

Therapie der chronischen Herzinsuffizienz – konservative vs. operative Möglichkeiten

“Drugs, Devices and Interventions”



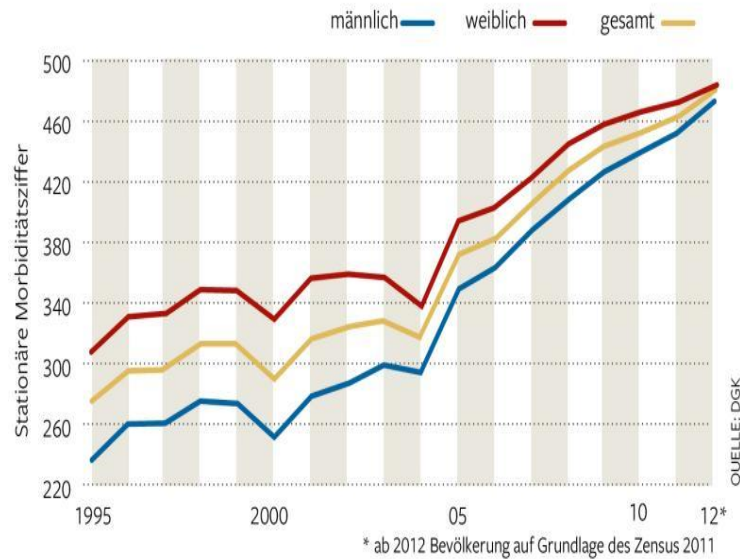
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Herzinsuffizienz

die häufigste, tödlichste und teuerste aller Herzerkrankungen

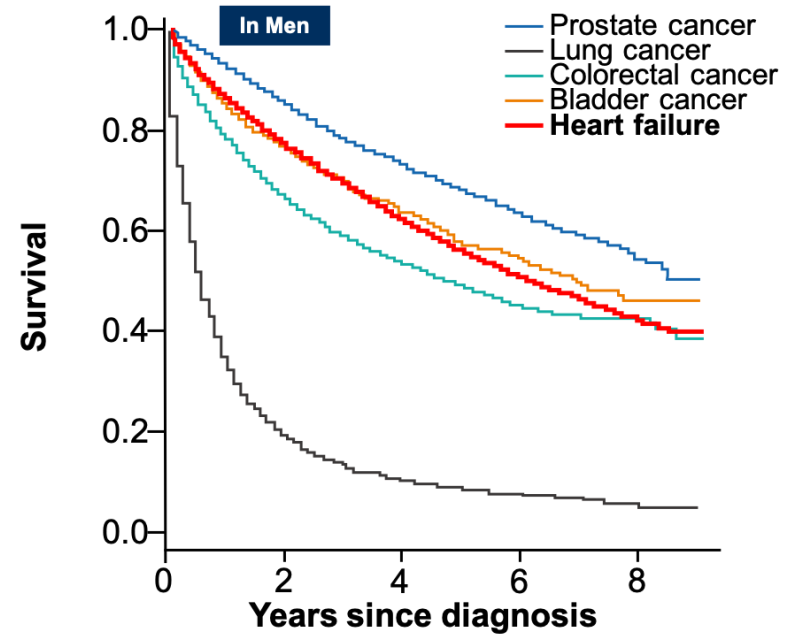
Prävalenz Herzinsuffizienz nimmt zu.
3-4% in der CH, ca. 300'000 Patienten

ZUNAHME DER HERZINSUFFIZIENZ in Deutschland

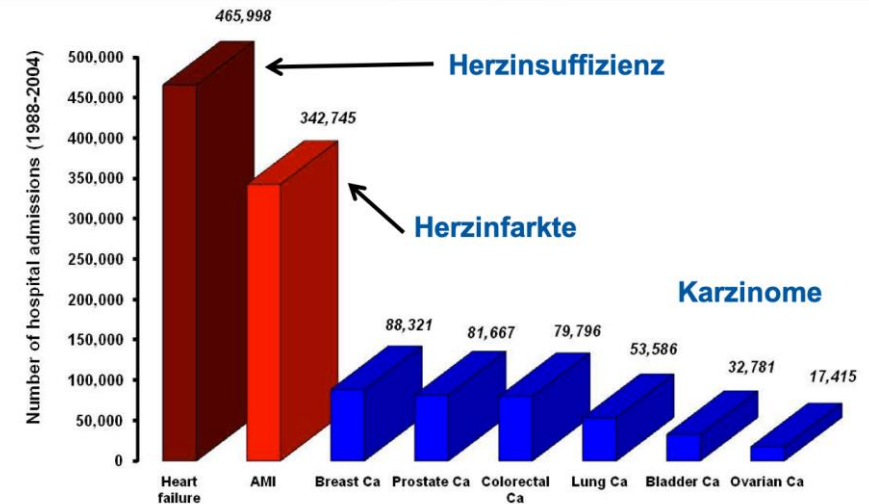


Statistisches Bundesamt

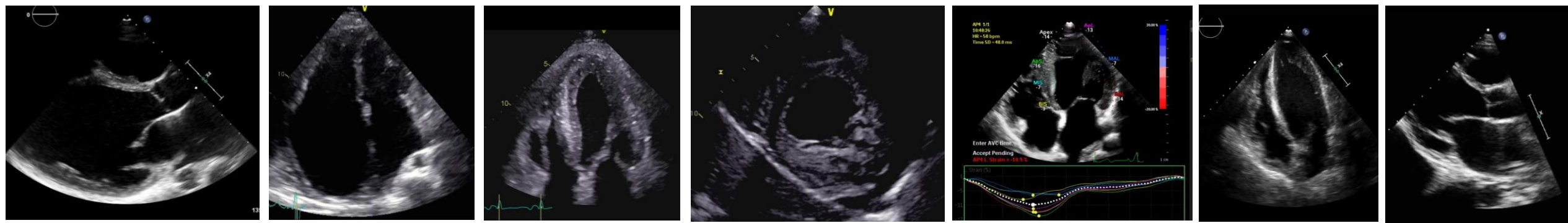
Prognose ist ähnlich wie bei häufigen
Karzinomen



Führt zu mehr Hospitalisationen als
Infarkte oder Tumore



Herzinsuffizienz ist ein klinisches Syndrom



Behandlung basiert auf dem LVEF-Phänotyp – nicht so sehr auf der Ätiologie

	HFrEF	HFmrEF	HFpEF	
	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a	
	LVEF ≤40%	LVEF 41–49% ^b	LVEF ≥50%	
	—	—	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c	

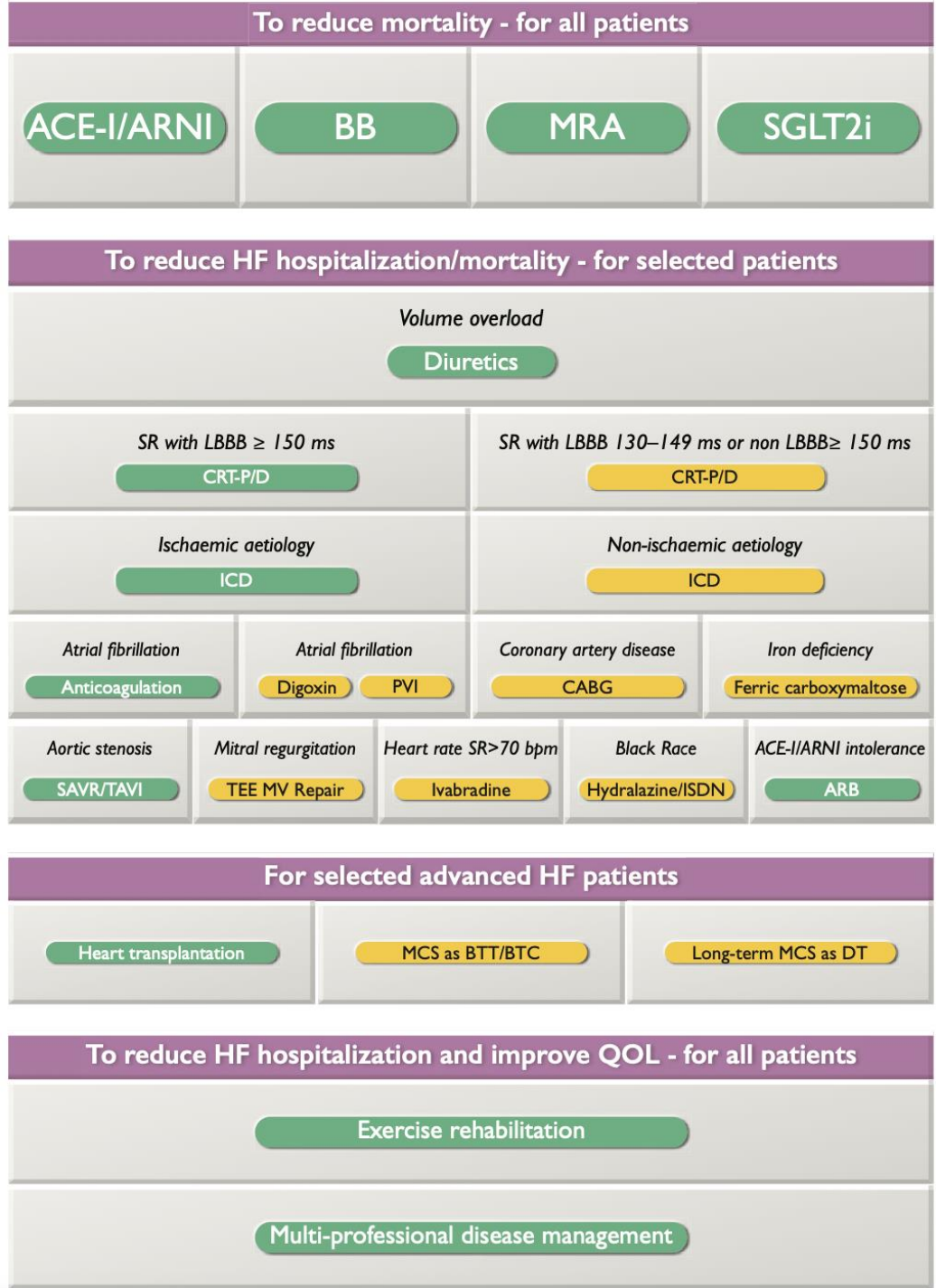
ALGORITHMUS ZUR BEHANDLUNG DER CHRONISCHEN HFrEF

Hochkomplexe Patienten –

Die grösste Herausforderung: welche Untersuchungen und Therapien braucht es wann?

Hierfür: **Herzinsuffizienz-Spezialist**

ESC GUIDELINES 2021

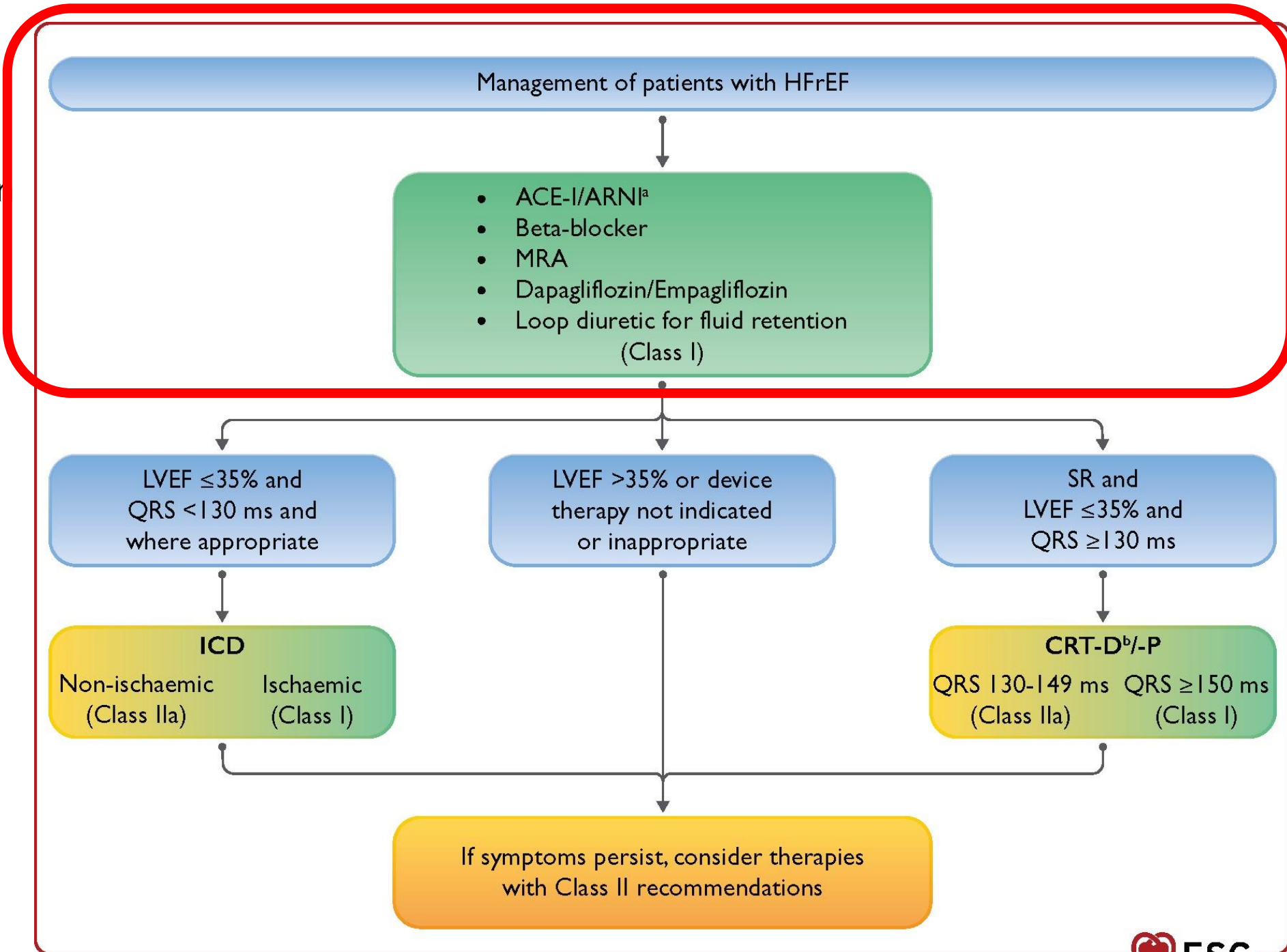


Patient mit einer
symptomatischen
Herzinsuffizienz und
reduzierter Auswurfraction
HFrEF

«konservative» Therapieprinzipien:

1. Hypervolämie behandeln
2. Neurohumorale Aktivierung durchbrechen
3. SGLT-2 hemmen

Alle gleichzeitig



Aktuell: 4 Pfeiler um die Mortalität bei Patienten mit einer HFrEF zu verbessern (Class I A or B)



