Azərbaycan
Kardiologiya
Cəmiyyəti

İleri Evre Kalp Yetersizliği Hastalarında Mekanik Destek Cihazı / Kalp Transplantasyonu Kime ? Ne zaman?

Prof Dr Sanem Nalbantgil, FESC, FHFA

Ege Üniversitesi Kardiyoloji AD

İzmir

2023 Haziran / Bakü

JACC: HEART FAILURE
VOL. 9, NO. 10, 2021

PUBLISHED BY ELSEVIER

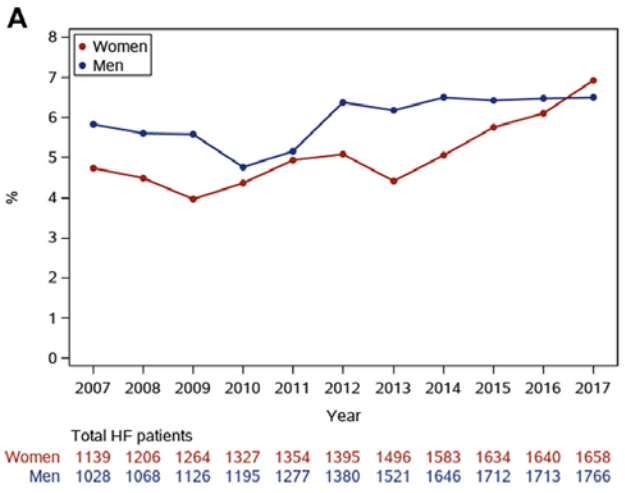
Advanced Heart Failure Epidemiology and Outcomes

