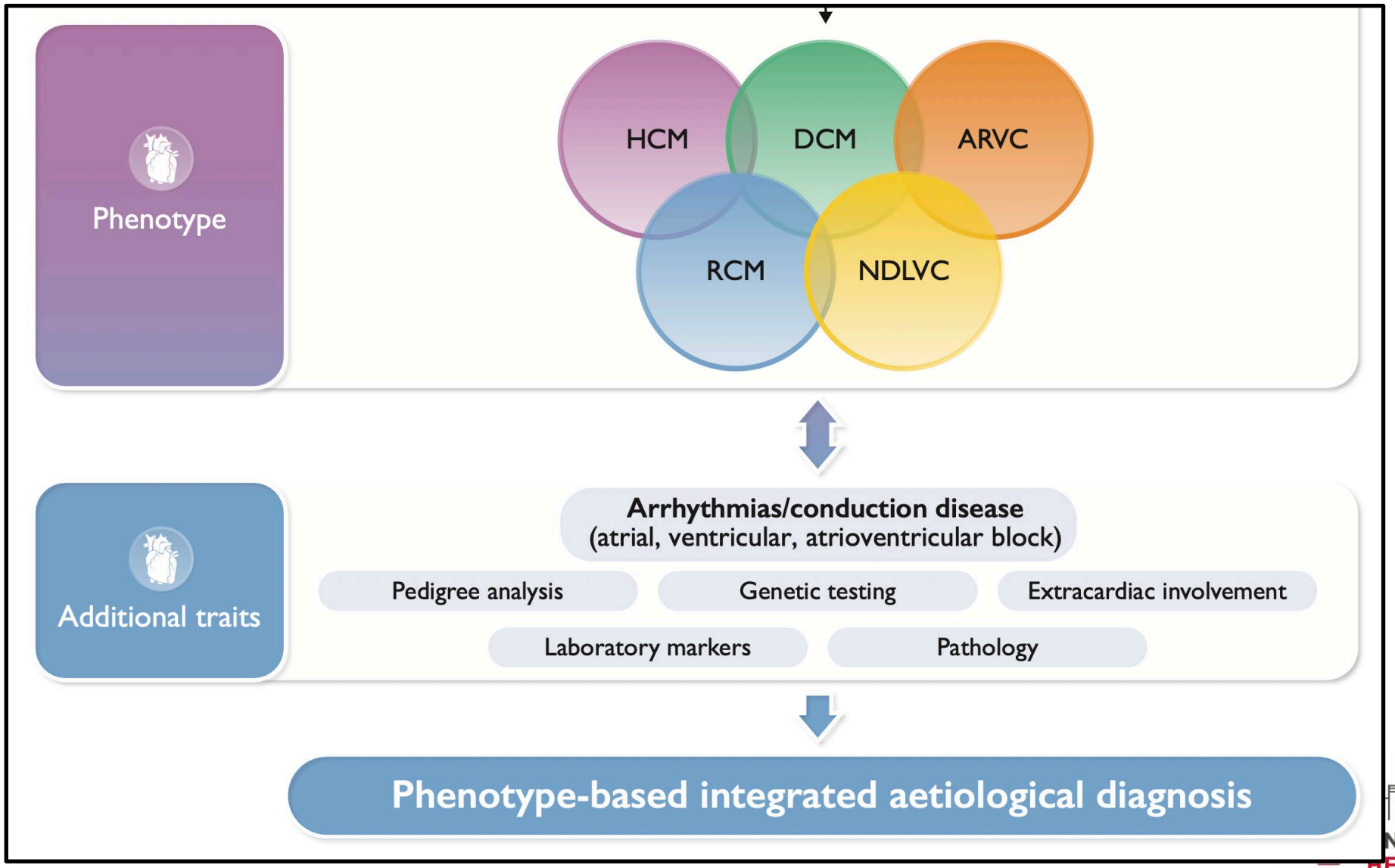
Diagnostisches Vorgehen



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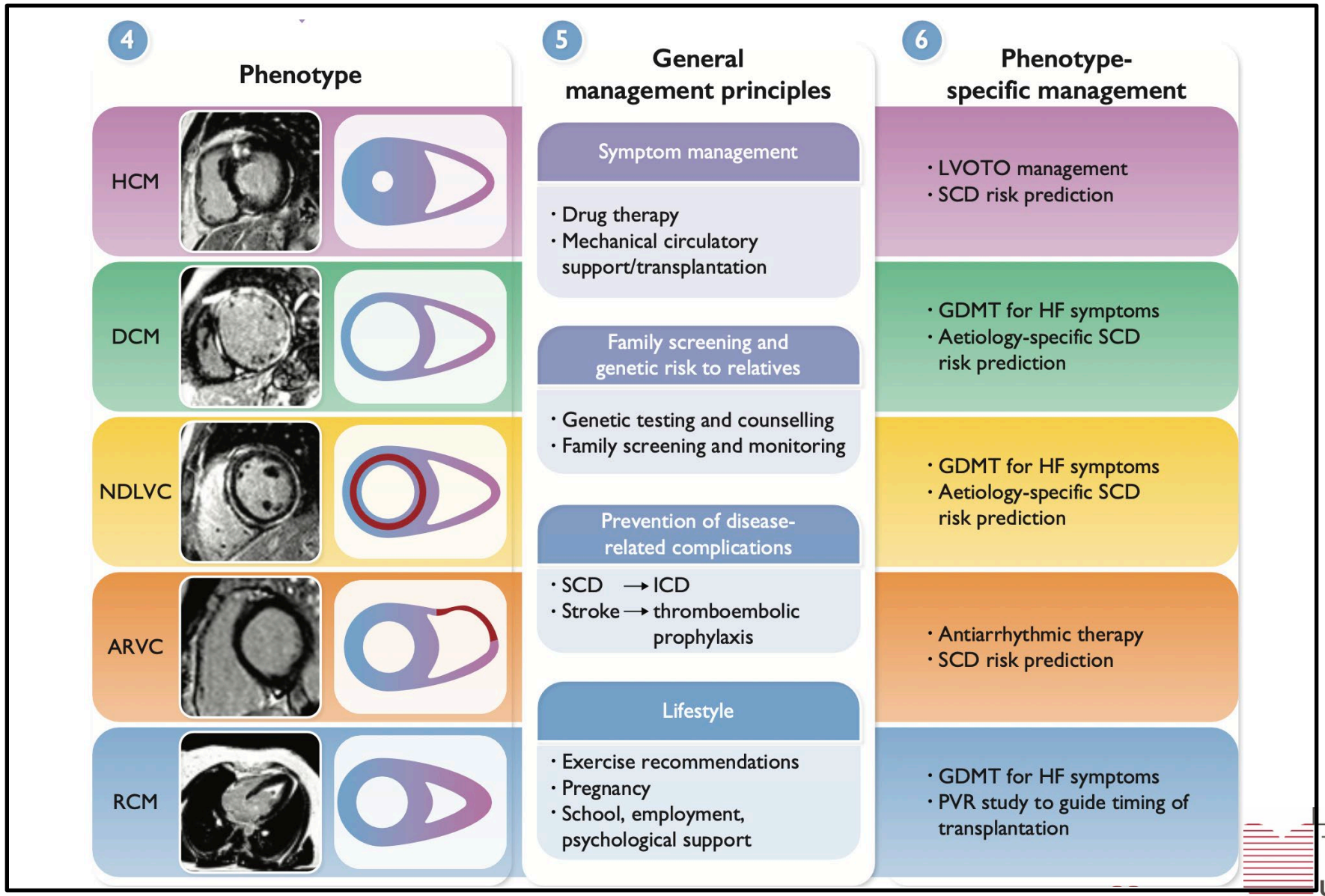
Therapeutisches Vorgehen



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Multidisziplinäre Therapie

Recommendations	Class[a]	Level[b]
It is recommended that all patients with cardiomyopathy and their relatives have access to multidisciplinary teams with expertise in the diagnosis and management of cardiomyopathies.	I	C

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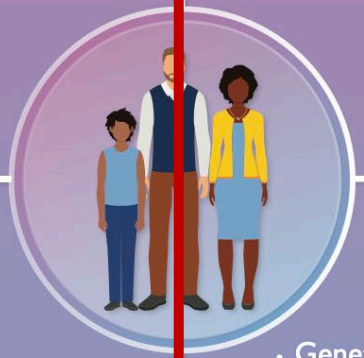
Cardiomyopathy specialists

- Cardiologist with cardiomyopathy expertise
- Paediatric cardiologist with cardiomyopathy expertise
- Specialist nurse
- Cardiac genetic counsellor

Patient support

- Family/carer(s)
- Psychologist
- Patient associations



Other related cardiology experts

- Heart failure team
- Arrhythmia team
- Cardiac imaging team
- Interventional cardiologist team
- Cardiologist with expertise in sports cardiology

Other related specialties[a]