**ACE-Inhibitor
Sacubitril/Valsartan
(ARB)**

Beta-Blocker

**Mineralocorticoid
Receptor Antagonist**

SGLT-2 Inhibitor

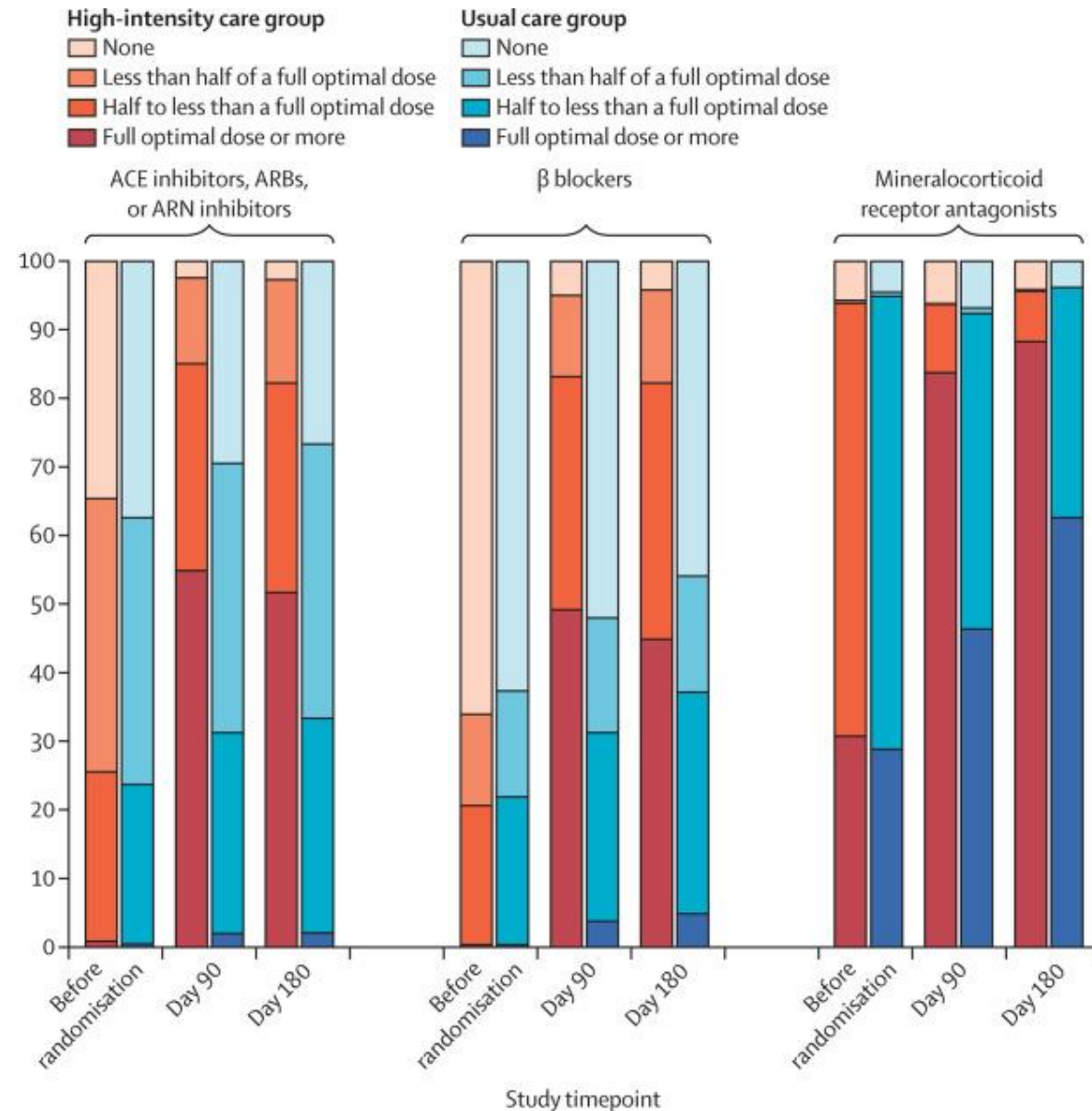
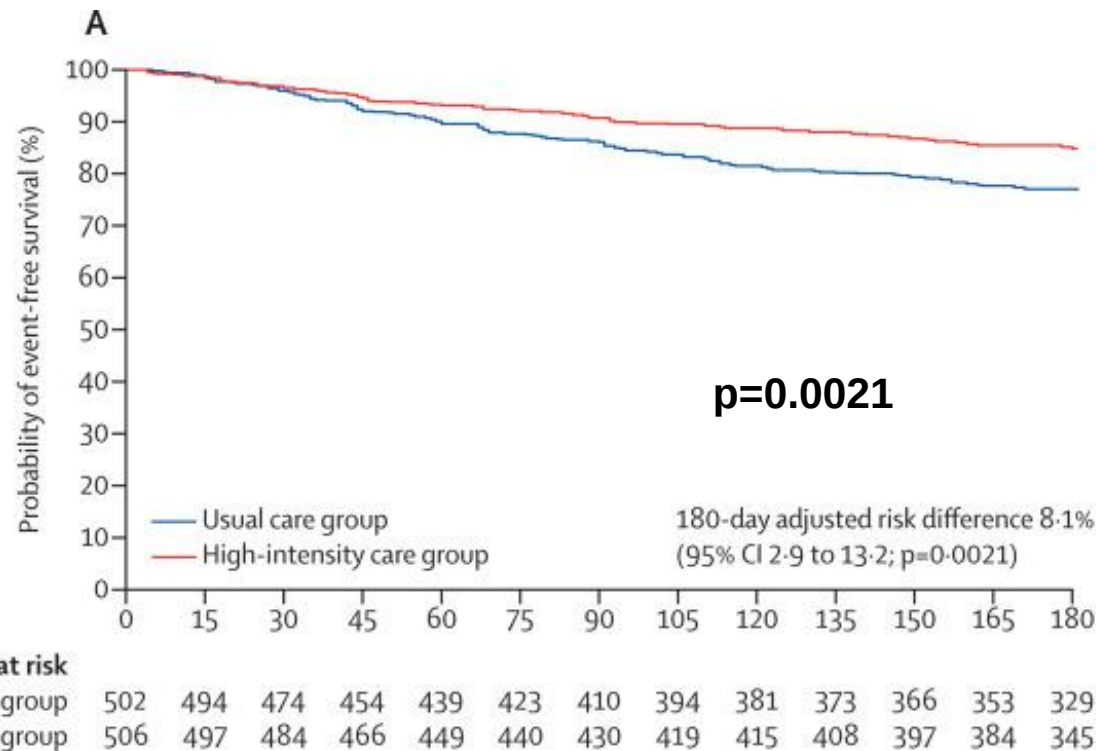
ACE-Hemmer mit Sacubitril/Valsartan ersetzen, um die Prognose weiter zu verbessern (Class 1B!)

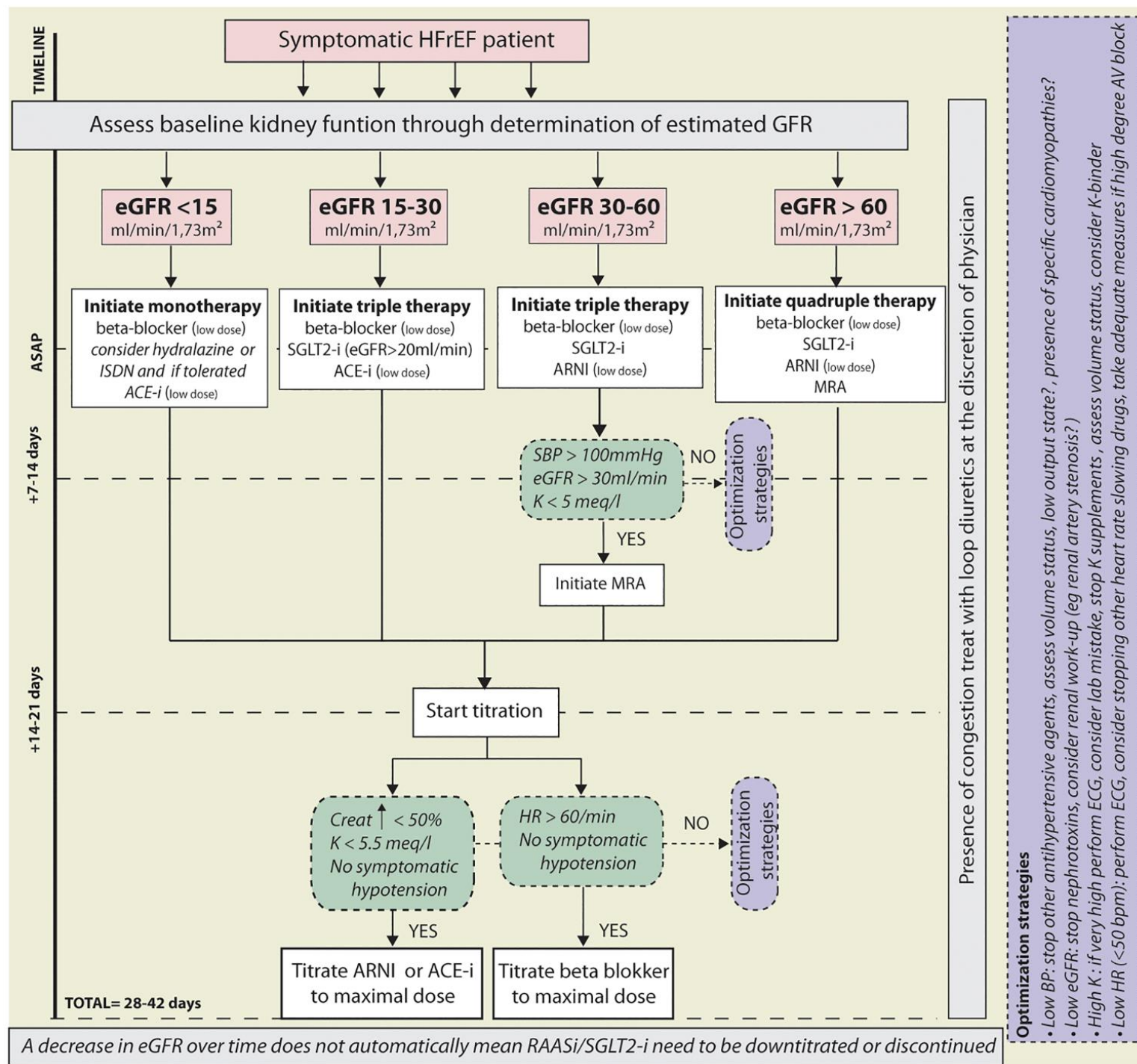
Standard Therapie bei allen Patienten

STRONG-HF – Herzinsuffizienz Medikamente gleichzeitig und zügig auftitrieren

- Multinationale, open-label, randomisierte, parallel-group Studie
- **Patienten mit akuter HI** und noch nicht auf optimaler empfohlener medikamentöser Behandlung
- 2 Gruppen: «**usual care**» oder «**high-intensity care**» mit Auftitrierung der Behandlung auf 100% der empfohlenen Dosen innert 2 Wochen nach Austritt. 4 ambulante Visiten innert 2 Monaten.

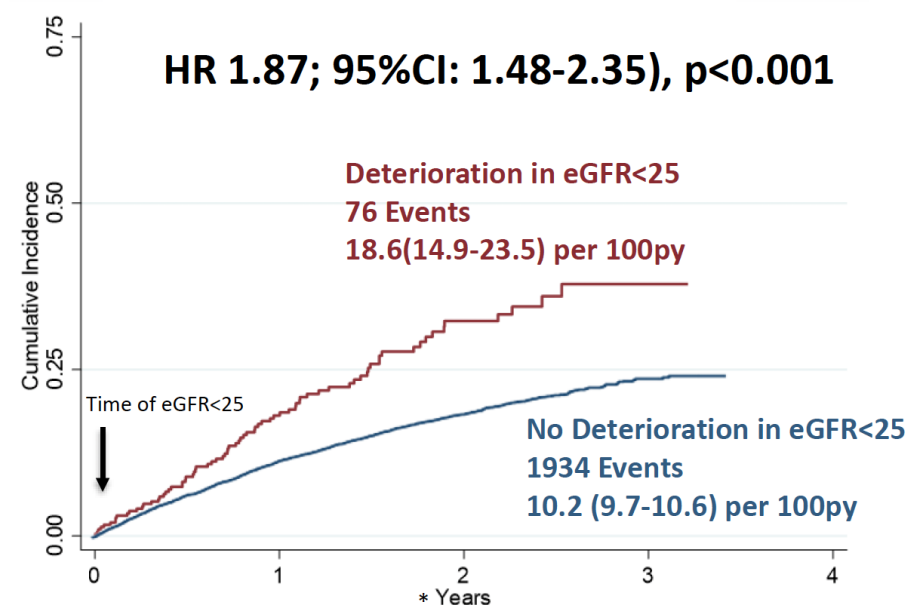
Primärer Outcome: 180 Tage «Readmission» für HI oder Tod.





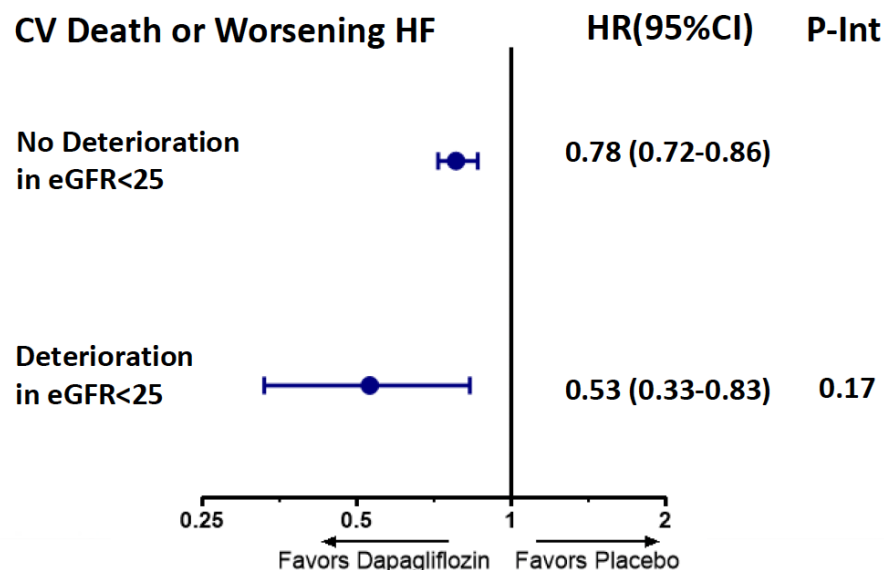
SGLT-2i bei Patienten mit einem GFR Abfall auf unter 25ml/min – Eine gepoolte Analyse der DAPA-HF and DELIVER Studien

- Patients with HF deterioration below 25ml/min have higher risk for subsequent CV outcomes
- Dapagliflozin: lower rates of CV death or worsening HF regardless of deterioration of GFR
- safety consistent

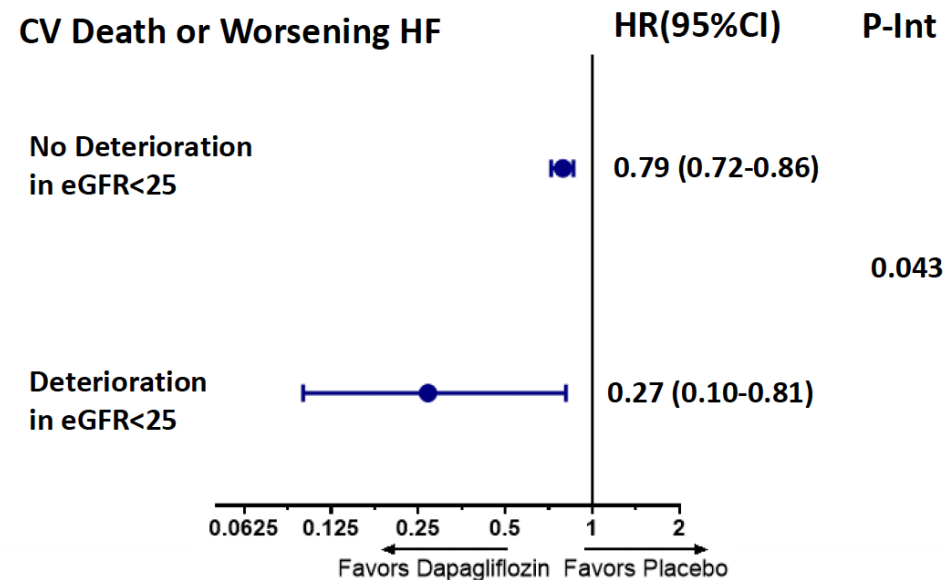


*Analysis time for patients not experiencing deterioration in eGFR<25 was time of randomization and time of eGFR<25 for those experiencing deterioration

Deterioration in eGFR<25 At Least Once



Persistent Deterioration in eGFR<25



Chatur S et al. JACC 23

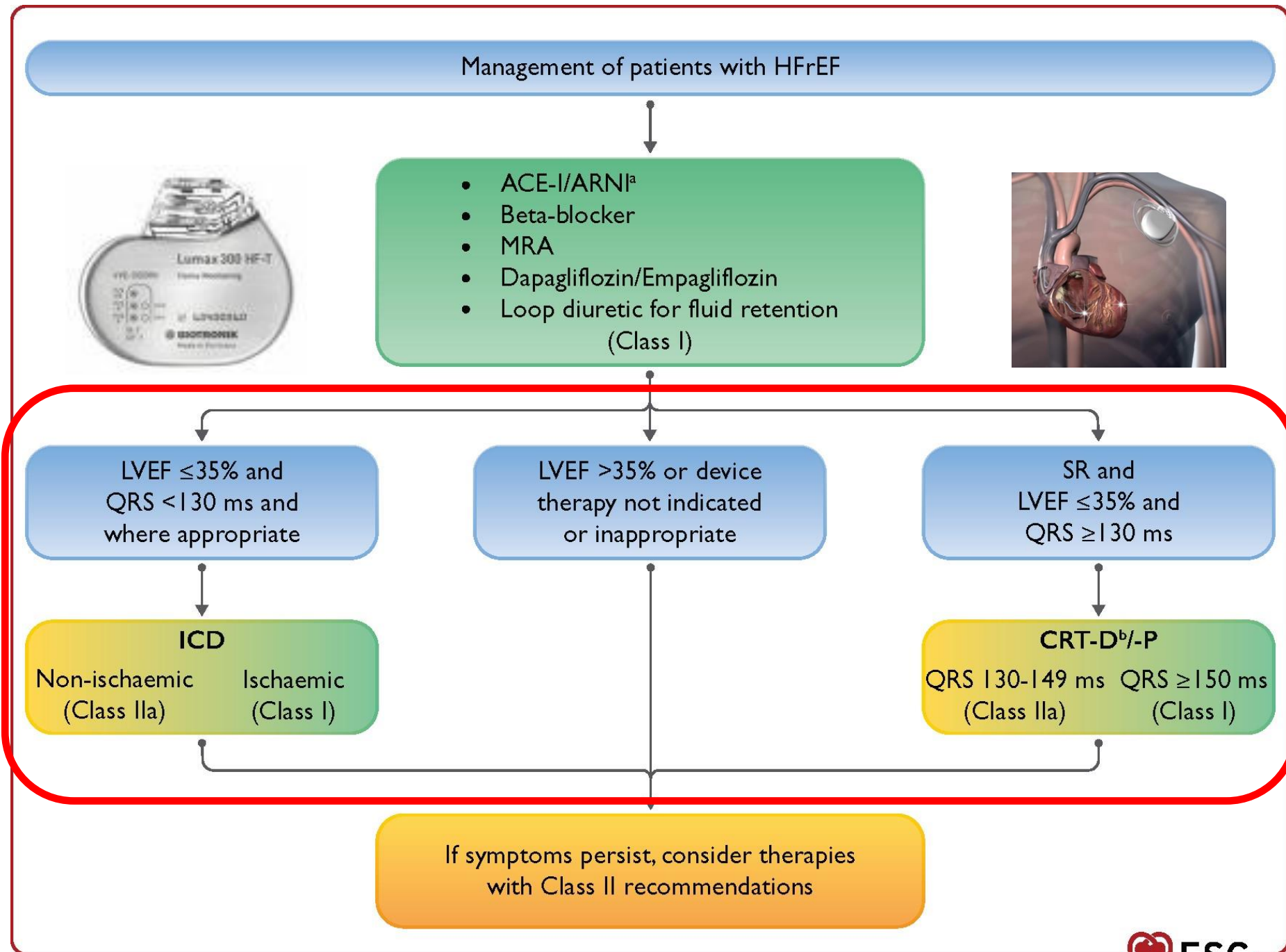
HFrEF

«operativ» - ICD und CRT

HFrEF Patienten mit EF < 35% trotz optimaler medikamentöser Therapie (die 4 Säulen ± Diuretika):

- **ICD** (vor allem bei ischämischer HK)
- **CRT** falls QRS > 130ms (insbesondere wenn > 150ms)

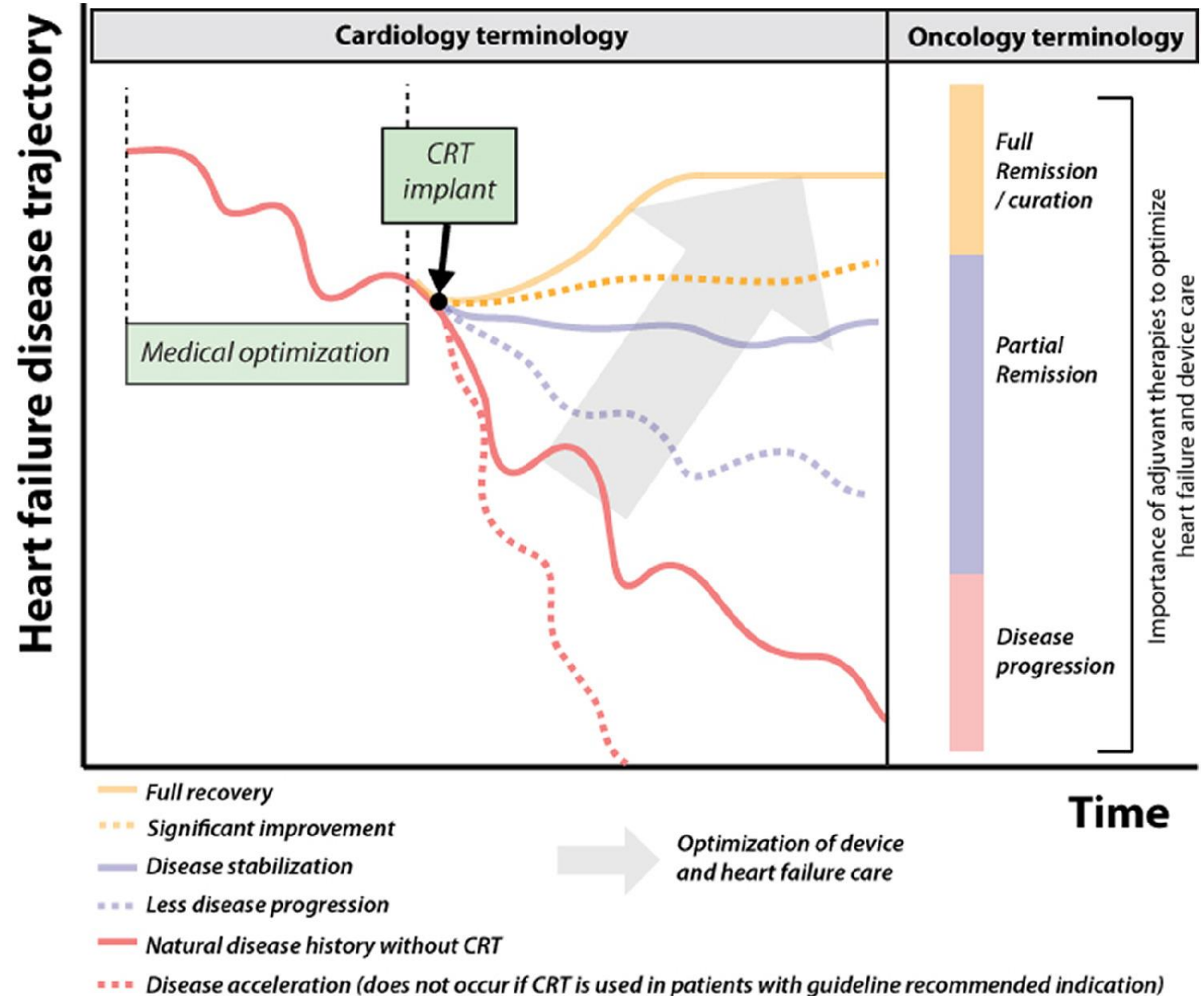
Tragbarer ICD bei Patienten mit hohem Risiko für einen plötzlichen Herztod als „Bridge to“ einem implantierbaren Device - IIb, B



Verlauf der Herzinsuffizienz unter Therapie

Der Erfolg der CRT darf nicht durch das Ausmaß des «reverse Remodellings» definiert werden, sondern durch das Ausmaß der Krankheitsmodifikation

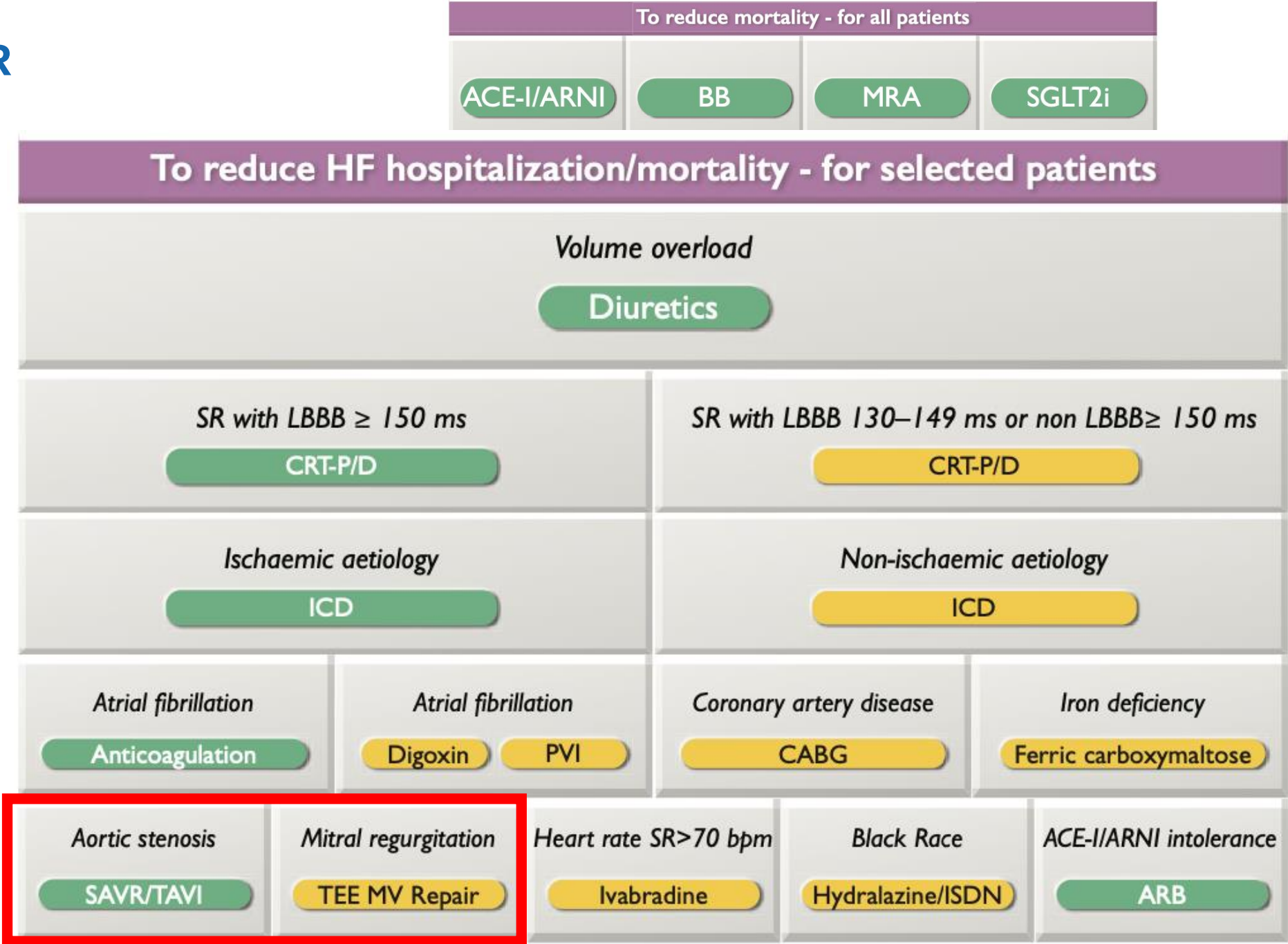
Mullens W et al, EJHF 2020



ALGORITHMUS ZUR BEHANDLUNG DER CHRONISCHEN HFrEF

„selected patients“

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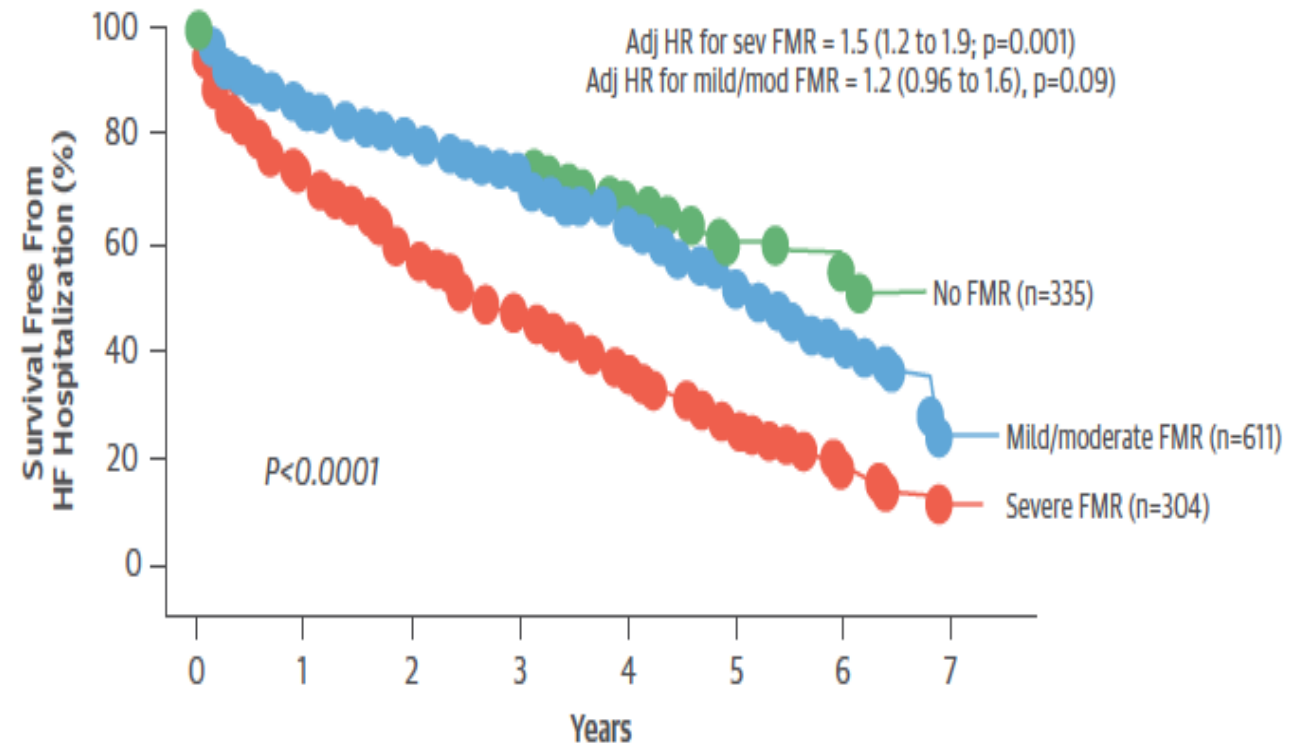
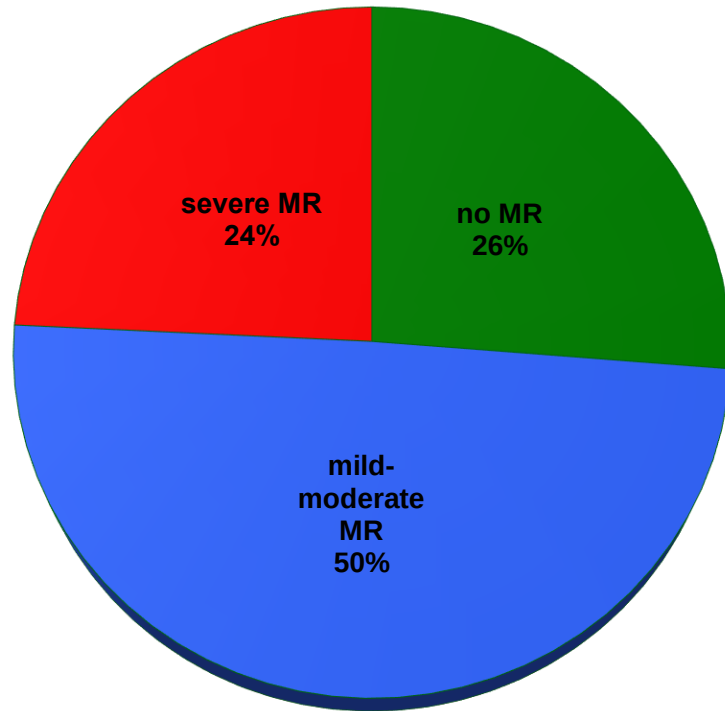


$\frac{3}{4}$ aller Patienten mit Herzinsuffizienz haben eine funktionelle bzw. sekundäre Mitralsuffizienz

Prognose ist bestimmt durch die zugrundeliegende Erkrankung

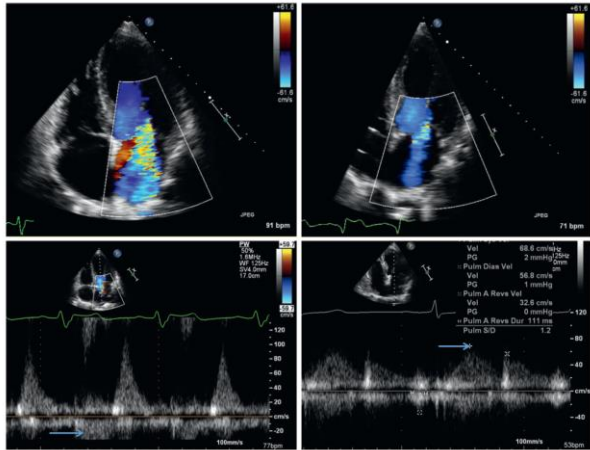
1256 Patienten mit ischämischer und nicht-ischämischer DCM (mean EF 32%)

Mitralsuffizienz ist mit erhöhter Mortalität assoziiert



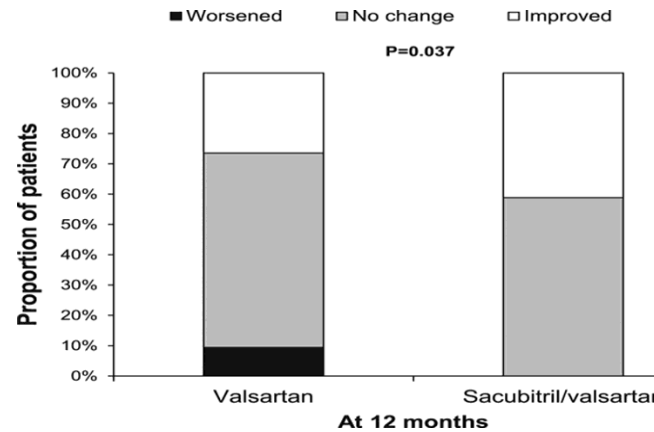
Optimale «konservative» medikamentöse Therapie reduziert die Mitralklappeninsuffizienz signifikant! (Remodelling, reduzierter Pre- und Afterload)

Diuretika: MI ist stark volumenabhängig



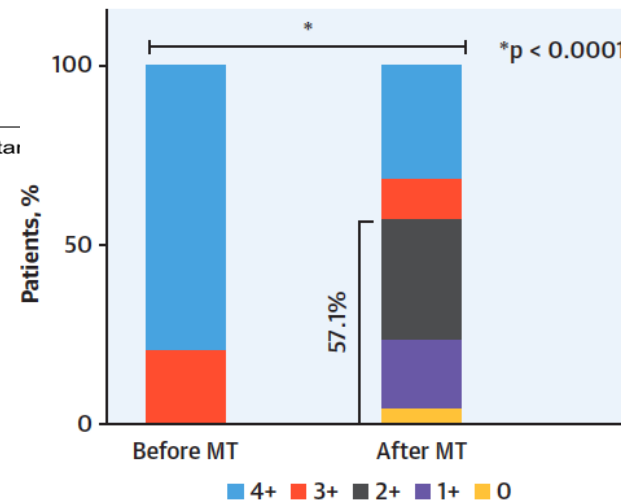
Grayburn PA, et al, JACC 2014

ARNI



Kann DH et al, Circulation 2019

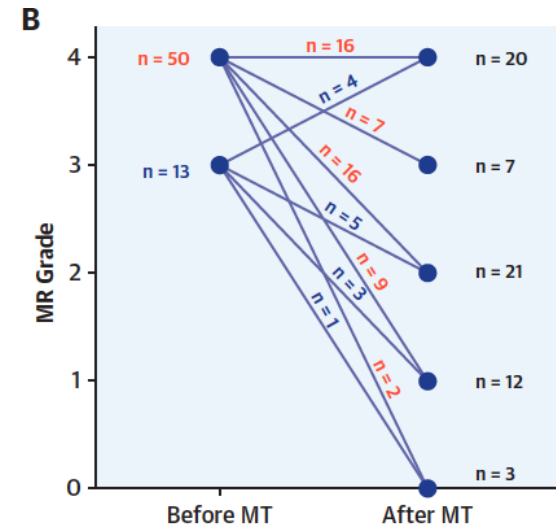
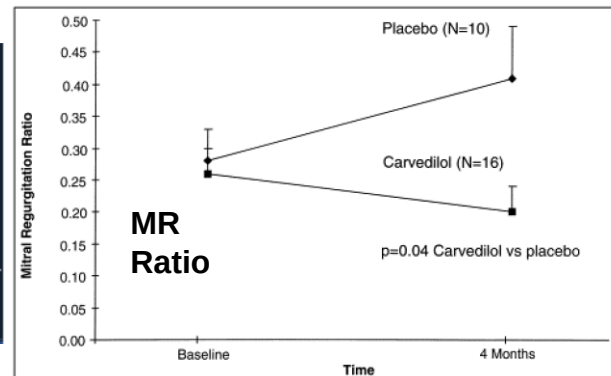
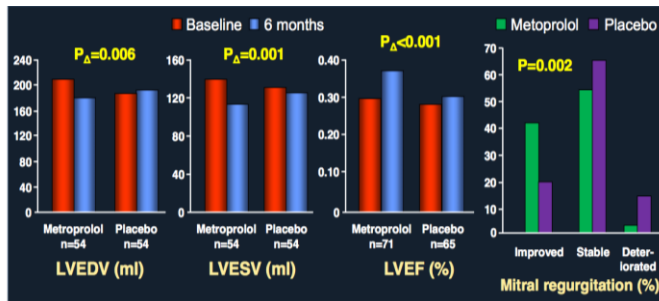
Effiziente medikamentöse Therapie zur Behandlung der sekundären Mitralinsuffizienzen