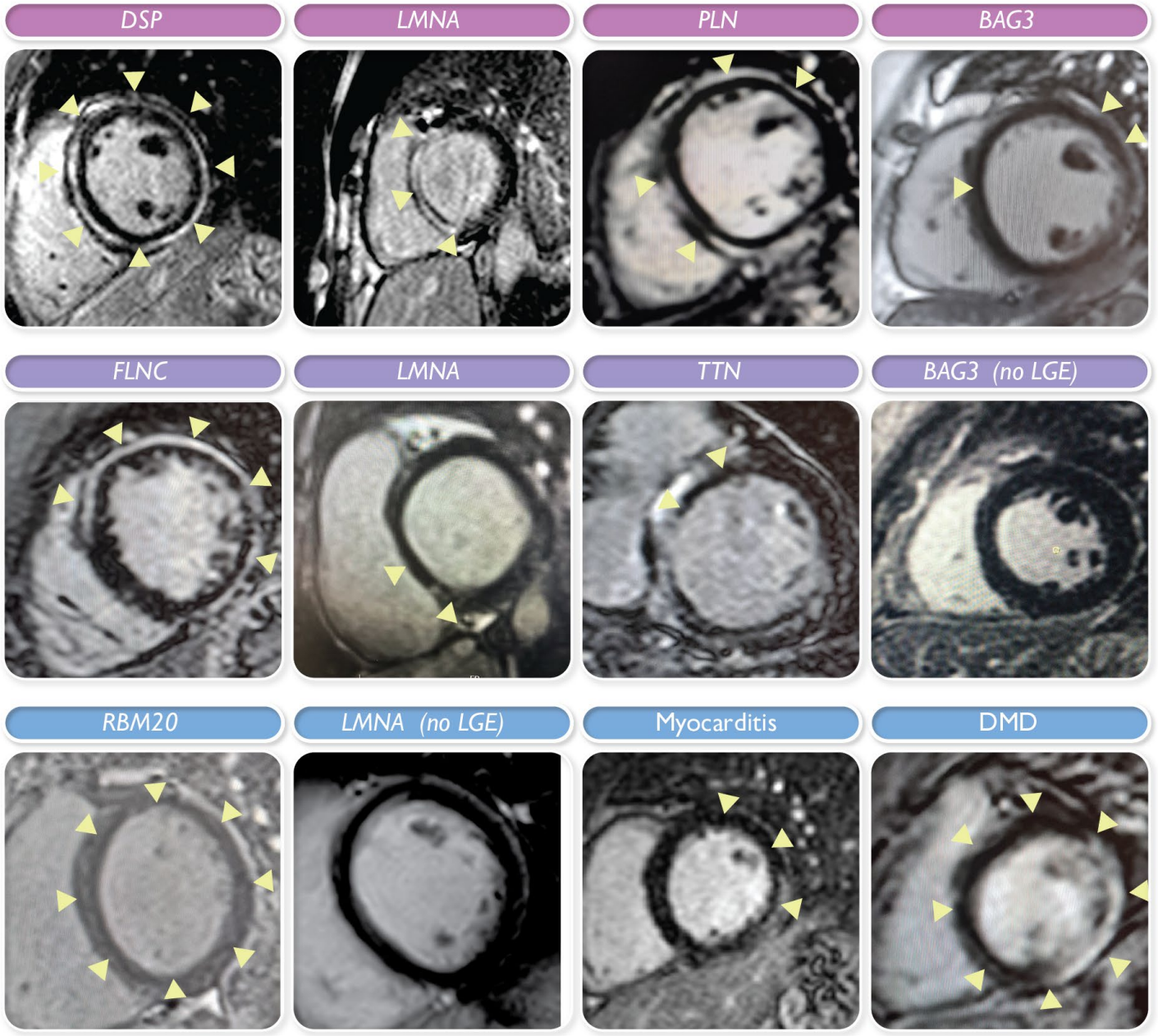
- Geneticist
- Pathologist
- Other: cardiac surgeon, primary care physician, paediatrician, internist, nephrologist, neurologist, dermatologist, endocrinologist, ophthalmologist, pharmacist, rheumatologist etc.

ESC

Neue Konzepte

- NDLVC Phänotyp
- Management der LVOT-Obstruktion in HCM
- SCD-Risikostratifizierung in DCM / NDLVC und ARVC

NDLVC Phänotyp und ätiologisches Korrelat



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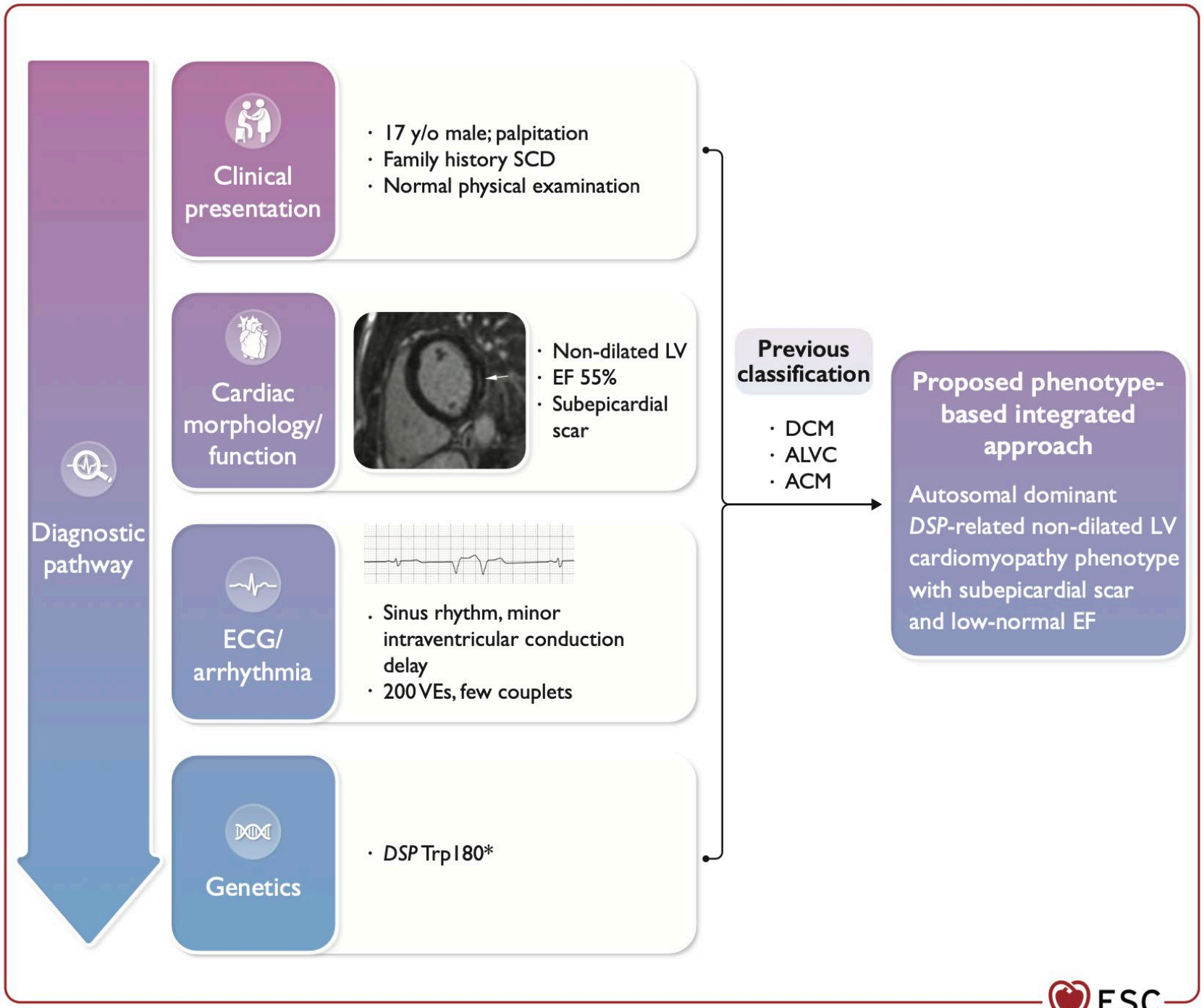
NDLVC Phänotyp – Beispiel