57% of patients with secondary MR have a reduction $\leq 2+$ (Data without ARNIs and SGLT2-Inhibitors)

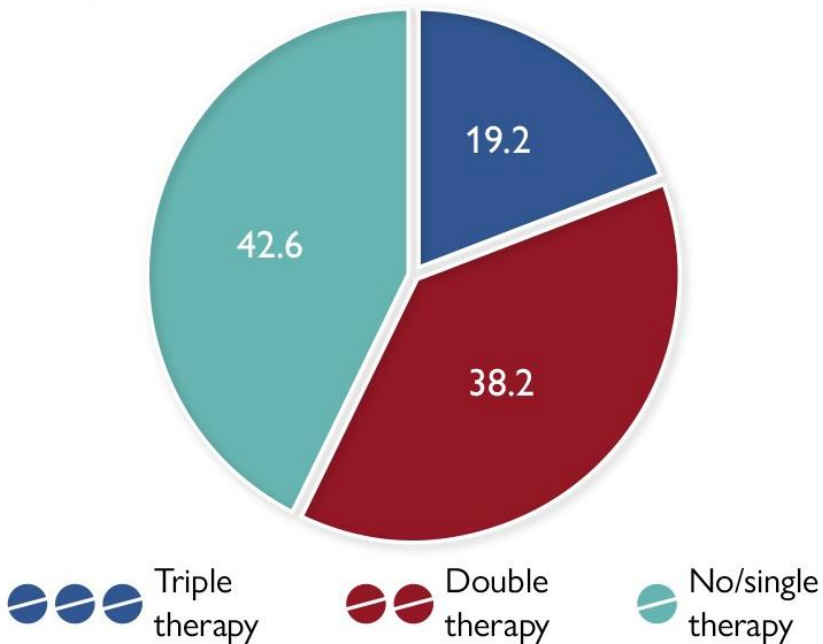
Sannino et al. JACC 2020

B-Blocker

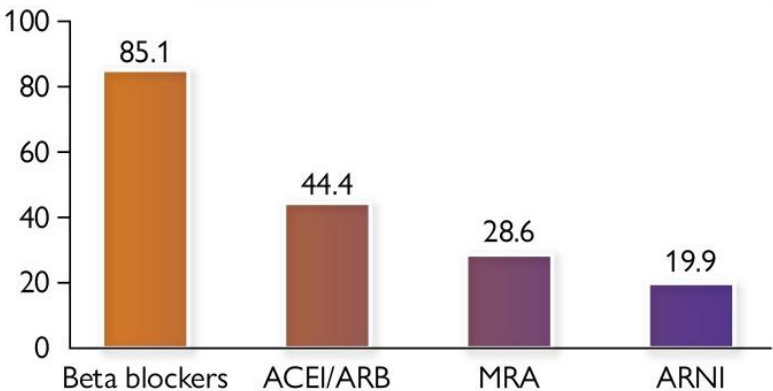


Leider bekommen die meisten Patienten keine adäquate Therapie vor einer Mitralklappen-Intervention

Pre-MTEER GMT utilization (N=4199; 449 Sites)



Pre-MTEER prescription rates (N=4199; 449 Sites)



Center-level pre-MTEER triple GMT rates

(N=144 sites performing 10+ MTEER annually)

- Range: 0-61%
- 10 sites with 0% triple therapy use
- ~1.5-fold variation in the likelihood that similar patients at 2 random sites were prescribed triple therapy

4199 patients. 2019-2022

Full Cohort

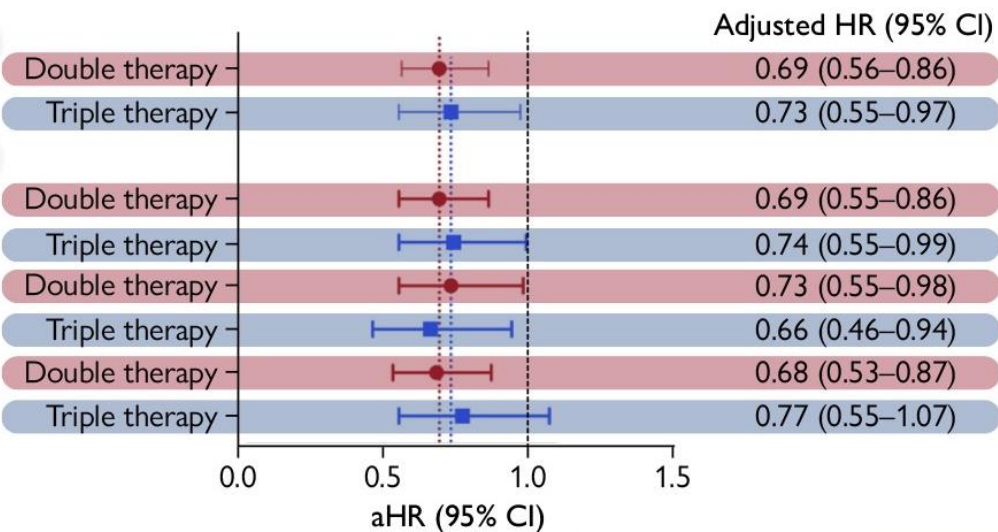
(N=2014)

Sensitivity analyses

Excluding LVEF>40% or NYHA Class 1 (N=1718)

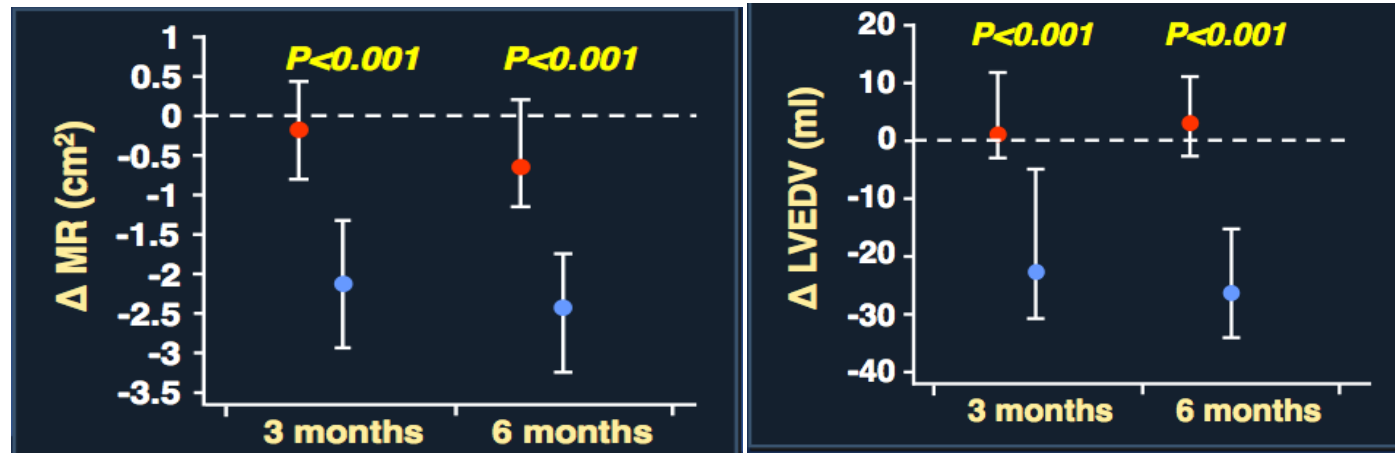
Procedurally Successful MTEER Only (N=1473)

Excluding NYHA Class IV (N=1619)



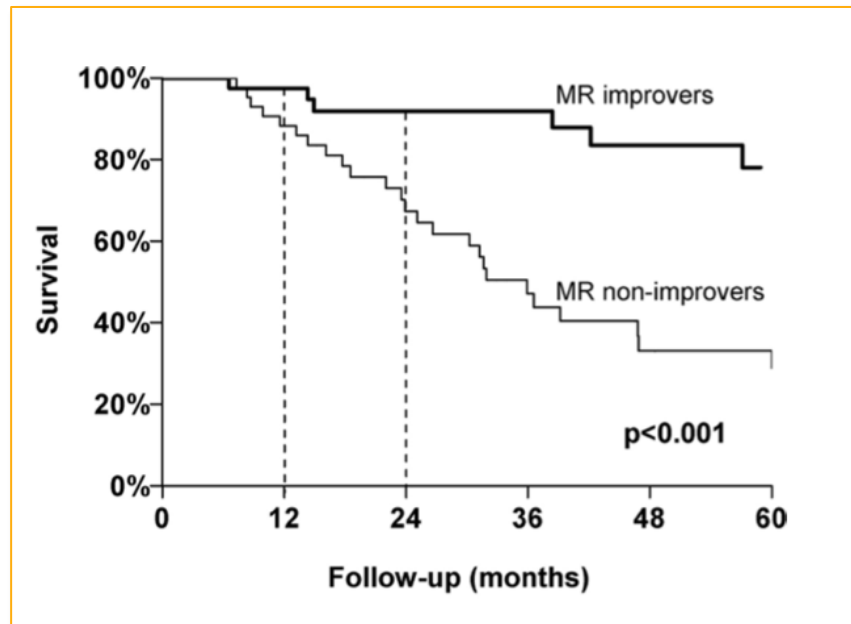
Varshney AS et al, EHJ 23

MIRACLE: CRT verbessert die Mitralinsuffizienz



450 pts with LVEF < 35% and QRS > 130 sec

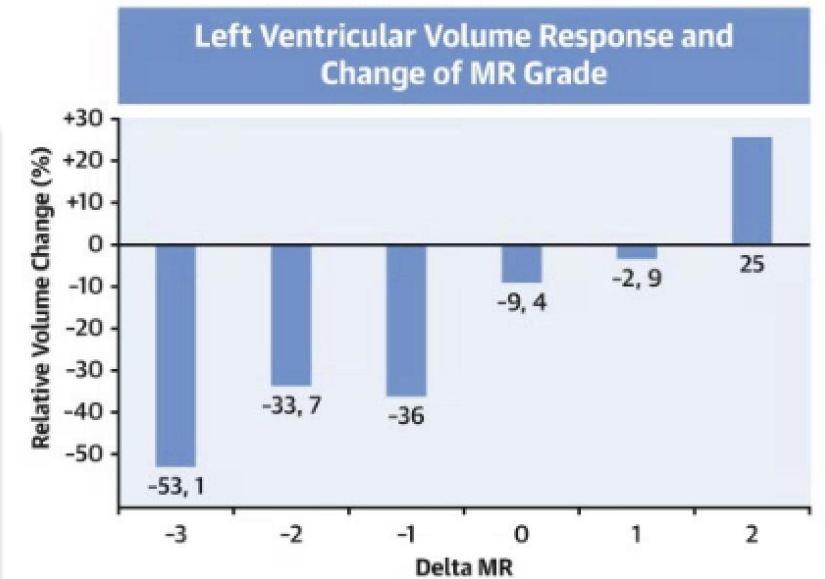
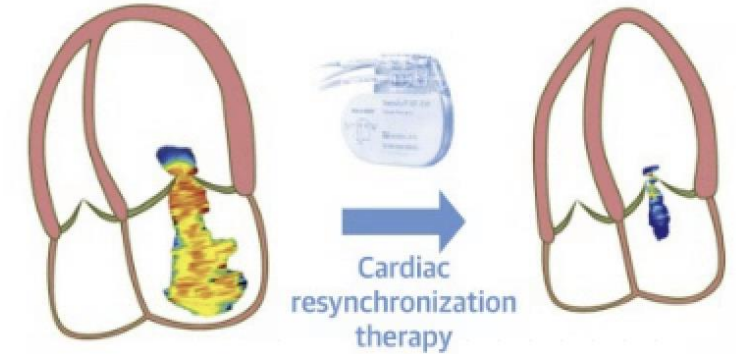
Sutton J et al, Circulation 2007



Bei Verbesserung der MI durch CRT verbessert sich auch die Prognose

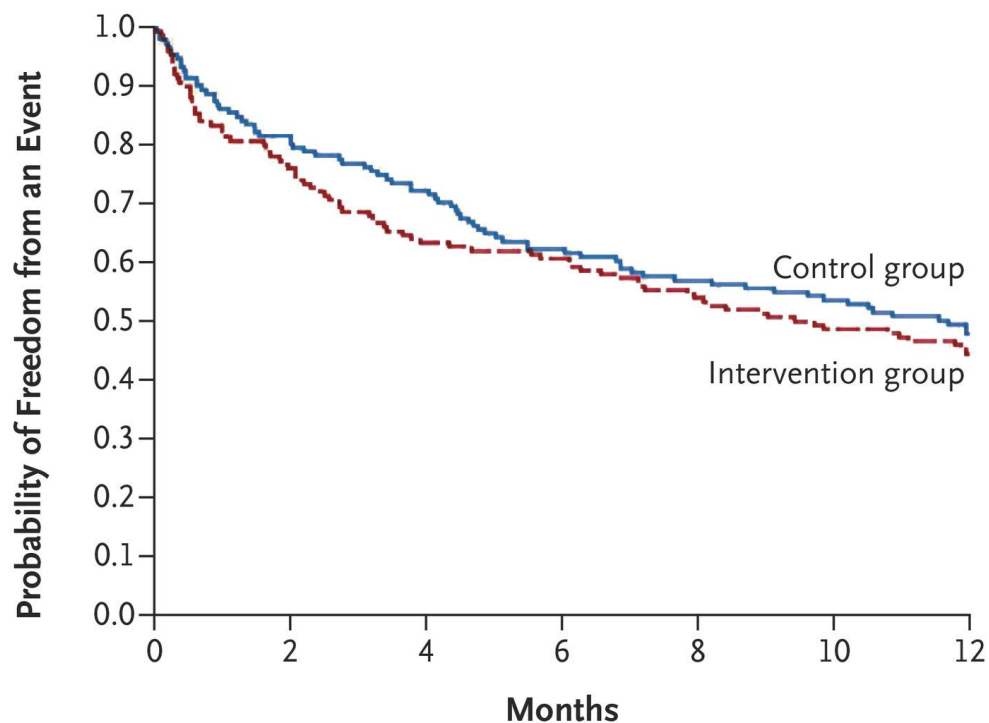
Van Bommel Circulation 2011

Reduktion der MI nach CRT und Remodelling



Vor 6 Jahren: TEER in FMR

Mitra.fr – «Niederlage»

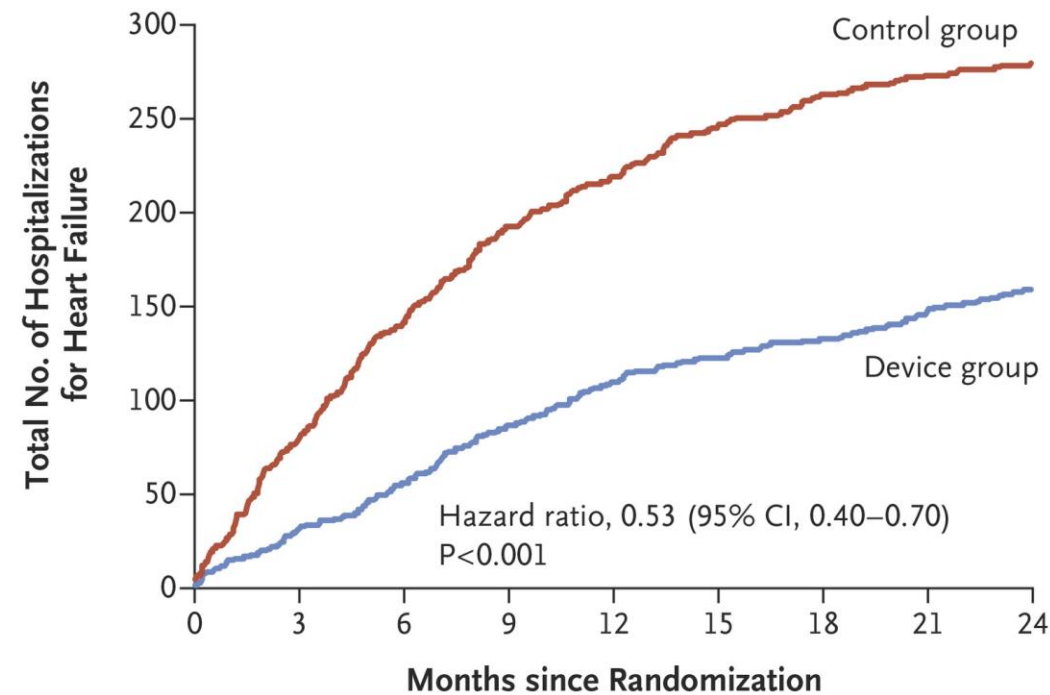


No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

Obadia JF al NEJM 2018

COAPT – «Revolution»

A Hospitalization for Heart Failure



No. at Risk									
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

Stone G et al NEJM 2018

RESHAPE-HF2 Trial –HFrEF und sekundäre Mitralinsuffizienz

Randomisiert, kontrolliert (nicht geblindet), mittelschwere bis schwere MI. 1:1 M-TEER mit GDMT oder nur GDMT.

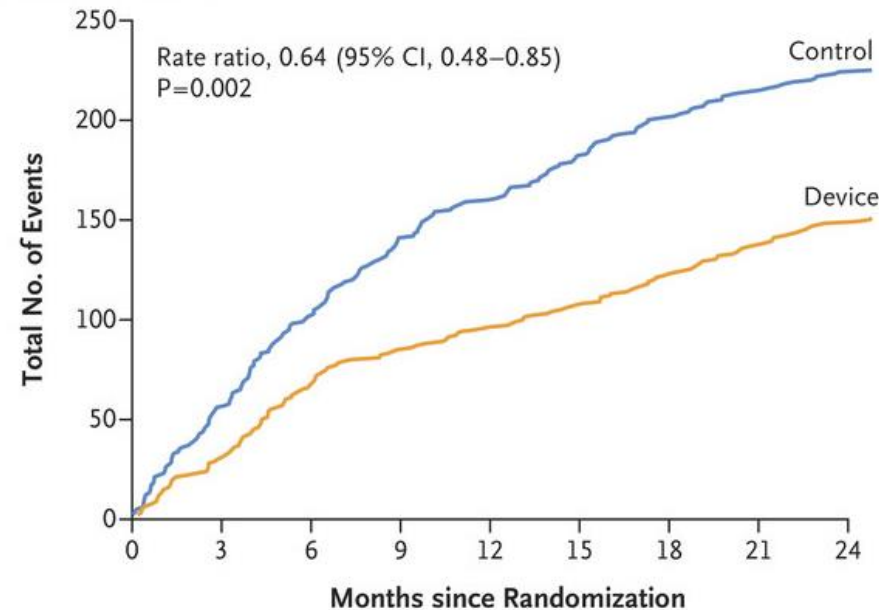
3 primäre Endpunkte:

- «rate of the composite of first or recurrent hospitalization for HF or CV death»
- «rate of first or recurrent hospitalization for HF»
- «QOL change from baseline to 12 months»

Charakteristika:

- 70-jährig, 80% Männer, 35% DM, 50% Hypertonie, 48% Afib
- Nicht-ischämische HF 35%
- NYHA III 60%
- HHF im letzten Jahr 66%
- NTproBNP 2700ng/ml, SBP 112mmHg, GFR 55ml/min
- **LVEF 32%**, LVEDV 200ml, med regurgitant Volume 35ml
- BB 95%, ACE, ARB or ARNI: 82%, MRA 80%, SGLT2 9%

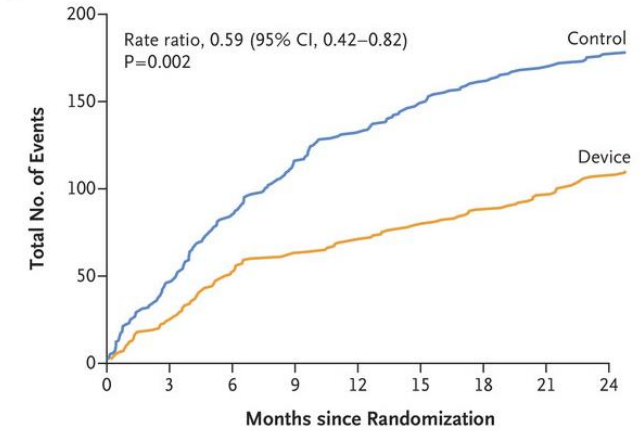
A Composite of Hospitalization for Heart Failure or Death from Cardiovascular Causes



No. at Risk

Control	255	240	223	204	189	179	165	155	146
Device	250	241	222	207	197	191	179	170	163

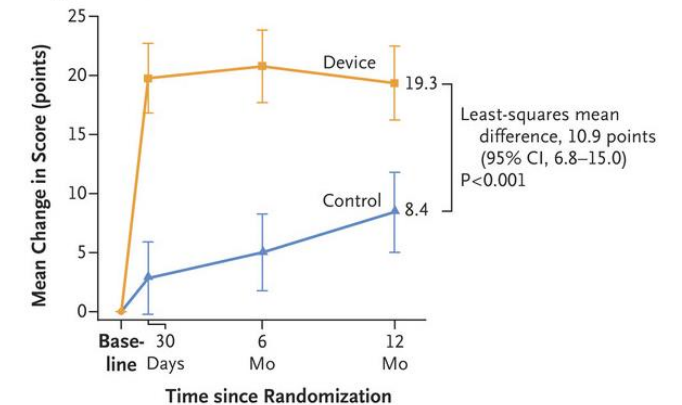
B Hospitalization for Heart Failure



No. at Risk

Control	255	240	223	204	189	179	165	155	146
Device	250	241	222	207	197	191	179	170	163

C KCCQ-OS Score



• RESHAPE-HF2 - Percutaneous repair of moderate-to-severe or severe functional mitral regurgitation...

Secondary Endpoints

Secondary end points				
Mitral regurgitation grade $\leq 2+$ at 12 mo — no./total no. (%)	132/146 (90.4)	43/119 (36.1)**	21.3 (10.7–45.8)††	<0.001¶
Mean change in 6-min walk distance from baseline to 12 mo — m	34.0±105.9	5.1±97.6	20.5 (0.3–40.7)‖	0.05‡‡
Rate of death from any cause during the complete* follow-up per 100 patient-yr (no. of events/total no. of patient-yr)	17.0 (142/836.7)	18.6 (142/765.2)	0.90 (0.71–1.13)	0.37
Rate of recurrent hospitalization for any cause during 24 mo per 100 patient-yr (no. of events/total no. of patient-yr)	48.7 (199/408.6)	61.0 (233/381.9)	0.82 (0.63–1.07)	0.15
NYHA functional class I or II heart failure at 12 mo — no./total no. (%)§§	140/188 (74.5)	96/164 (58.5)	2.35 (1.48–3.77)††	<0.001¶

*Follow-up times for 24 months assessments:

- Overall: median 24.0 months (IQR 12.0–25.0); Device group: 24.2 (IQR 15.7–25.0); Control group: 23.6 (IQR 10.4–24.9).

Follow-up times for all-cause mortality assessment:

- Overall: median 29.4 months (IQR 14.0–61.1); Device group: 34.3 (IQR 16.0–63.1); Control group: 27.0 (IQR 11.6–58.0)



Stefan Anker
Germany



#ESCCongress

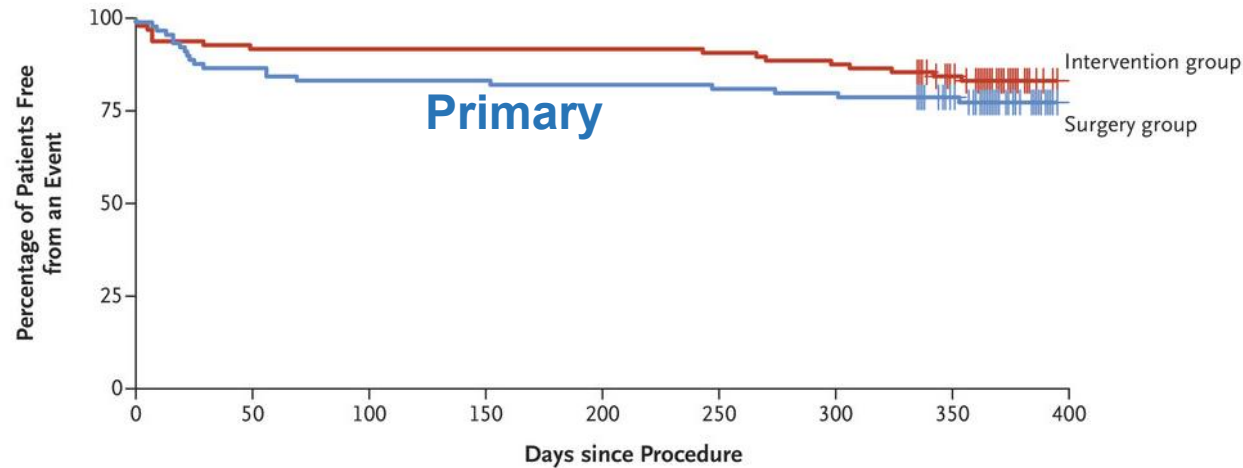
MATTERHORN – Transcatheter Repair vs. Mitral-Valve Surgery for secondary MR

Wenn die FMR angegangen wird, dann eher interventionell als chirurgisch

Nicht-Unterlegenheitsstudie bei HFrEF und fMR bei Patienten mit Symptomen trotz GDMT. 1:1 M-TEER oder Operation.

Primärer Endpunkt: Zusammengesetzt aus Tod, Krankenhausaufenthalt wegen HF, Mitralklappen-Wiederintervention, Assist Device oder Schlaganfall innerhalb eines Jahres. Sicherheit: Wichtige unerwünschte Ereignisse innerhalb von 30 Tagen

A Primary End-Point Event



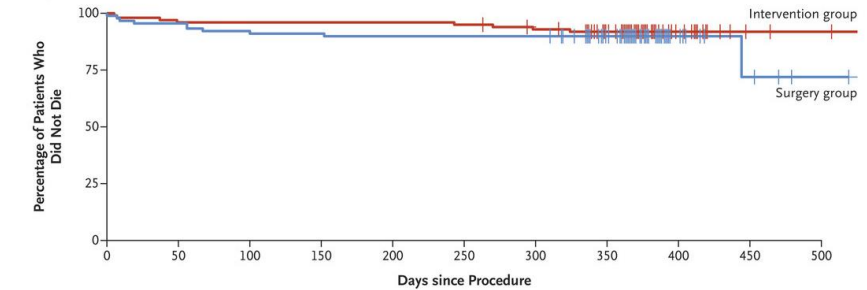
No. at Risk (%)										
Intervention group	96 (100)	88 (92)	88 (92)	88 (92)	88 (92)	87 (91)	84 (88)	71 (74)	0 (0)	
Surgery group	89 (100)	77 (87)	74 (83)	74 (83)	73 (82)	72 (81)	71 (80)	58 (65)	0 (0)	

Characteristics:

- 70 Jahre, Frauen 38%, BMI 27, DM 25%, Hypertonie 83%
- GFR 57ml/min, EuroSCORE 2.0,
- CRT 13%, RAAS Inhibitor 70%, 3er HI-Medi-Kombi bei Entlassung 19%

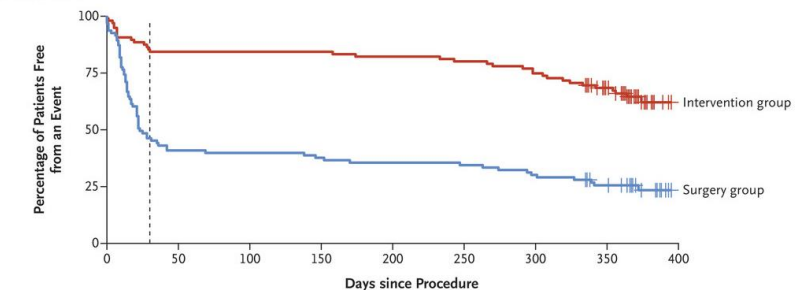
Death

B Death from Any Cause



No. at Risk (%)											
Intervention group	99 (100)	95 (96)	95 (96)	95 (96)	95 (96)	94 (95)	90 (91)	77 (78)	15 (15)	3 (3)	2 (2)
Surgery group	89 (100)	85 (96)	82 (92)	81 (91)	80 (90)	80 (90)	80 (90)	63 (71)	10 (11)	4 (4)	1 (1)

C Major Adverse Event

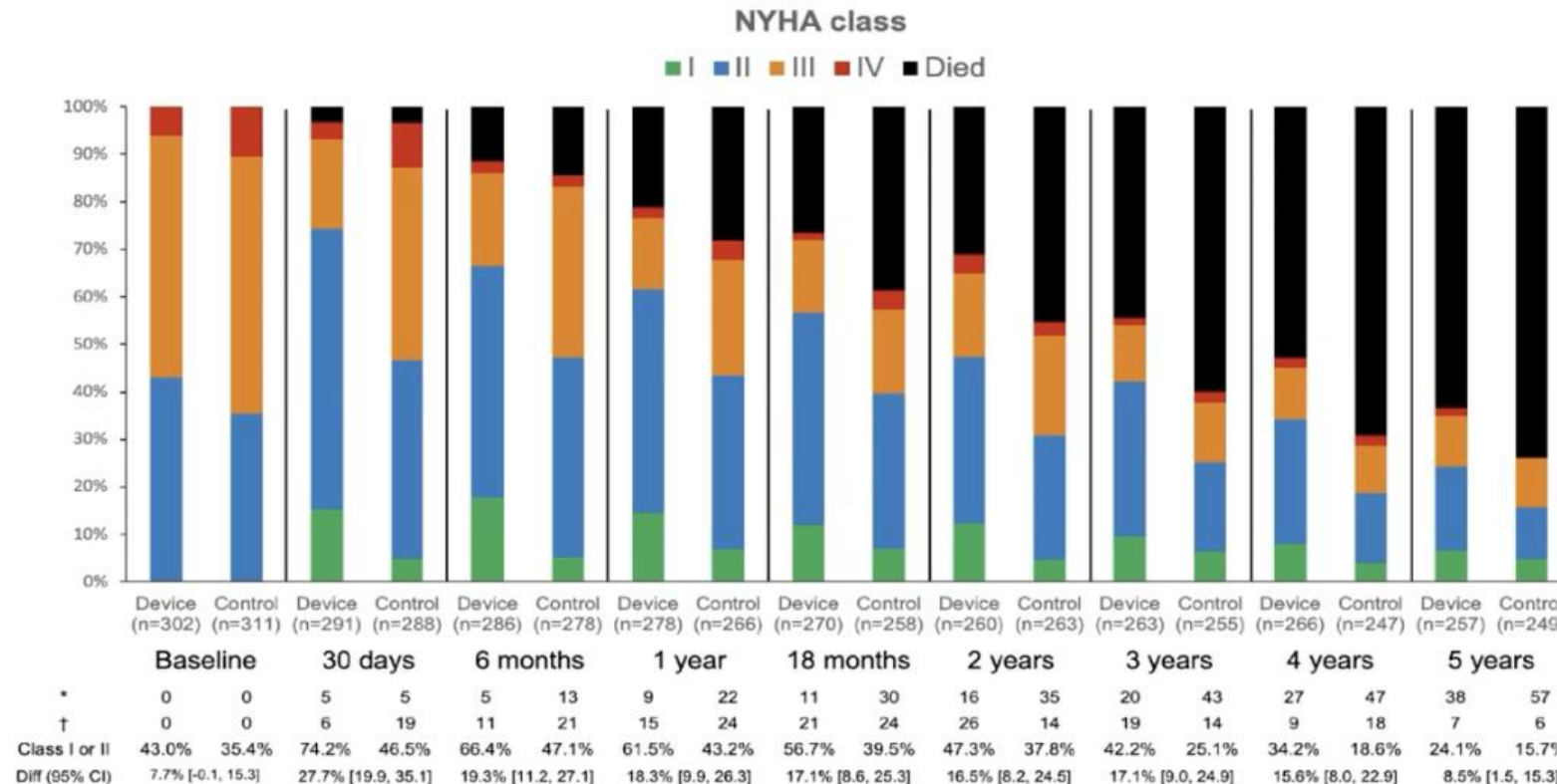


No. at Risk (%)										
Intervention group	95 (100)	80 (84)	80 (84)	80 (84)	78 (82)	76 (80)	71 (75)	57 (60)	0 (0)	
Surgery group	93 (100)	38 (41)	37 (40)	35 (38)	33 (35)	32 (34)	28 (30)	21 (23)	0 (0)	

Major adverse events

Das ist die Population....

Matterhorn Trial: Implications from COAPT



Stone et al *NEJM* 2023

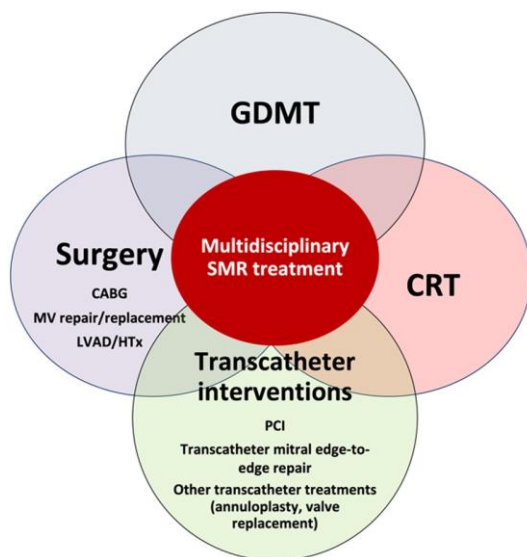


ESC-Guidelines: Class I Empfehlungen für den «Heart Team» Ansatz

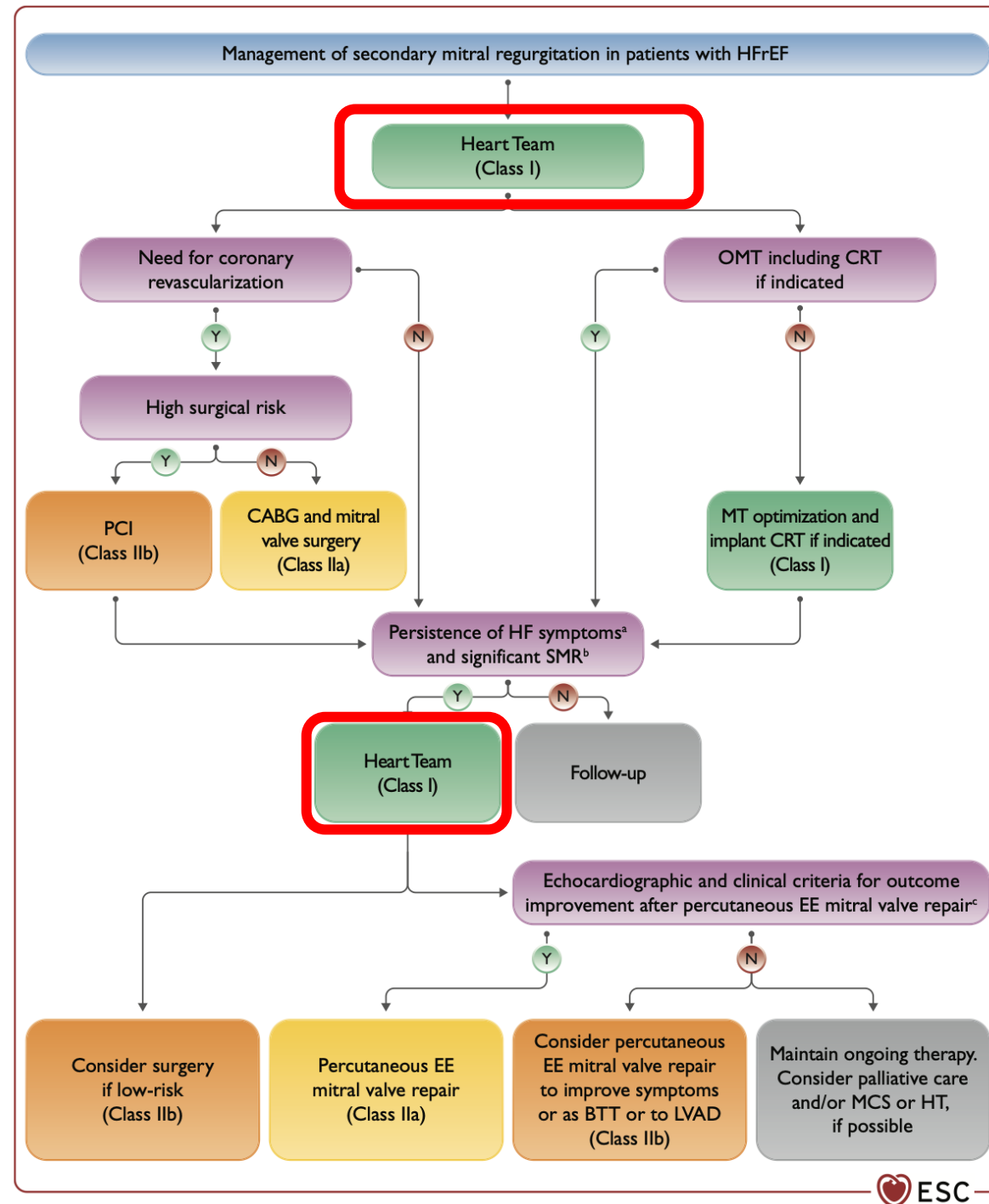
Therapieentscheidungen nur im «Herzteam»
mit einem **Herzinsuffizienz Spezialisten**