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Neue Konzepte

- NDLVC Phänotyp
- Management der LVOT-Obstruktion in HCM
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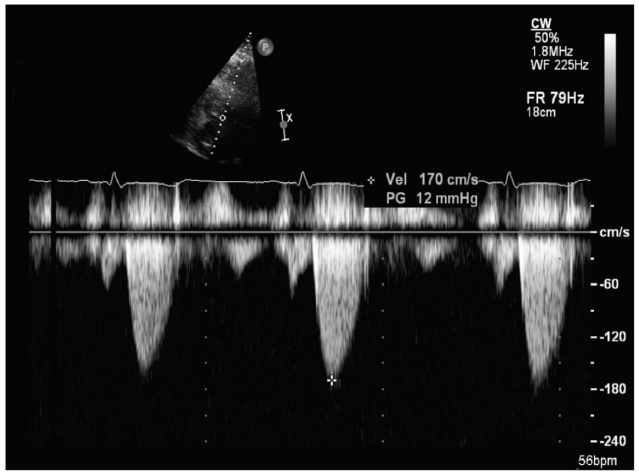
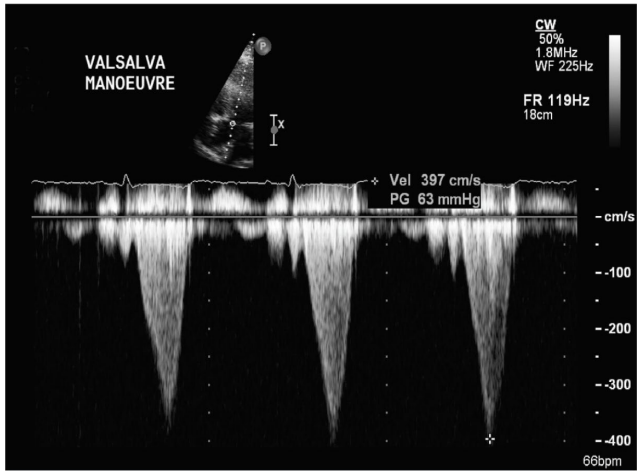
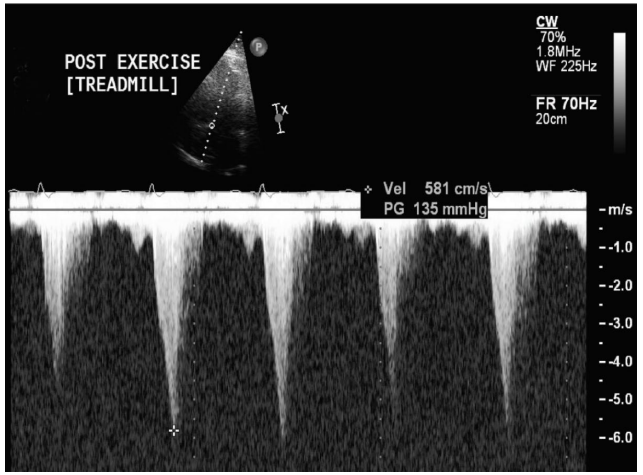
LVOT Obstruktion bei hypertropher Kardiomyopathie



RUHE: 12 mmHg



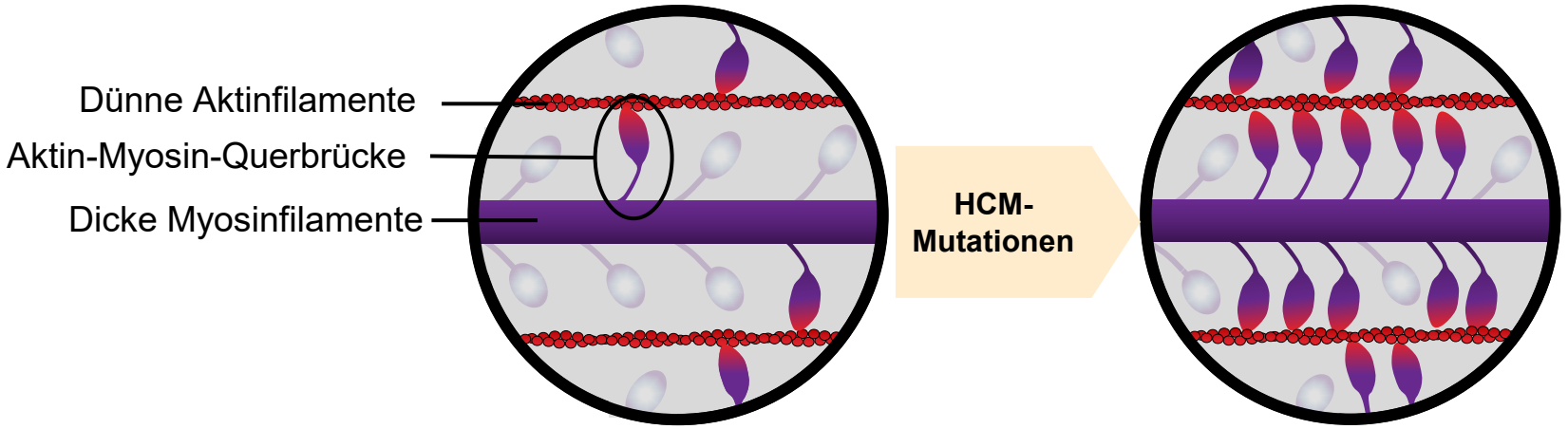
VALSALVA: 63 mmHg



STRESS: 135 mmHg

Maron et al. *Circulation* 2006

Pathophysiologie der HCM
Exzessive Bildung von Aktiv-Myosin Querbrücken



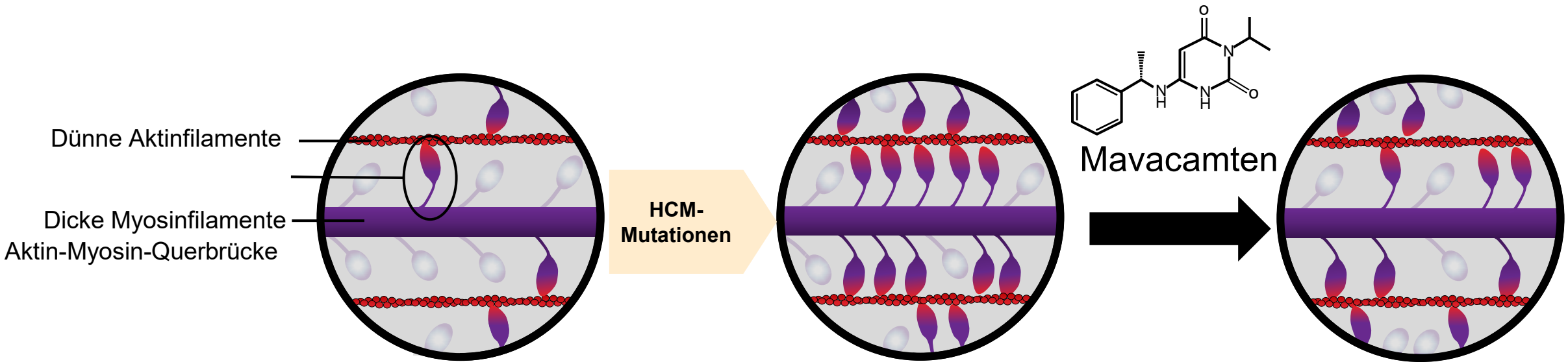
Normales Sarkomer

HCM-Sarkomer

- Hyperkontraktilität
- Erhöhter Energiebedarf
- Ungeordnete Sarkomere
- Versteifung des Myokards

Ho et al. *Circ Heart Fail* 2020, Kawas et al. *J Biol Chem* 2017, Nag et al. *Nat Struct Mol Biol* 2017

Präzisionstherapie: Myosin-Modulation



Normales Sarkomer

HCM-Sarkomer

- Hyperkontraktilität
- Erhöhter Energiebedarf
- Ungeordnete Sarkomere
- Versteifung des Myokards

HCM-Sarkomer + Mavacamten

- reduzierte Hyperkontraktilität

Ho et al. *Circ Heart Fail* 2020, Kawas et al. *J Biol Chem* 2017, Nag et al. *Nat Struct Mol Biol* 2017

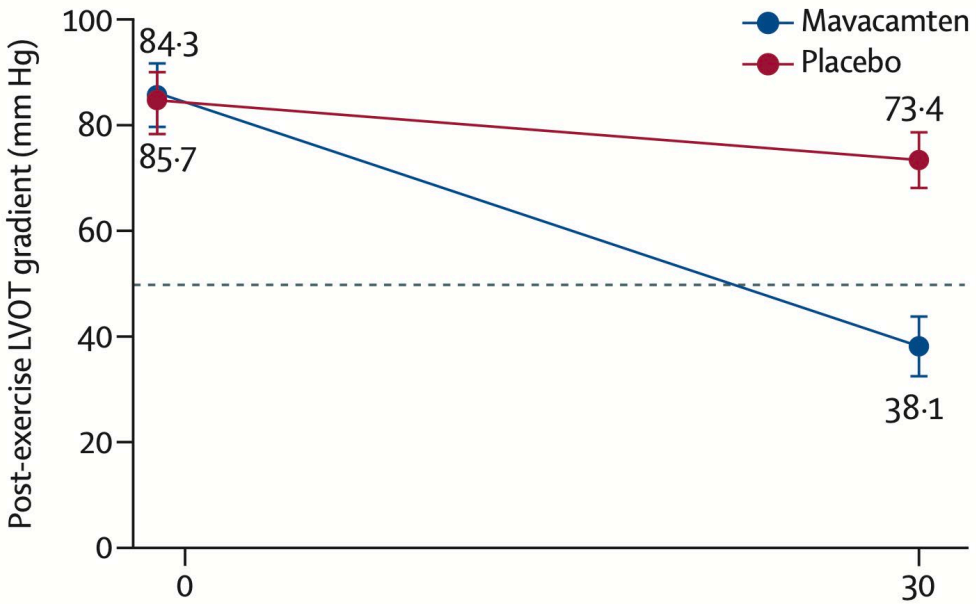
Mavacamten – “first in class” Myosin-Inhibitor