Revaskularisation und optimale
medikamentöse und CRT Behandlung

Coats AJ et al,
joint position
statement from
HFA, EACVI,
EHRA and
EAPCI, EHJ
2021

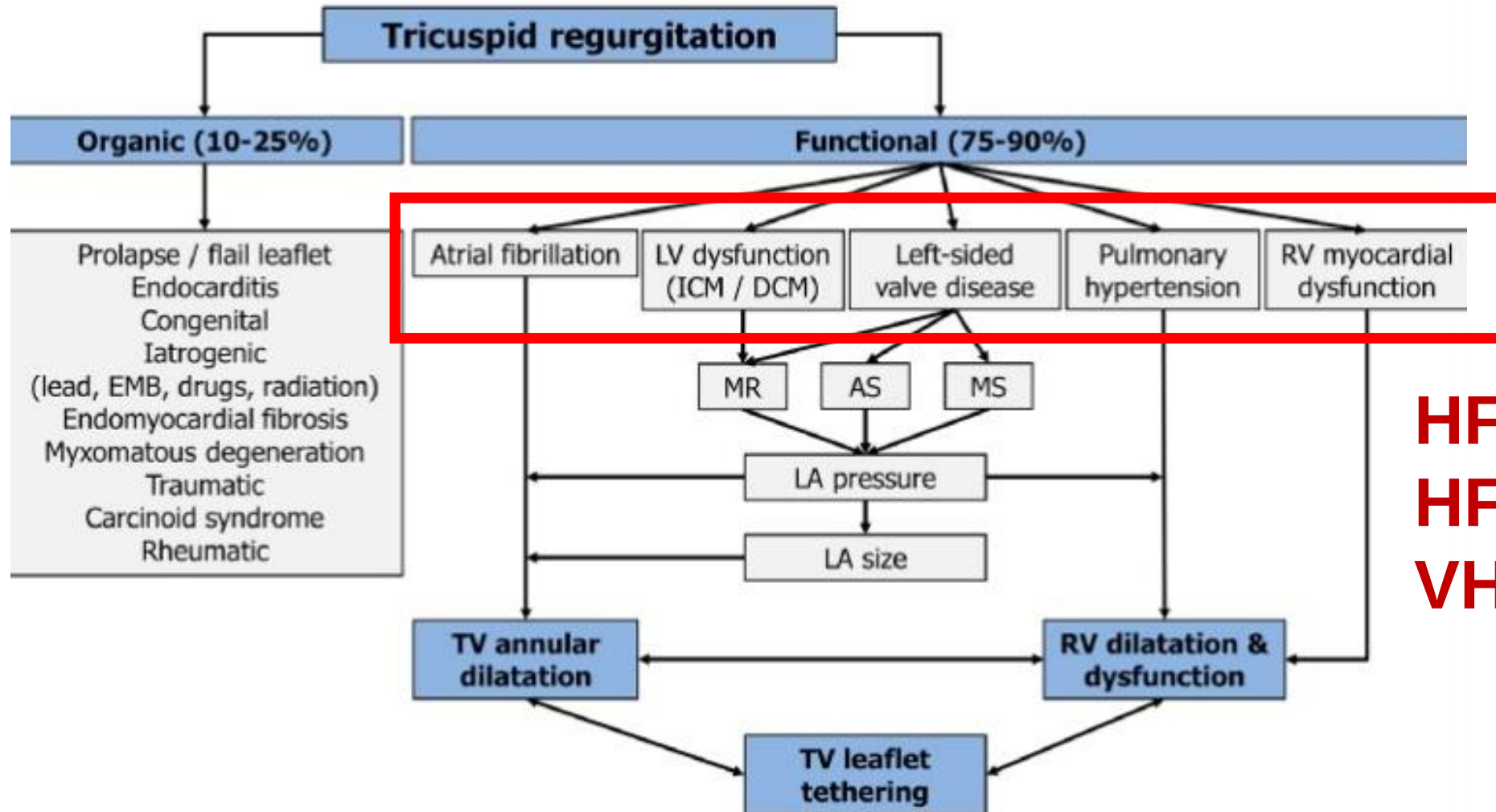


ESC Guidelines 2021



Muss jede schwere Trikuspidalinsuffizienz weg? – Nicht immer

Ursachen der Trikuspidal-Klappen Insuffizienz



HFrEF!
HFpEF!
VHF!

Trikuspidalinsuffizienz: Verschiedene Devices vermindert den Schweregrad

Heisst das auch, dass sich die
Prognose verbessert?

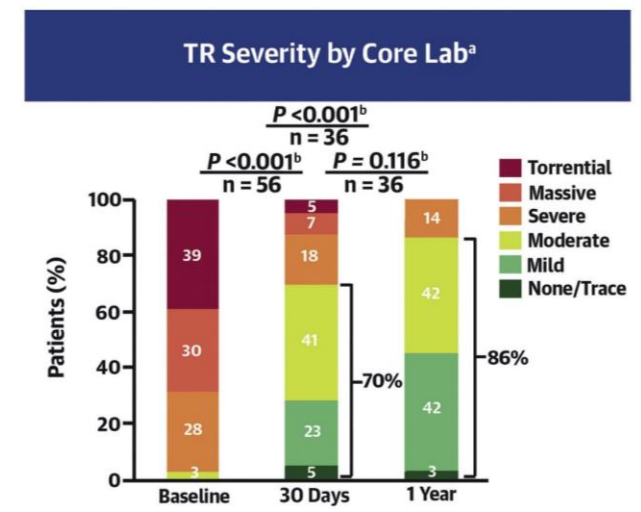
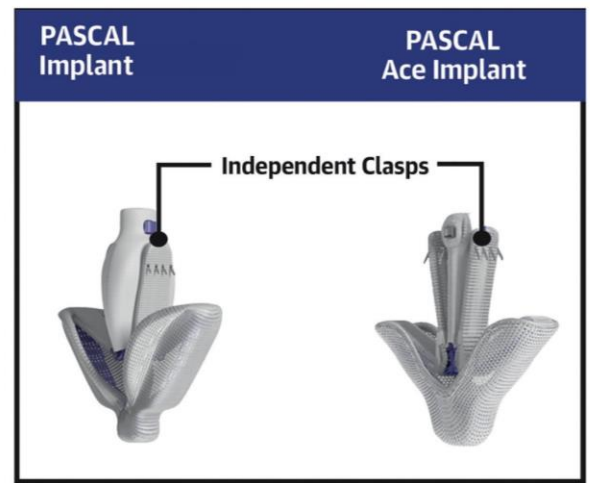
Guidelines?

Transcatheter treatment of symptomatic secondary severe tricuspid regurgitation may be considered in inoperable patients at a Heart Valve Centre with expertise in the treatment of tricuspid valve disease.^f

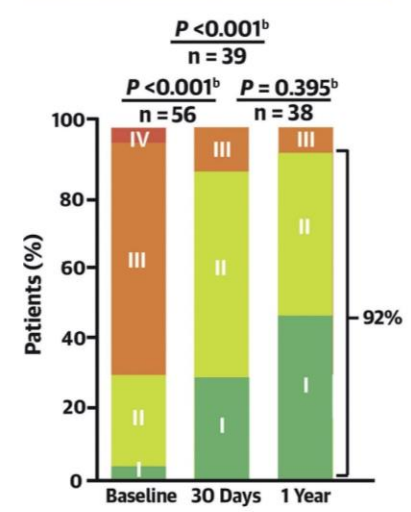
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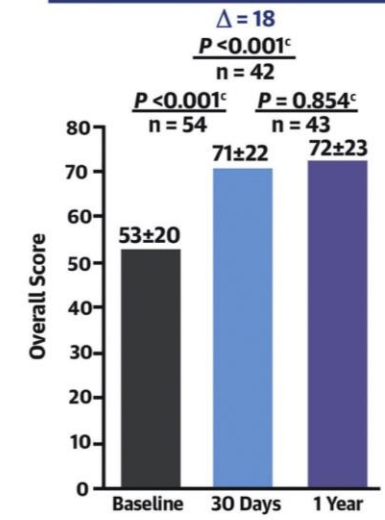
ESC Guidelines for Valve Disease 2021



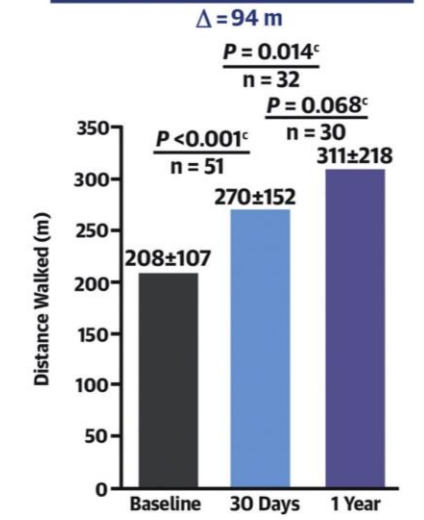
NYHA Functional Class



Overall KCCQ Score



6-Minute Walk Distance

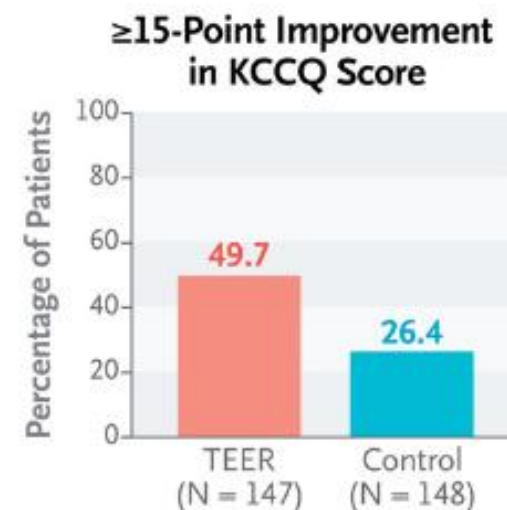
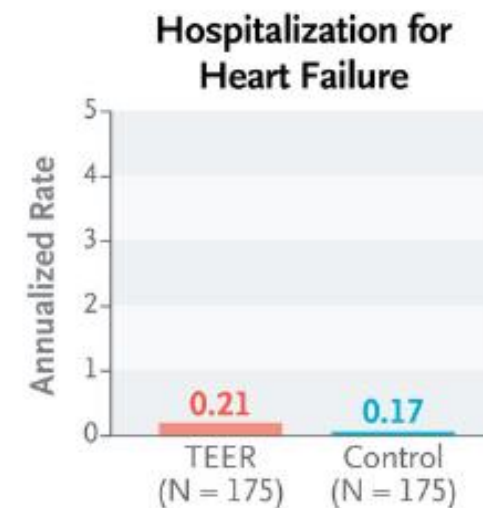
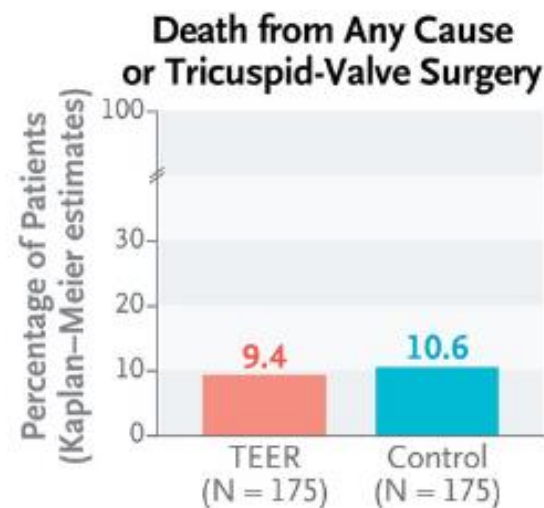


Transcatheter Repair for Patients with Tricuspid Regurgitation – TRILUMINATE

- Prospektive randomisierte Studie
- Symptomatische schwere TR
- 1:1-Verhältnis entweder TEER oder OMT
- Hierarchischer zusammengesetzter Endpunkt einschließlich Tod, oder Trikuspidalklappen-chirurgie, HHF, Verbesserung der Lebensqualität (QOL)
- 350 Patienten
- Durchschnittsalter 78 Jahre, 55 % Frauen
- VHF 90 %, Hypertonie 80 %, GFR 55 ml/min
- LVEF=59 %, LVEF <50 %: 22 %

Hierarchischer Endpunkt – positiv «nur» aufgrund QOL-Verbesserung

	TEER Group	Control Group
	(N = 175)	(N = 175)
Hierarchical composite — no. of wins	11,348	7643



TRI.fr - Multicentric randomized evaluation of T-TEER for severe TR



First Academic Randomized Trial about transcatheter correction of TR

Population

Symptomatic (NYHA functional class II to IV) with $\geq$ severe TR Signs and symptoms of heart failure in the previous 12-months, Ineligibility for surgery

Intervention

Percutaneous procedure using the TriClip™ device (T-TEER) on top of GDMT



Main Objective

To assess safety and efficacy of T-TEER + GDMT compared to GDMT alone

Charakteristika:

- 36% Männer, 78.5 Jahre, BMI 25, NYHA III 41%
- Hypertension 69%, HFH 40%, VHF 95%
- 6MWT 305m

Primary Endpoint (ITT) (1)

At 1-year follow-up, 109 patients (74.1%) in the T-TEER group improved, compared to 58 patients (40.6%) in the GDMT group

The T-TEER group has a probability of a better rank of 0.67; 95% confidence interval, 0.61 to 0.72; $P < .0001$

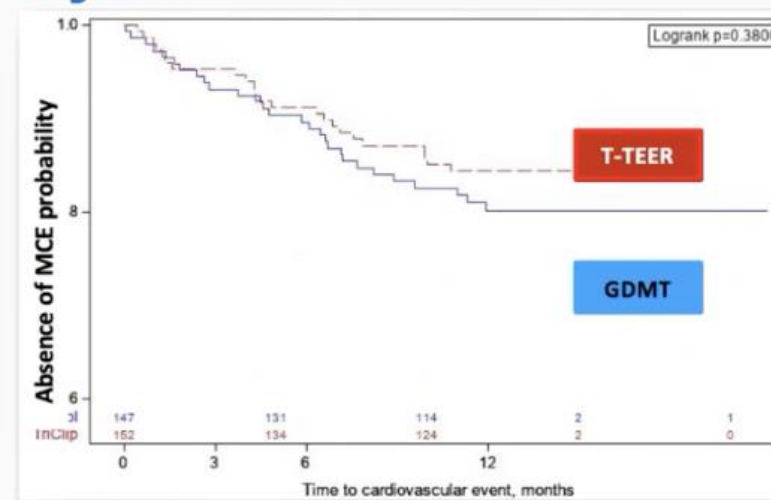


Erwan Donal et al, ESC 2024

Hierarchical Composite Endpoint/MCE

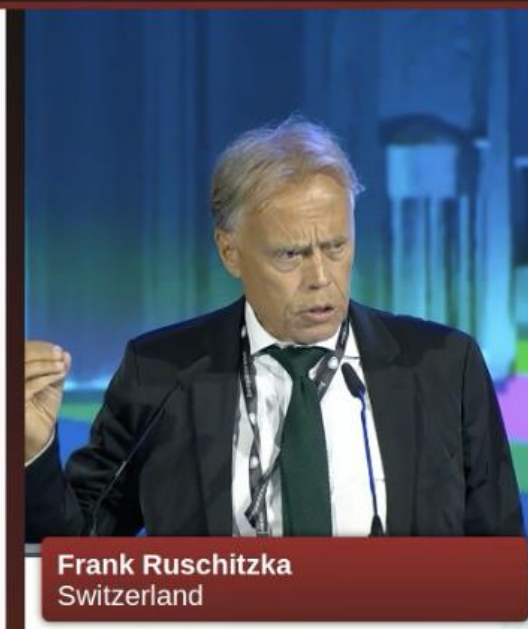
No differences in the incidence of death or hospitalization for heart failure at 1 year

Hierarchical Clinical Composite Endpoint	Control N = 148	T-TEER N = 152
Improved		
Favorable change in NYHA class , n	39	70
Mild, moderate or marked improvement on PGA (< 4) , n	19	39
Worsened		
Unscheduled hospitalization for HF , n	20	15
Died, n	8	5
Unfavorable change in NYHA-class at last visit, n	15	3
Slight, moderate or marked worsening on PGA (> 4), n	25	7
Unchanged: none of the above, n	17	8
Missing	5	5



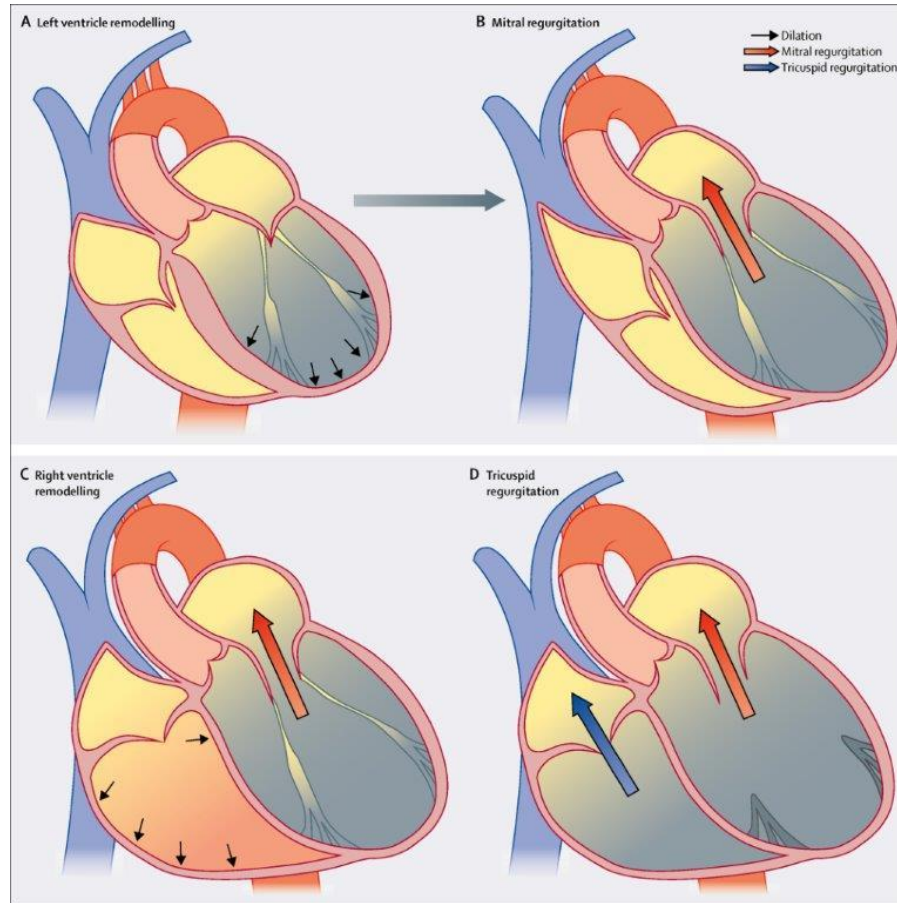
one-year mortality 3.4%

Major cardiovascular events during the one-year follow-up (MCE): myocardial infarction, or unstable angina, or revascularization, or stroke, or cardiovascular death, or heart failure hospitalization



Frank Ruschitzka
Switzerland

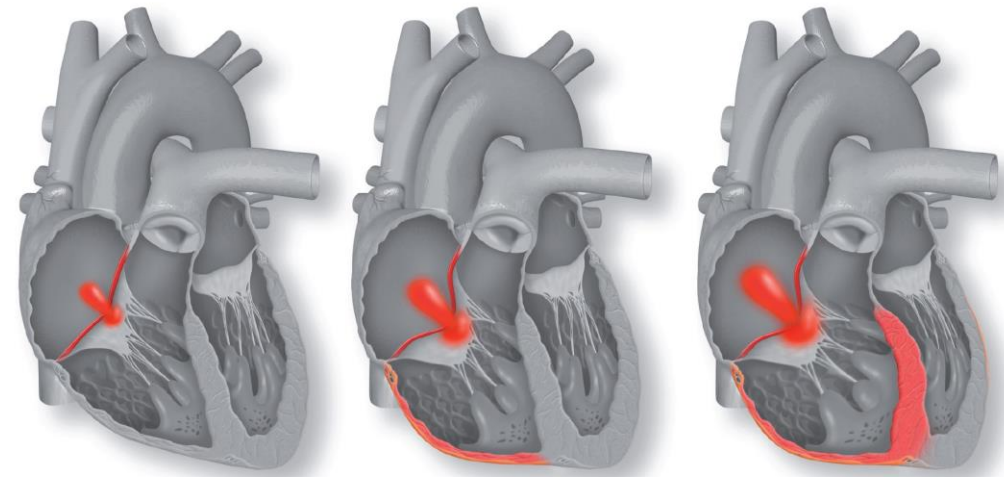
Typische Entstehung der sekundären TI mit zunehmender Beeinträchtigung der RV-Funktion



Bax J et al Lancet 2019
 Bartko PE et al, EHJ 2020
 Bartko PA et al; JACC Cardiovasc Imag
 2019

Secondary Tricuspid Regurgitation

HFpEF / HFmrEF / HFrEF

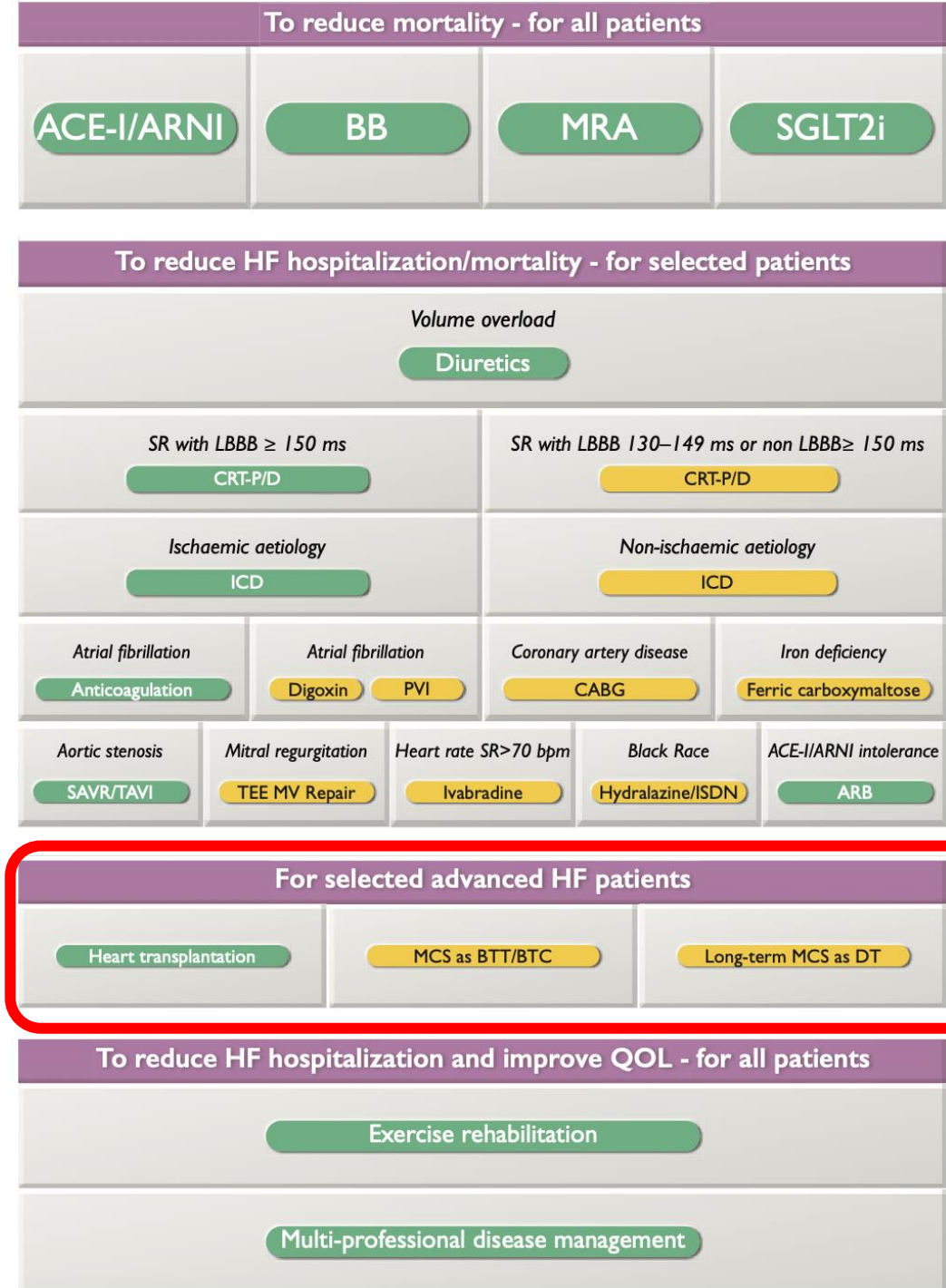


- | Phase I | Phase II | Phase III |
|--|---|--|
| <ul style="list-style-type: none"> • Increased RV systolic pressure • sPAP ↑ • RV dilatation • TV annular dilatation | <ul style="list-style-type: none"> • Progressive RV dilatation • RA dilatation • TV annular dilatation | <ul style="list-style-type: none"> • RV dilatation and distortion • sPAP ↑ • RA dilatation • TV annular dilatation • Tethering of TV leaflets |

HFpEF oft mit einer sekundären TI assoziiert. Zugrundeliegende LV-Pathologie wird häufig verpasst und die Herzinsuffizienz-Symptome werden fälschlicherweise der TI zugeschrieben.

NEUER THERAPIE ALGORITHMUS FÜR HFrEF

ESC GUIDELINES 2021



Advanced heart Failure „Fortgeschrittene Herzinsuffizienz

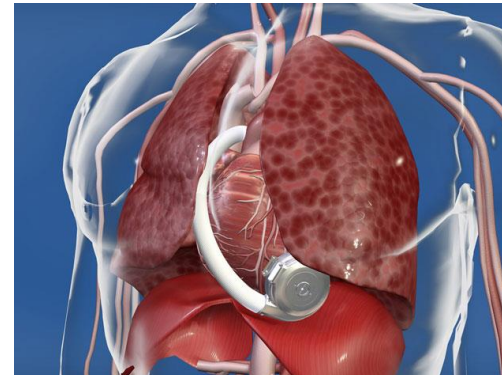
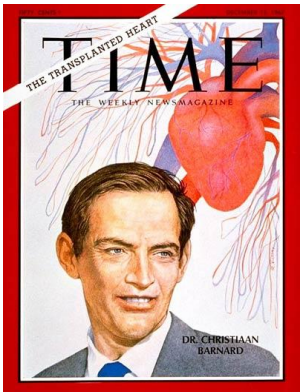
For selected advanced HF patients

Heart transplantation

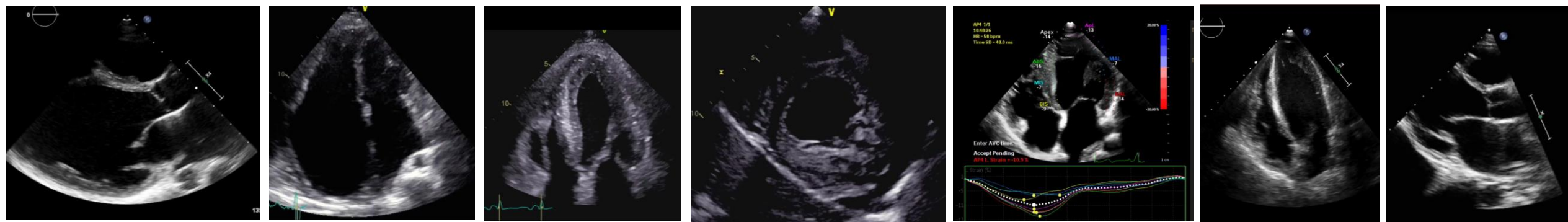
MCS as BTT/BTC

Long-term MCS as DT

MCS = mechanical circulatory support



Herzinsuffizienz ist ein klinisches Syndrom



Behandlung basiert auf dem LVEF-Phänotyp – nicht so sehr Ätiologie

	HFrEF	HFmrEF	HFpEF	
	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a	
	LVEF ≤40%	LVEF 41–49% ^b	LVEF ≥50%	
	—	—	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c	

EMPEROR Preserved

Empagliflozin versus Placebo in Patients with HFpEF: Composite Endpoint of CV Death or Hospitalization for HF

5988 patients, NYHA class II-IV and EF >40%

Empagliflozin 10mg or placebo

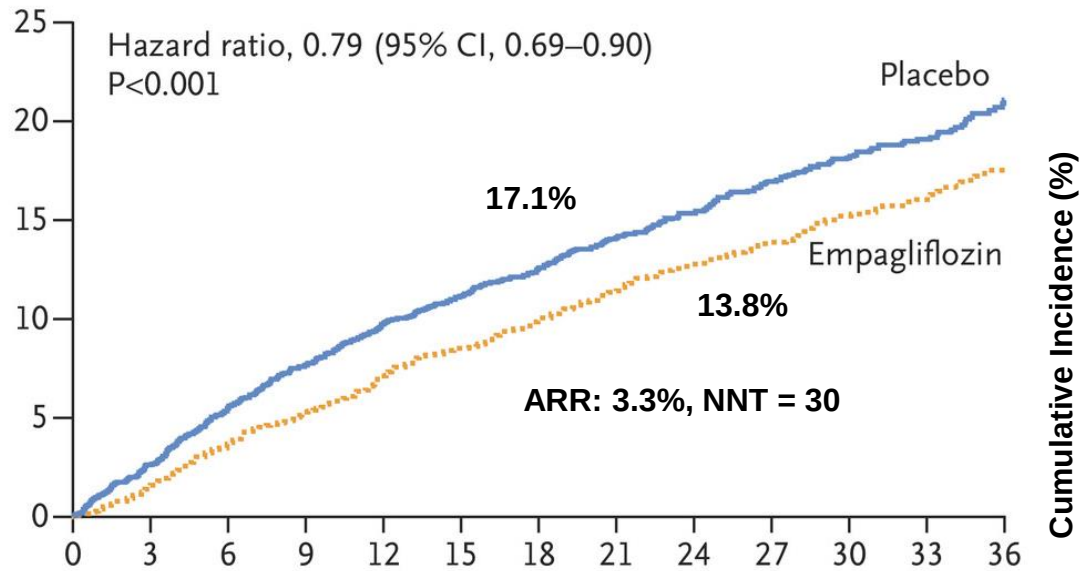
FU 26.2 months

Age 71.8 years, 44.6% female, 81.5% NYHA II, BMI 29.8, BP 132mmHg, LVEF (mean) 54.3%, 33% EF 40-50%, NTproBNP 995pg/ml

35% ischemic, 51% Afib, **49% Diabetic**, 90% Hypertension, eGFR 60.6ml/min

RAAS inhibitors: 81%, Sac/Val: 2.2%

MRA: 37.5%, BB; 86.8%, Statins: 69%



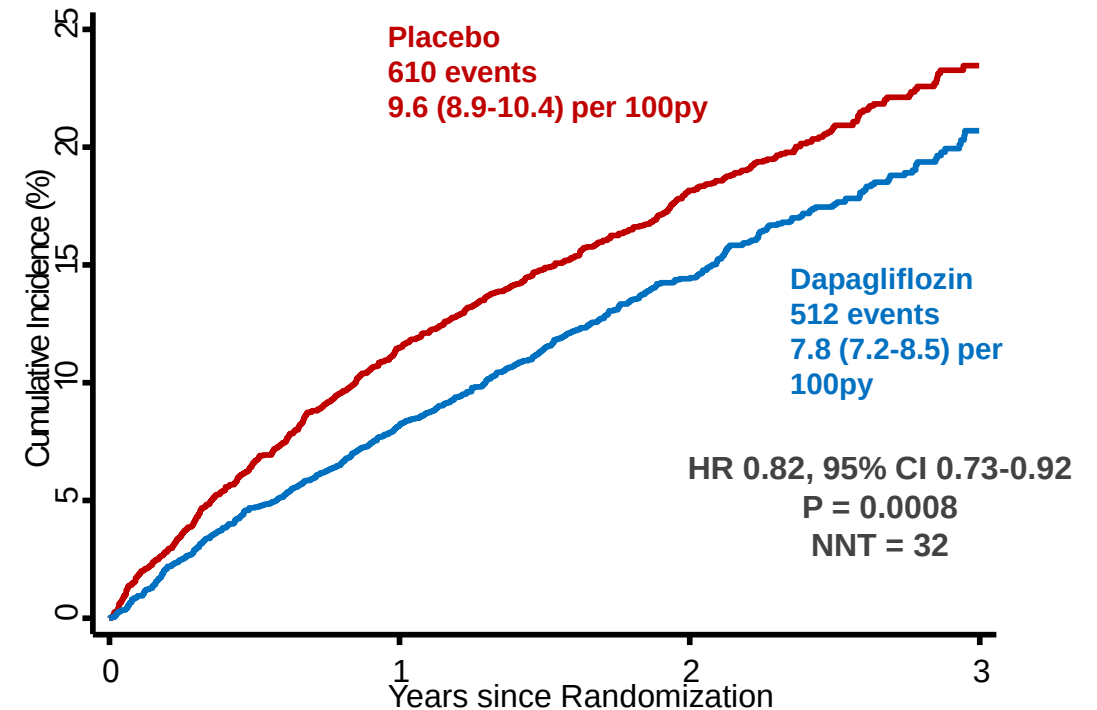
Bestätigung 2022 in HFmrEF und HFpEF:

DELIVER-Trial: Dapagliflozin 10mg vs. Placebo in HFmrEF and HFpEF. Composite Endpoint of CV death or worsening heart failure (HF Hospitalization or Urgent HF Visit)

Age >40 years, NYHA II-IV, EF >40% (including prior EF < 40%), structural heart disease (LVH or LA enlargement), Elevated BNP

Age 71.5 years, 44% female, EF 54%, prior EF > 50%: 18.4%, EF>60%: 30%, Afib: 42%, eGFR: 61%