EXPLORER-HCM Studie

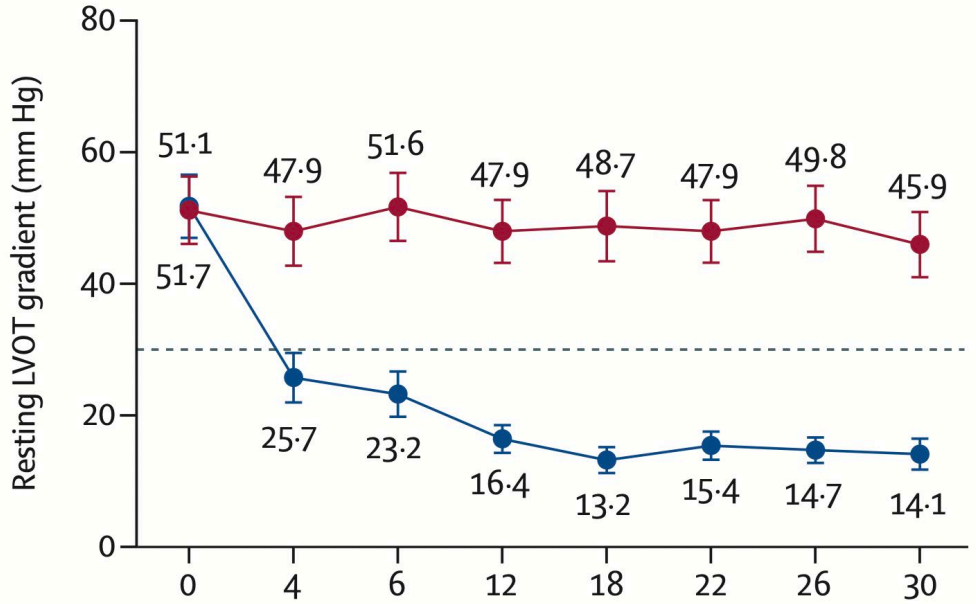
	Mavacamten group (n=123)	Placebo group (n=128)	Difference* (95% CI), p value
Primary endpoint†			
Either ≥1·5 mL/kg per min increase in pVO_2 with ≥1 NYHA class improvement or ≥3·0 mL/kg per min increase in pVO_2 with no worsening of NYHA class	45 (37%)	22 (17%)	19·4 (8·7 to 30·1; p=0·0005)
≥1·5 mL/kg per min increase in pVO_2 with ≥1 NYHA class improvement	41 (33%)	18 (14%)	19·3 (9·0 to 29·6)
≥3·0 mL/kg per min increase in pVO_2 with no worsening of NYHA class	29 (24%)	14 (11%)	12·6 (3·4 to 21·9)
Both ≥3·0 mL/kg per min increase in pVO_2 and ≥1 NYHA class improvement	25 (20%)	10 (8%)	12·5 (4·0 to 21·0)

Olivotto et al. *Lancet* 2020

Mavacamten – Reduktion des LVOT-Gradients



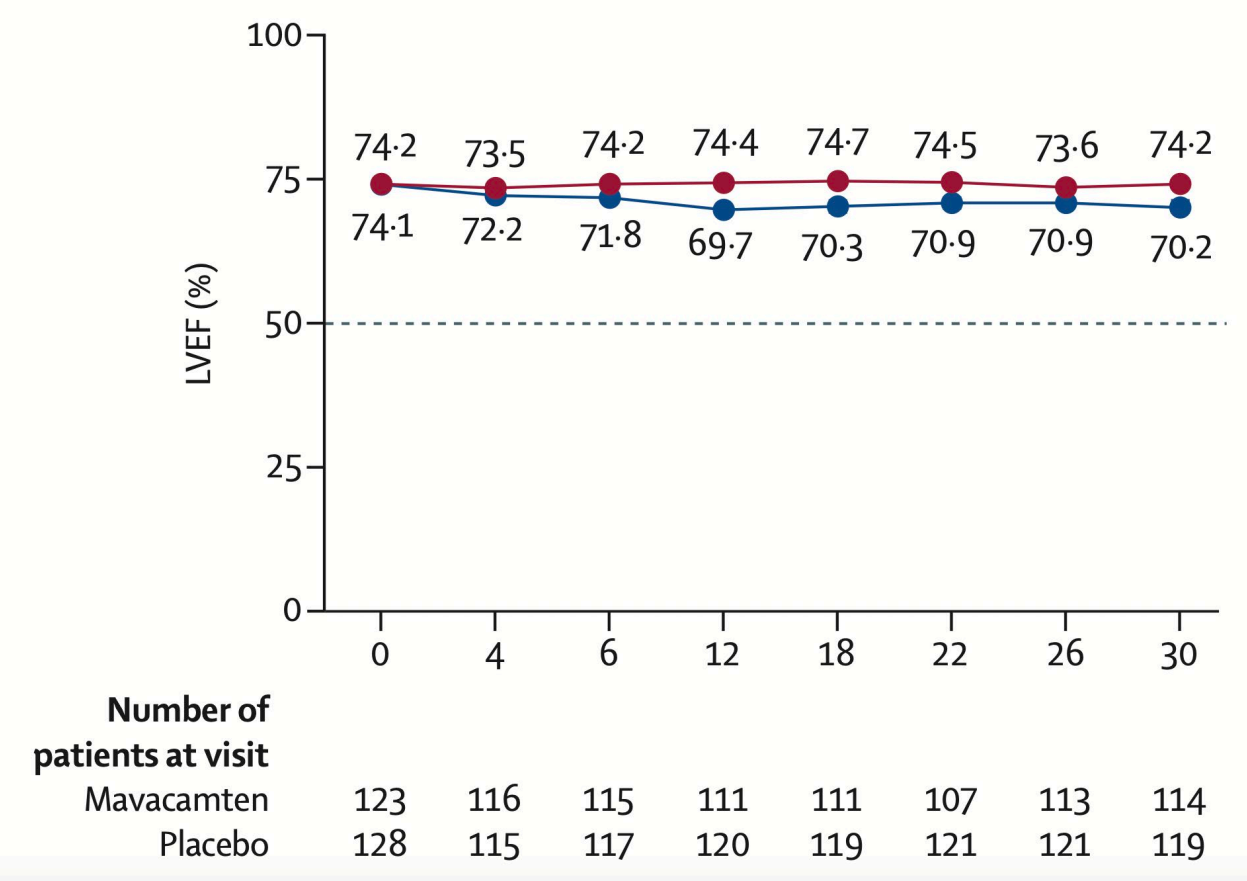
Number of patients at visit		
Mavacamten	122	118
Placebo	127	123



Number of patients at visit								
Mavacamten	123	119	119	118	116	118	120	117
Placebo	128	121	122	125	122	125	125	123

Olivotto et al. *Lancet* 2020

Mavacamten – Sicherheitsprofil



Number of patients at visit								
Mavacamten	123	116	115	111	111	107	113	114
Placebo	128	115	117	120	119	121	121	119

LVEF <50%:

* EXPLORER-HCM trial 5.7% (n=7)

** VALOR-HCM trial 12.5%

*** MAVA-LTE trial 8.7%

Olivotto et al. *Lancet* 2020

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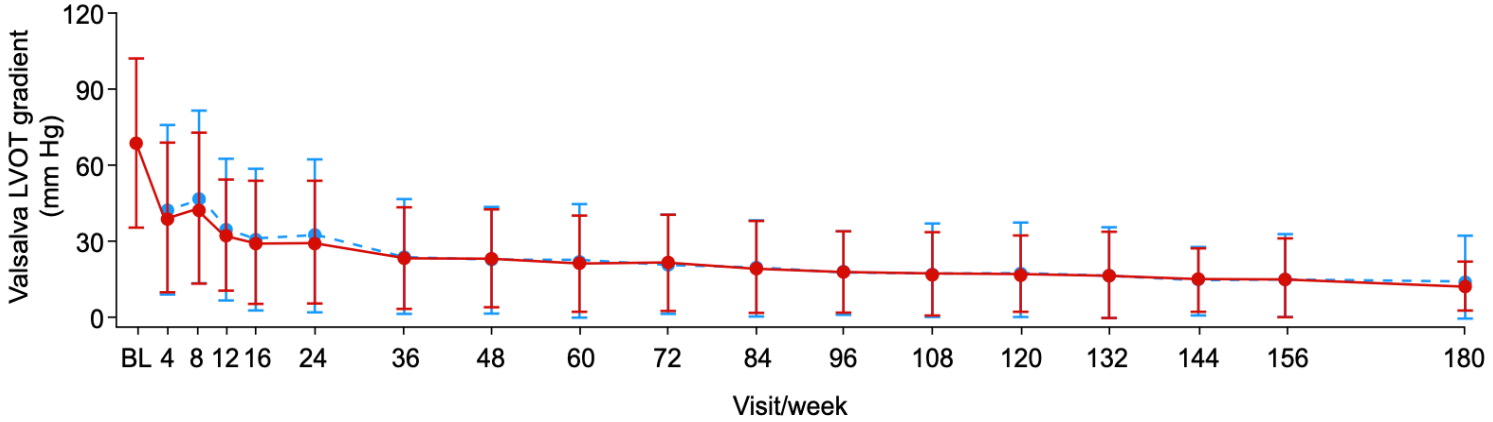
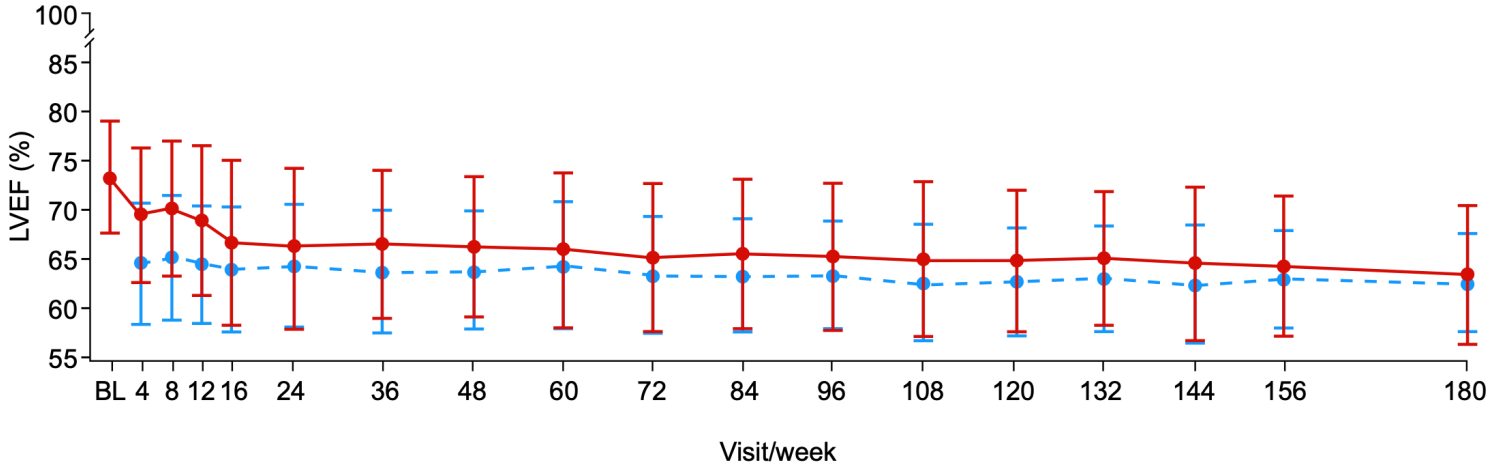
MAVA-LTE Studie (Woche 180)





Garcia Pavia et al, *EHJ* 2024

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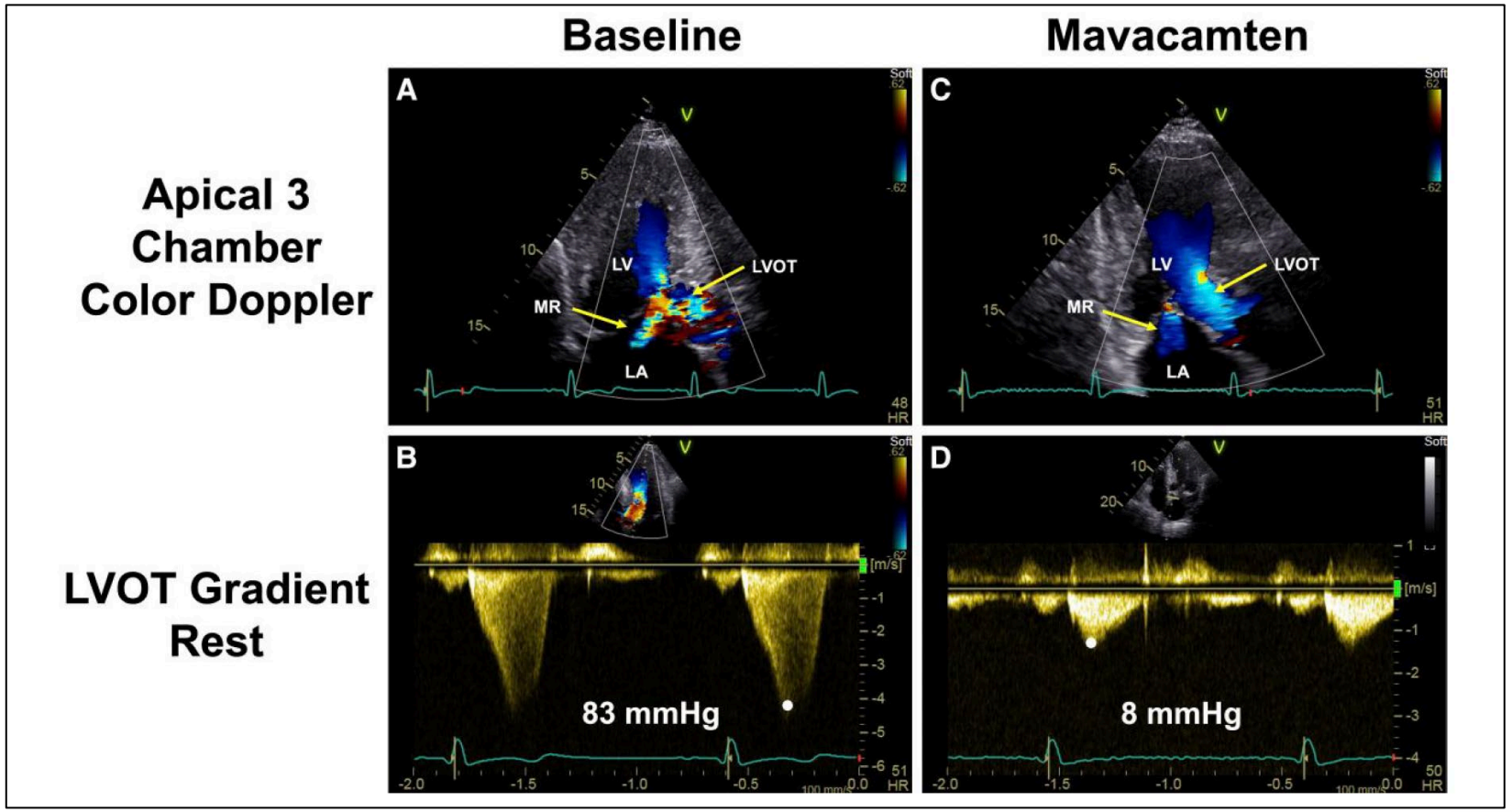
Reduktion des LVOT-Gradients



Braunwald et al. *EHJ* 2023

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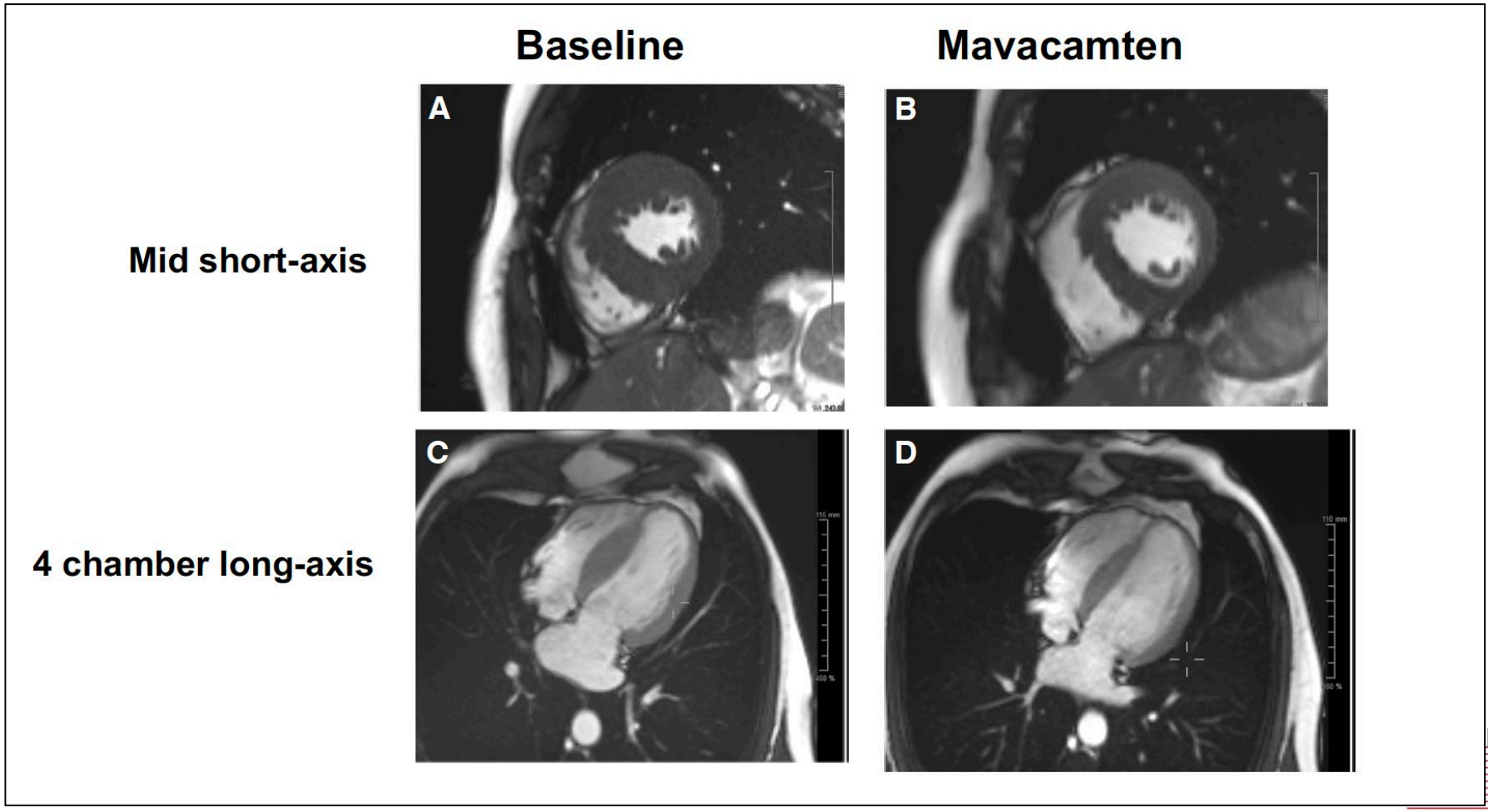
Reduktion der Hypertrophie