Diuretics 76%, ACEi 36%, ARB 36%, ARNI 5%, BB 82%, MRA 42%



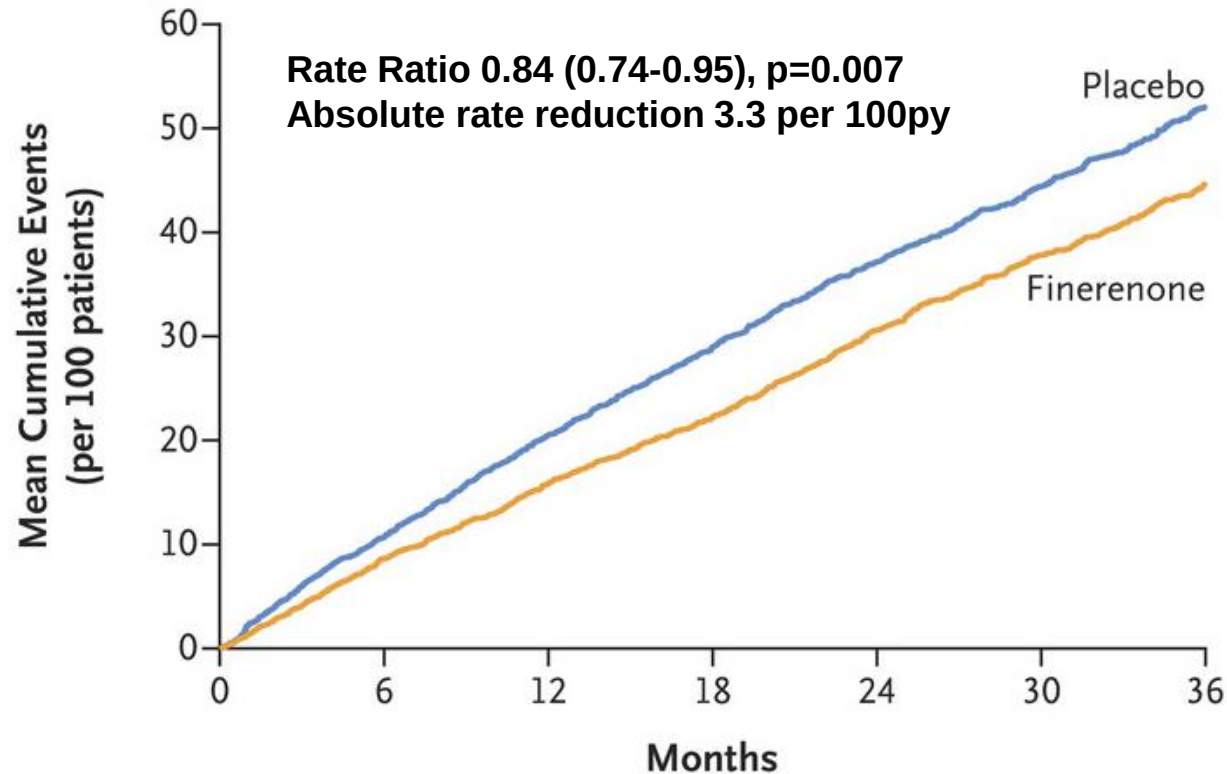
FINEARTS-HF trial

Internationale, doppelblinde Studie in Patienten mit **HFmrEF und HFpEF (EF > 40%)**, 1:1 Finerenone 20-40mg oder Placebo.

Endpunkt:

«Composite of total worsening heart failure events (event= first or recurrent unplanned Hosp or urgent visit for HF) and death from CV cause»

A Total Worsening Heart Failure Events and Death from Cardiovascular Causes

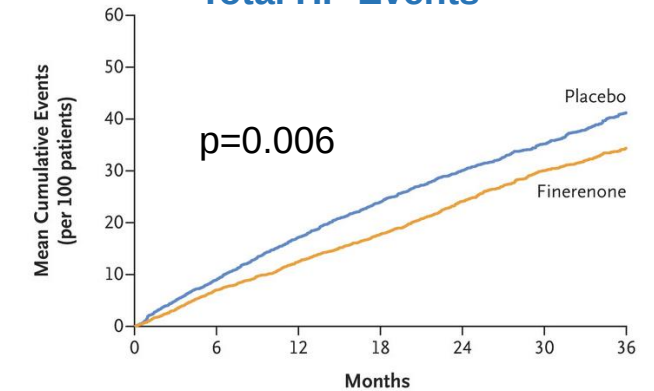


Characteristics:

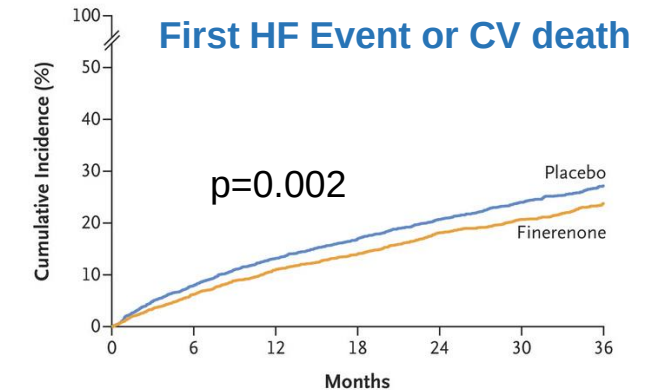
- 72J, 45% Frauen, vorherige HI-Hosp 60%
- BD 129mmHg, BMI 30, GFR 62ml/min, K 4.4mmol/l
- LVEF 52.5% (36%<50%), NTproBNP 1030ng/l, NYHA II-III
- 88% Hypertonie, 40% DM2, 38% VHF, 25% MI
- 85% BB, 36% ARB, 35% ACEI, 8% Sac/Val, 13% SGLT2, 87% Schleifendiuretika

Solomon SD et al, NEJM 2024

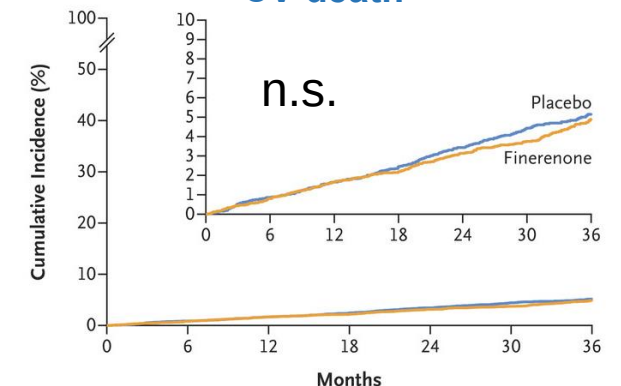
Total HF-Events



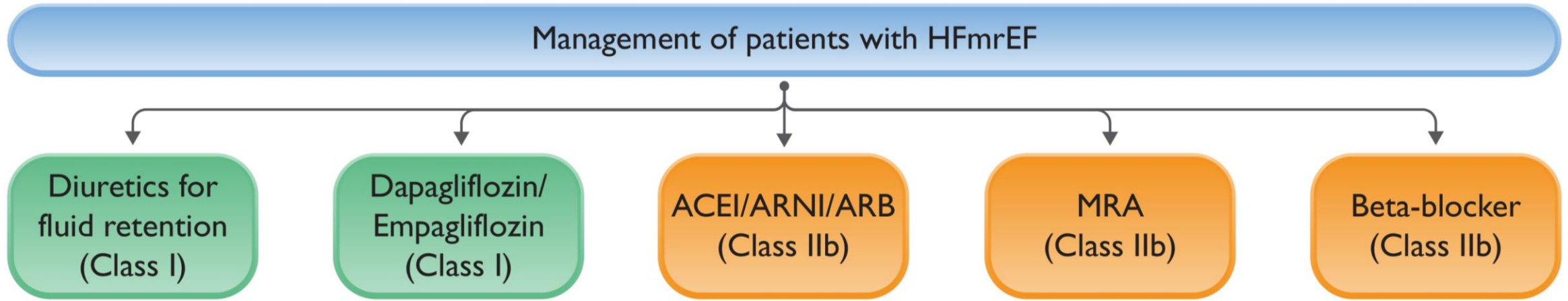
D First Worsening Heart Failure Event or Death from Cardiovascular Causes



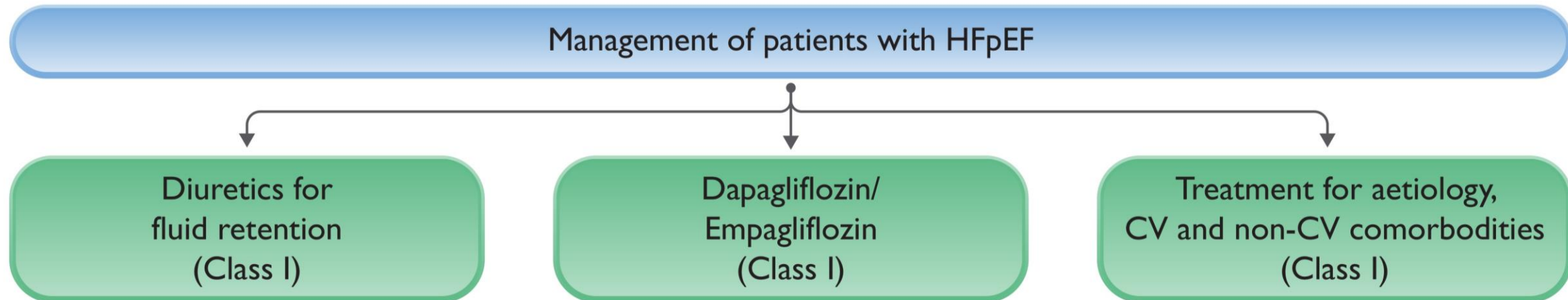
CV death



Treatment of HFmrEF – Update 2023



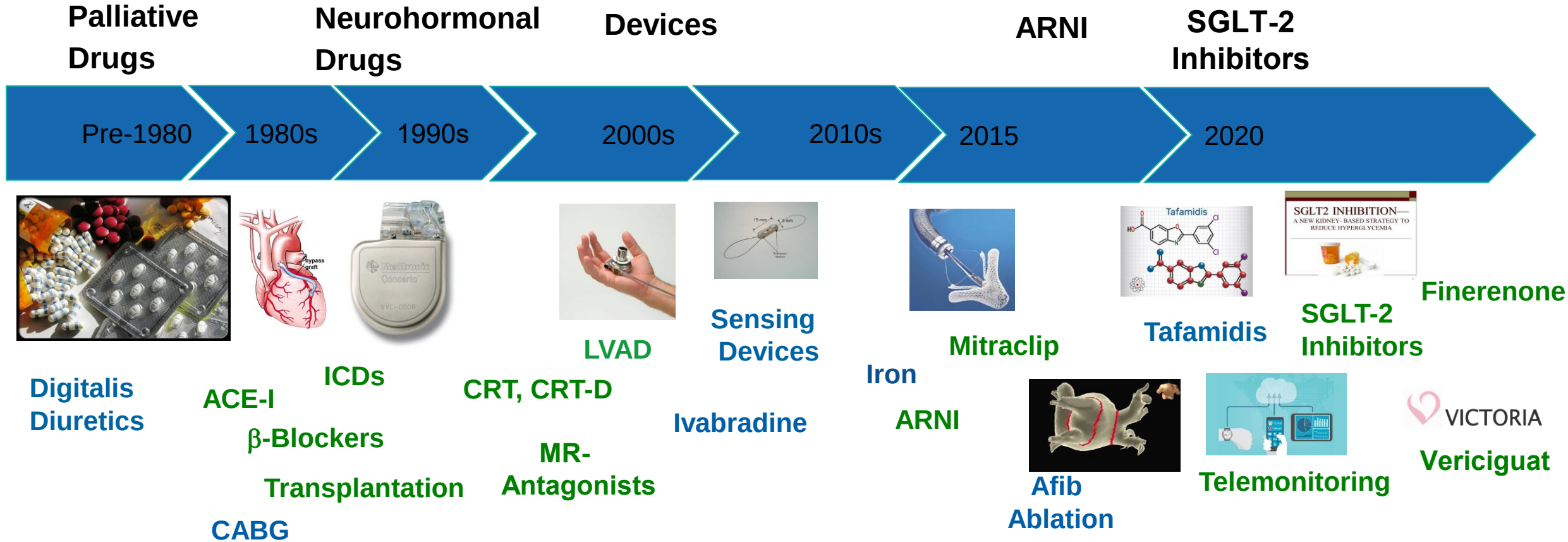
Treatment of HFpEF – Update 2023



MRA?

(R)evolution der Herzinsuffizienz-Therapie

Drugs, Devices, Interventions





**Danke für die
Aufmerksamkeit!**

Prof. Dr. med. Andreas Flammer
Kardiologie
Universitätsspital Zürich
andreas.flammer@usz.ch

Vereinfachte COAPT Kriterien

YES

COAPT criteria

Indication CoR IIa LoE B for M-TEER in SMR

NO

- Severe SMR
- Optimised HF treatments according to 2021 ESC guidelines
- NYHA Class II, III or ambulatory IV
- LVEF 20-50%
- LV end-systolic diameter ≤ 70 mm
- At least one HF hospitalisation within the previous year or increased NP levels^a
- Anatomy judged suitable for M-TEER^b

- Haemodynamic instability^c
- Stage D HF^d
- Moderate or severe RV dysfunction
- Systolic pulmonary pressure >70 mmHg
- COPD requiring oxygen or steroid
- Coronary, aortic or tricuspid valve disease requiring surgery
- Hypertrophic, restrictive or infiltrative cardiomyopathy

^aBNP ≥ 300 pg/ml or NT-proBNP $\geq 1,500$ pg/ml

^bincluding MVA >4.0 cm²

^csystolic pressure ≤ 90 mmHg, cardiogenic shock or the need for inotropic and/or mechanical supports

^dACC/AHA classification.

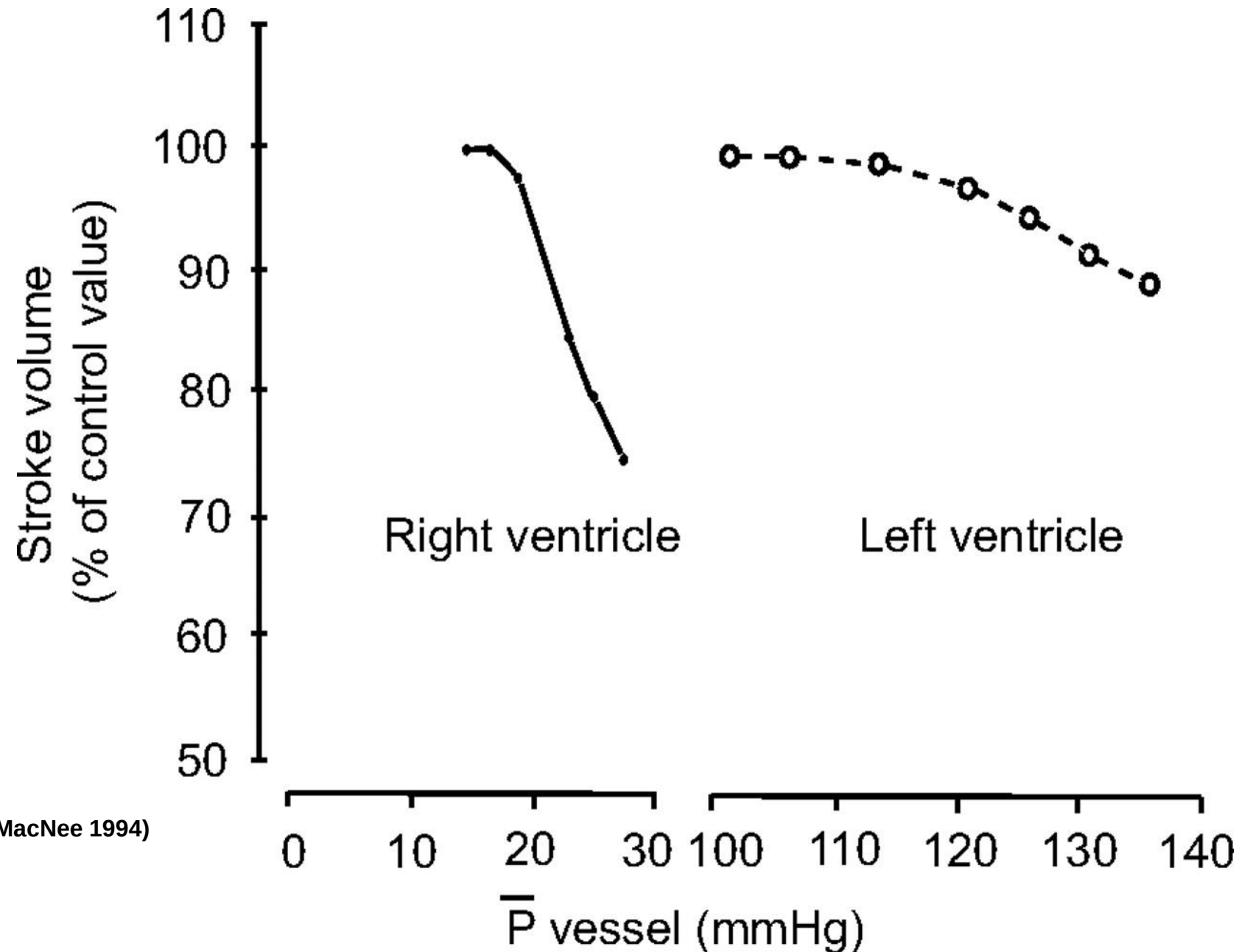
State-of-the-Art
Review

Hausleiter J et al,
Eurointervention
2023

ENTSCHEIDEND: Der rechte Ventrikel

Das dünne Myokard (1/3 des linken Ventrikels) ist flexibler, um große Schwankungen im venösen Rückfluss auszugleichen, **ABER ES HAT EINE ERHÖHTE EMPFINDLICHKEIT GEGENÜBER VERÄNDERUNGEN IM NACHLAST**

-> TR (Trikuspidalinsuffizienz) wird besser toleriert als eine erhöhte Nachlast aufgrund von linksseitiger Herzerkrankung.



François Haddad et al. Circulation. 2008 (Original MacNee 1994)