Braunwald et al. *EHJ* 2023

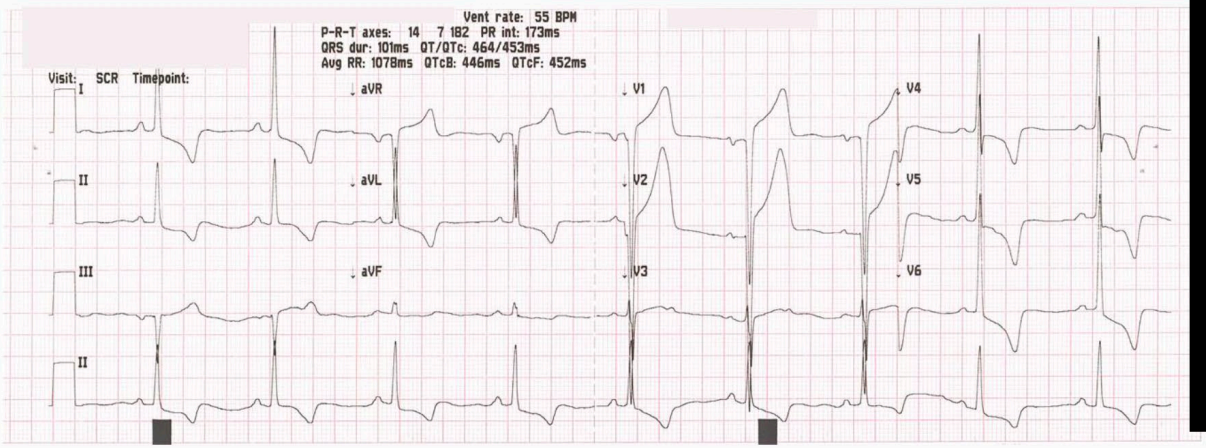
Full recovery

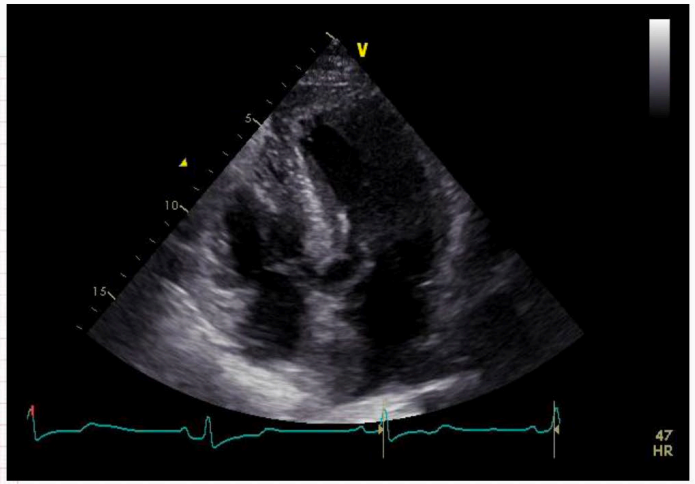
Baseline

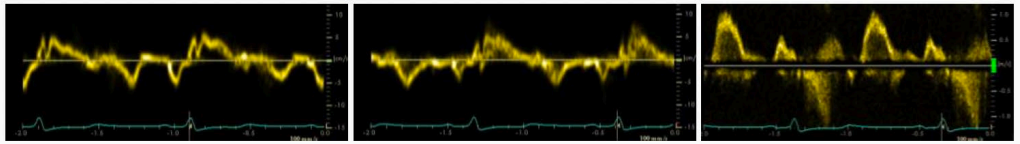
NT-proBNP = 1025 pg/ml

- **Mild dyspnea, tiredness, fatigue, palpitations and chest pain**

(HCM Symptom Questionnaire score: 4)



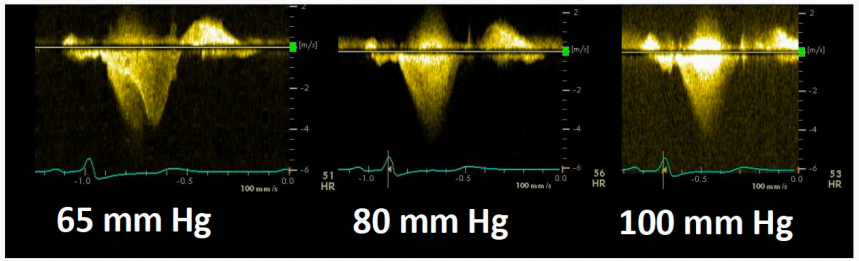




Septal e' = 6 cm/s

Lateral e' = 6 cm/s

E = 109 cm/s



65 mm Hg

80 mm Hg

100 mm Hg

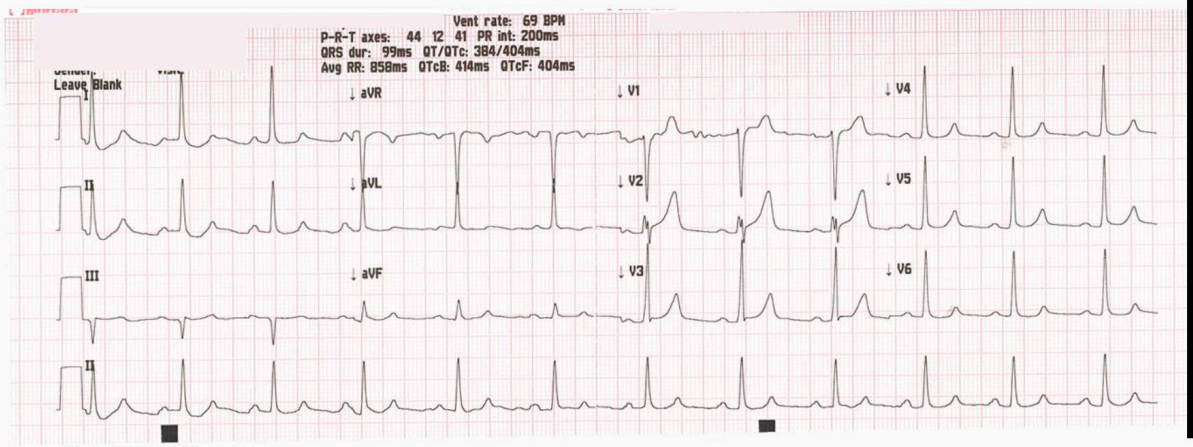
Full recovery

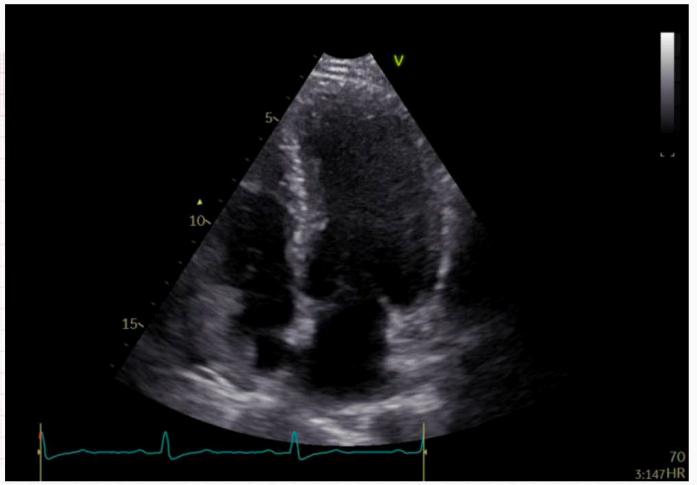
3 years post mavacamten treatment

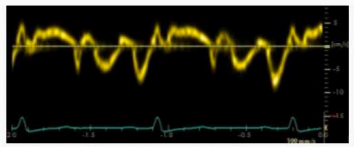
NT-proBNP = 17 pg/ml

- **Free of dyspnea, tiredness, fatigue, palpitations and chest pain**

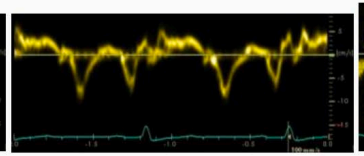
(HCM Symptom Questionnaire score: 1)



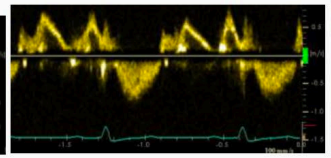




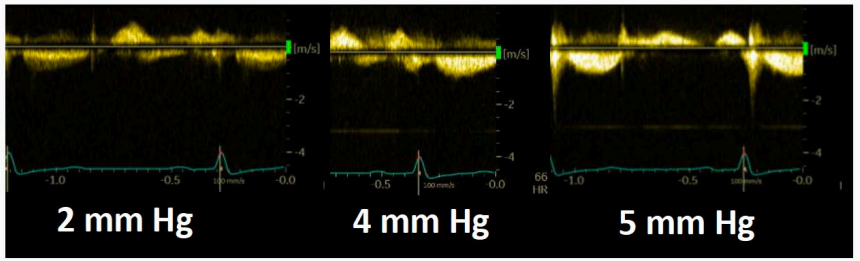
Septal e' = 6 cm/s



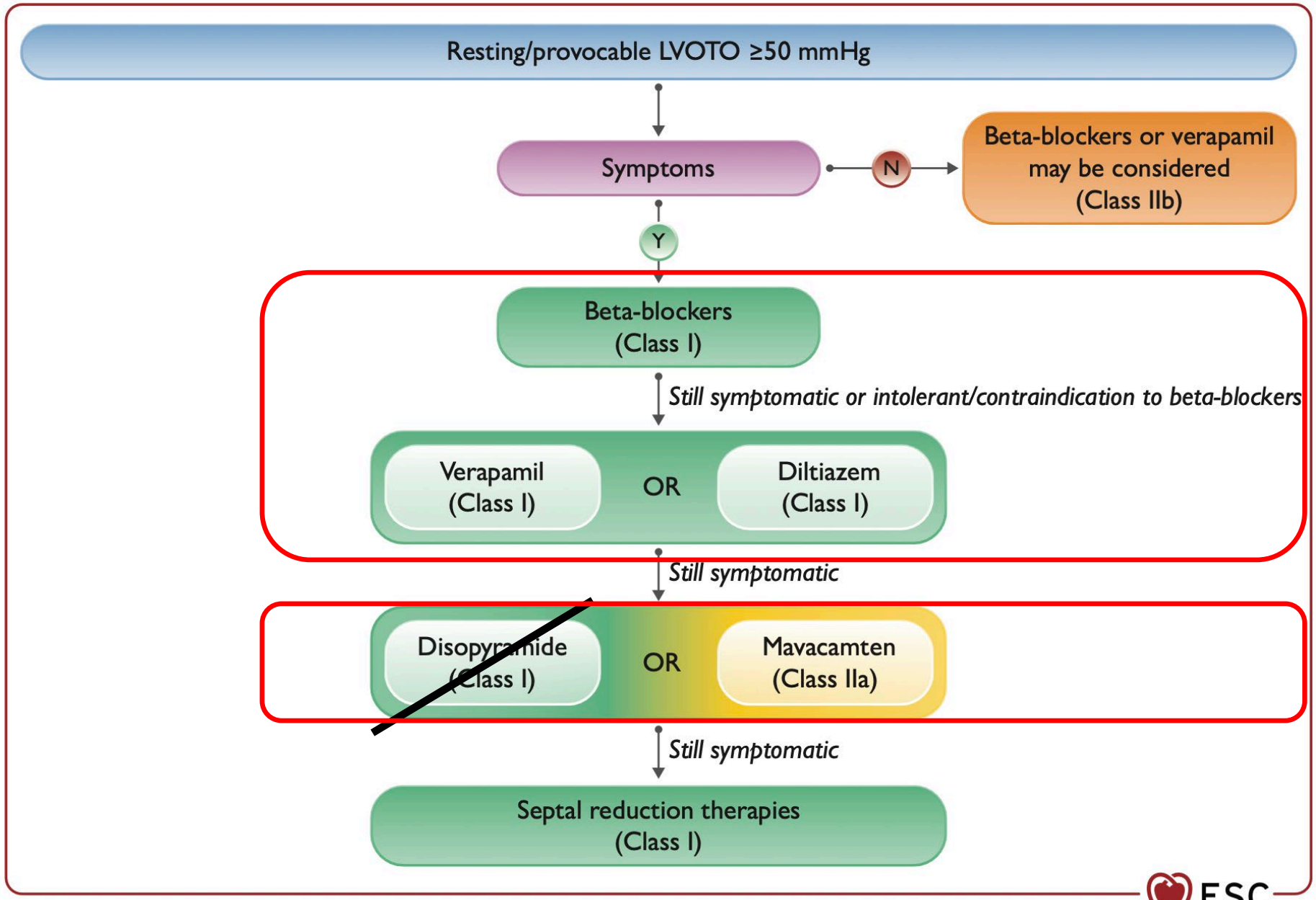
Lateral e' = 10 cm/s



E = 78 cm/s



Management der LVOT-Obstruktion



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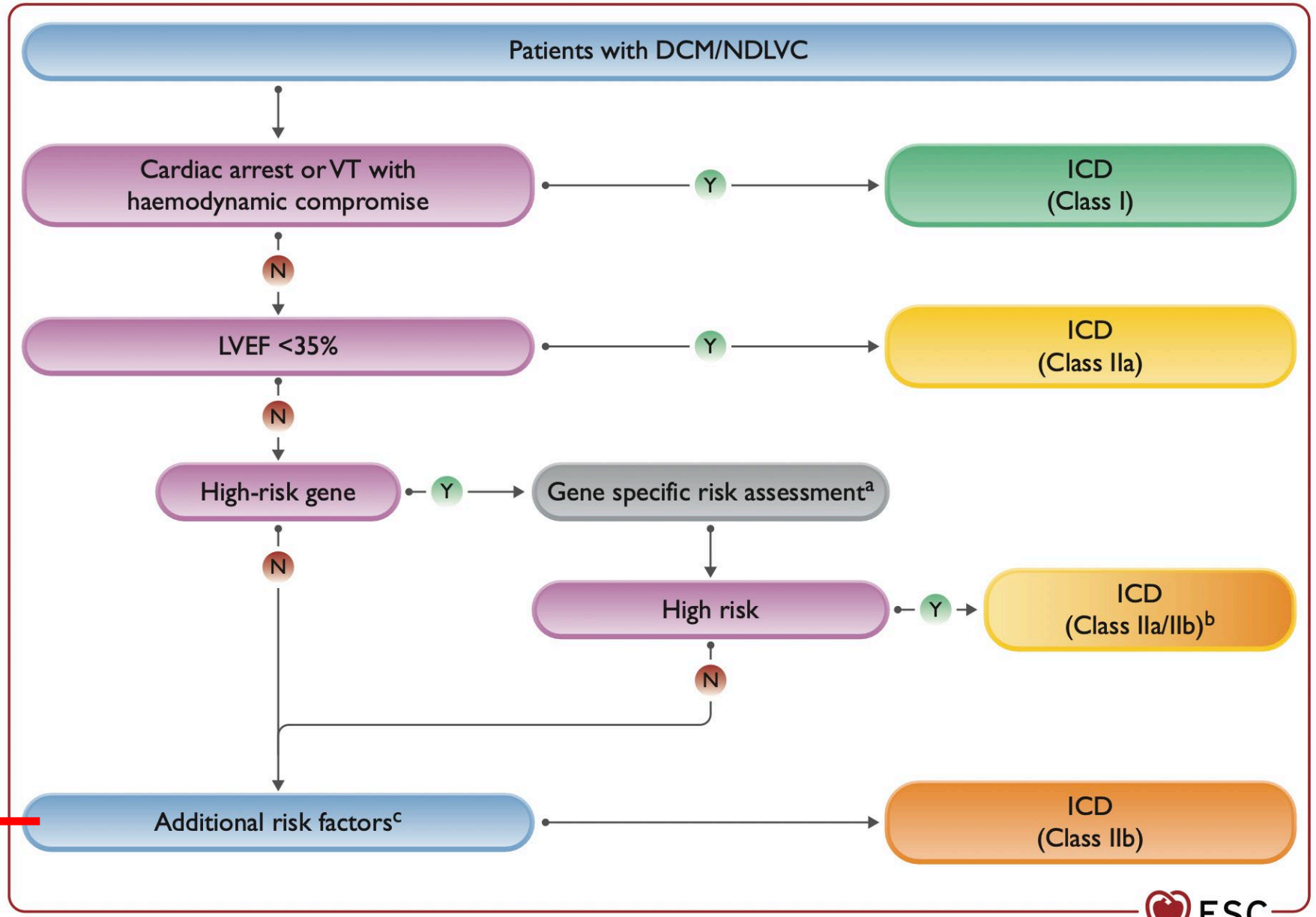
Neue Konzepte

- NDLVC Phänotyp
- Management der LVOT-Obstruktion in HCM
- SCD-Risikostratifizierung in DCM / NDLVC und ARVC

DCM - ICD Indikationen



- Synkope
- LGE

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Hochrisiko Genotyp und SCD-Prädiktoren (1)

Gene	Annual SCD rate	Predictors of SCD
LMNA	5–10%	Estimated 5-year risk of life-threatening arrhythmia using LMNA risk score https://lmna-risk-vta.fr
***FLNC*-truncating variants**	5–10%	LGE on CMR LVEF<45%
TMEM43	5–10%	Male Female and any of the following: LVEF <45%, NSVT, LGE on CMR, >200 VE on 24h Holter ECG

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Hochrisiko Genotyp und SCD-Prädiktoren (2)

Gene	Annual SCD rate	Predictors of SCD
PLN	3–5%	Estimated 5-year risk of life-threatening arrhythmia using *PLN* risk score https://plnriskcalculator.shinyapps.io/final_shiny LVEF<45% LGE on CMR NSVT
DSP	3–5%	LGE on CMR LVEF<45%
RBM20	3–5%	LGE on CMR LVEF<45%

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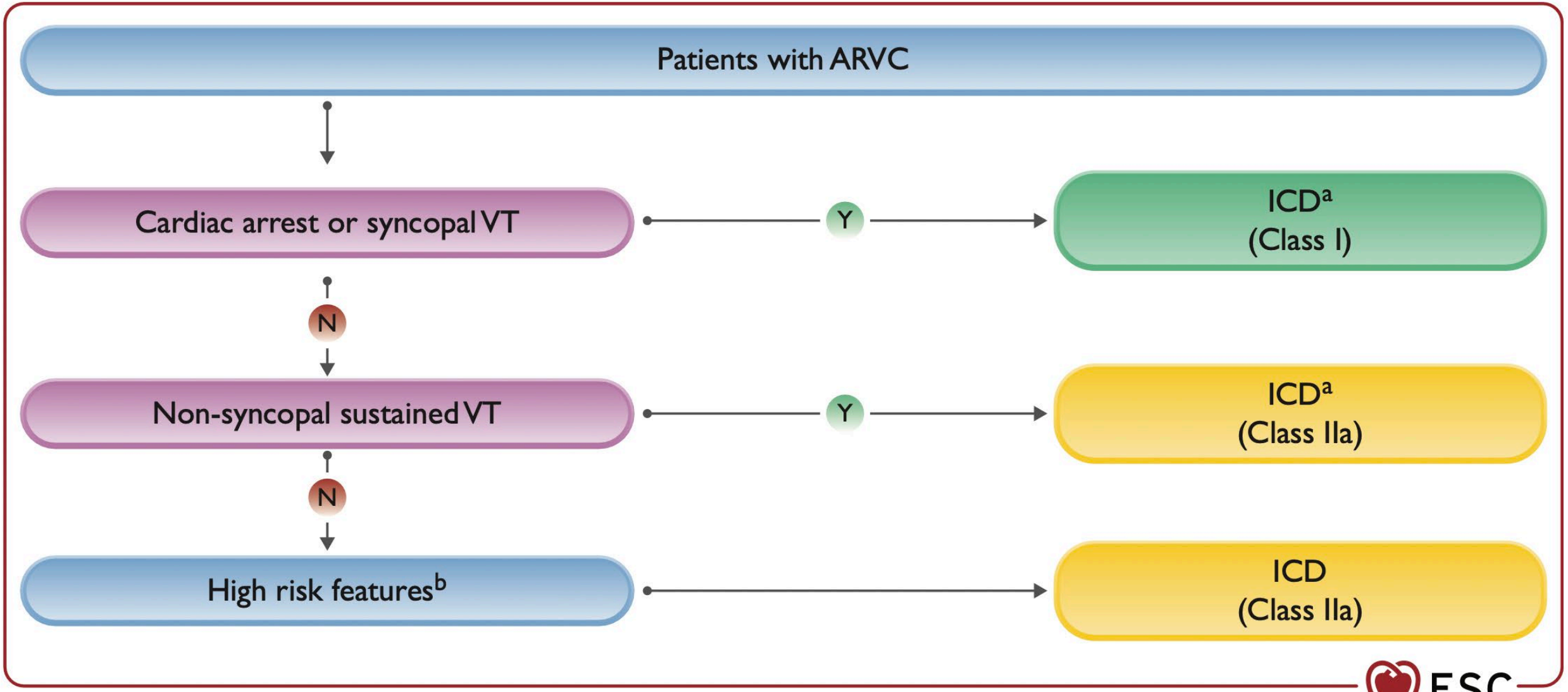
DCM - ICD Indikationen

Primary prevention		
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with DCM, symptomatic heart failure, and LVEF ≤35% despite >3 months of OMT.[861,885]	IIa	A
The patient's genotype should be considered in the estimation of SCD risk in DCM.[185,186,869,886]	IIa	B
An ICD should be considered in patients with DCM with a genotype associated with high SCD risk and LVEF >35% in the presence of additional risk factors (see *Table 21*).[541,542,867,869,873,878,881,886]	IIa	C
An ICD may be considered in selected patients with DCM with a genotype associated with high SCD risk and LVEF >35% without additional risk factors (see *Table 21*).[869,873,881,886]	IIb	C

ARVC - ICD Indikationen



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ARVC - ICD Indikationen

Primary prevention		
High-risk features[c] should be considered to aid individualized decision-making for ICD implantation in patients with ARVC.[538,939]	IIa	B
The updated 2019 ARVC risk calculator should be considered to aid individualized decision-making for ICD implantation in patients with ARVC.[d,524,526,536–539]	IIa	B

- **Synkope**
- **NSVT**
- **RVEF < 40%**
- **SMVT in PES**

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Vielen Dank für Ihre Aufmerksamkeit !

„Denn es muss von Herzen kommen, **was auf das Herz wirken soll.“**

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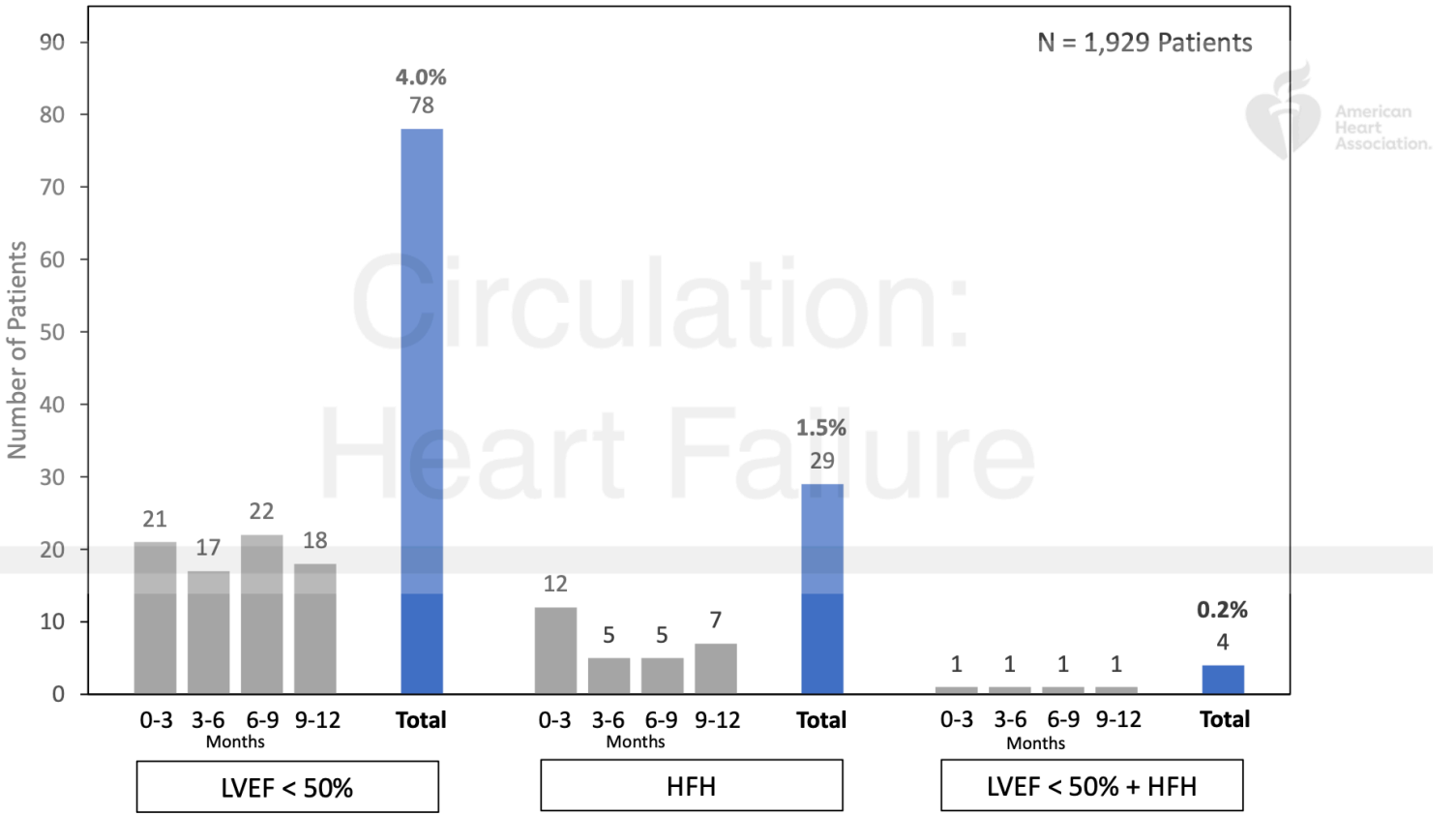
Mavacamten – Sicherheitsprofil

Risk Evaluation & Mitigation Strategy (REMS) Programm



Desai et al. *AHA2024 & Circ Heart Fail* 2024