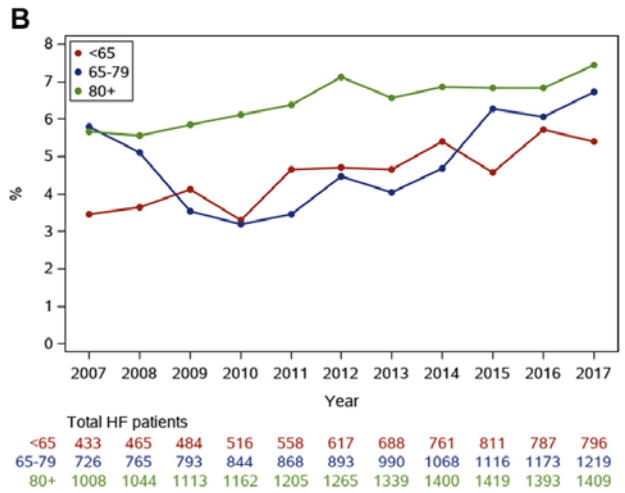
A Population-Based Study

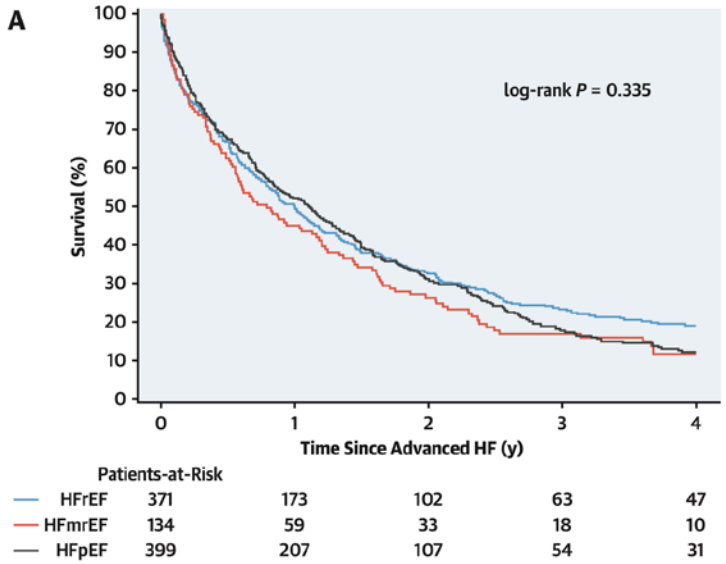
6836 hasta: %13.7 ileri evre KY hastası

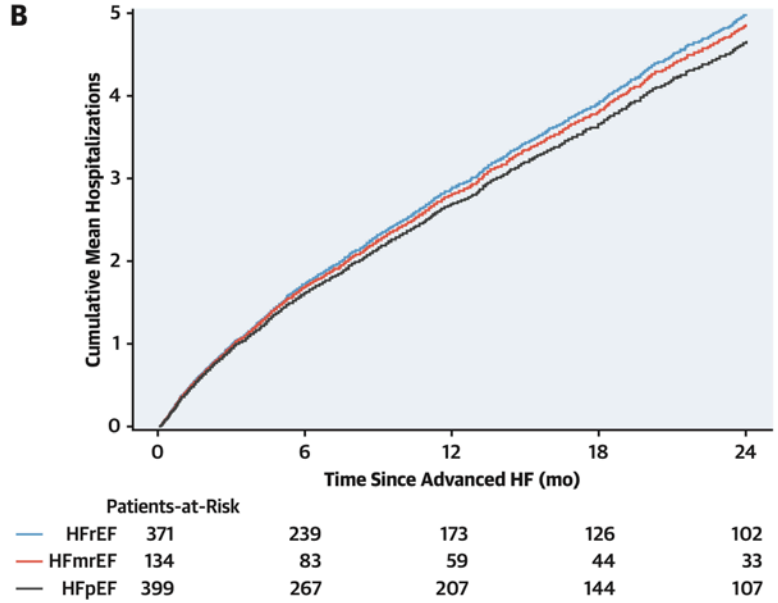
%42.3: DEF-KY, %14.3: HaEF-KY, %43.4:KEF-KY

Tanıdan ölüme kadar geçen süre: 12.2 ay

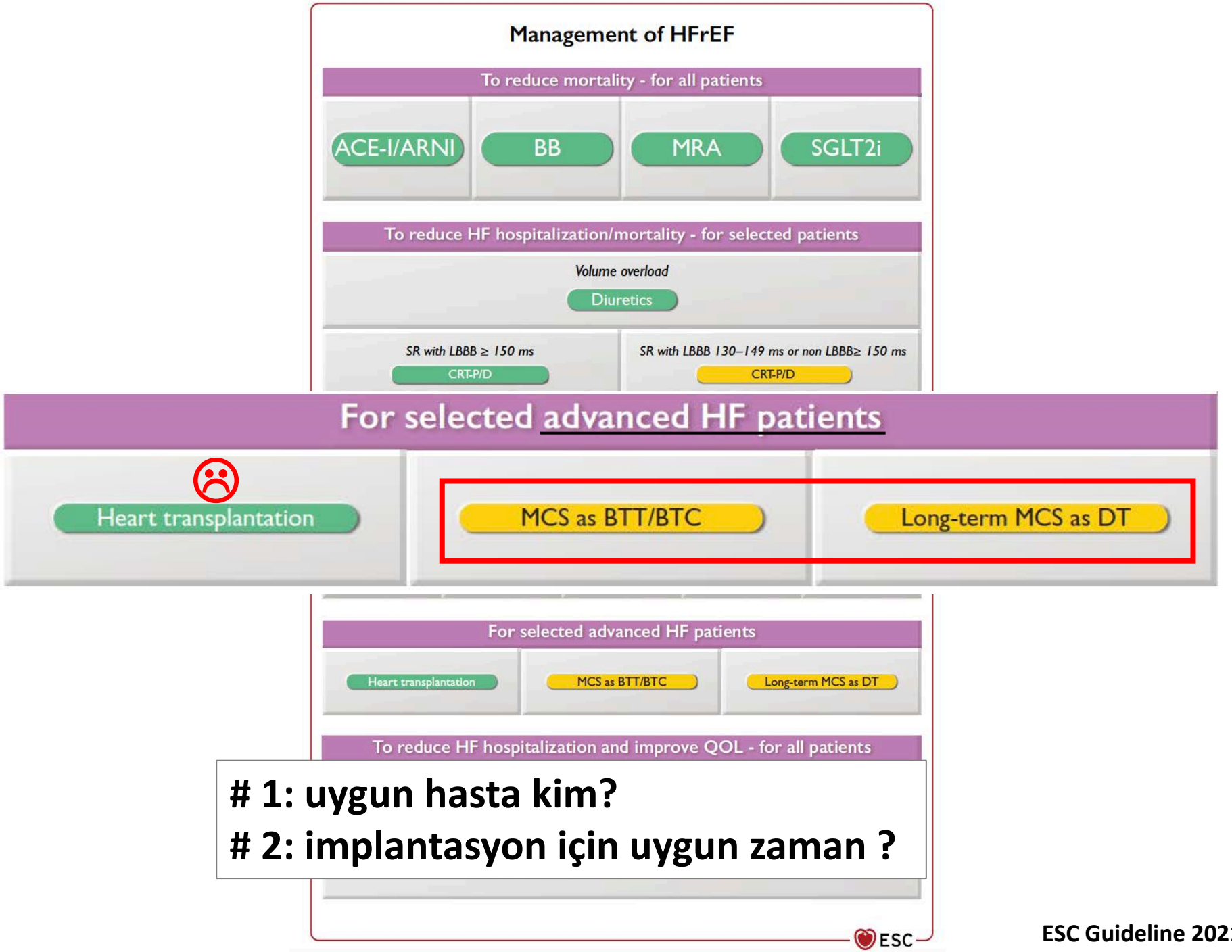








Dunlay SM et al. J Am Coll Cardiol HF. 2021;9(10):722-732



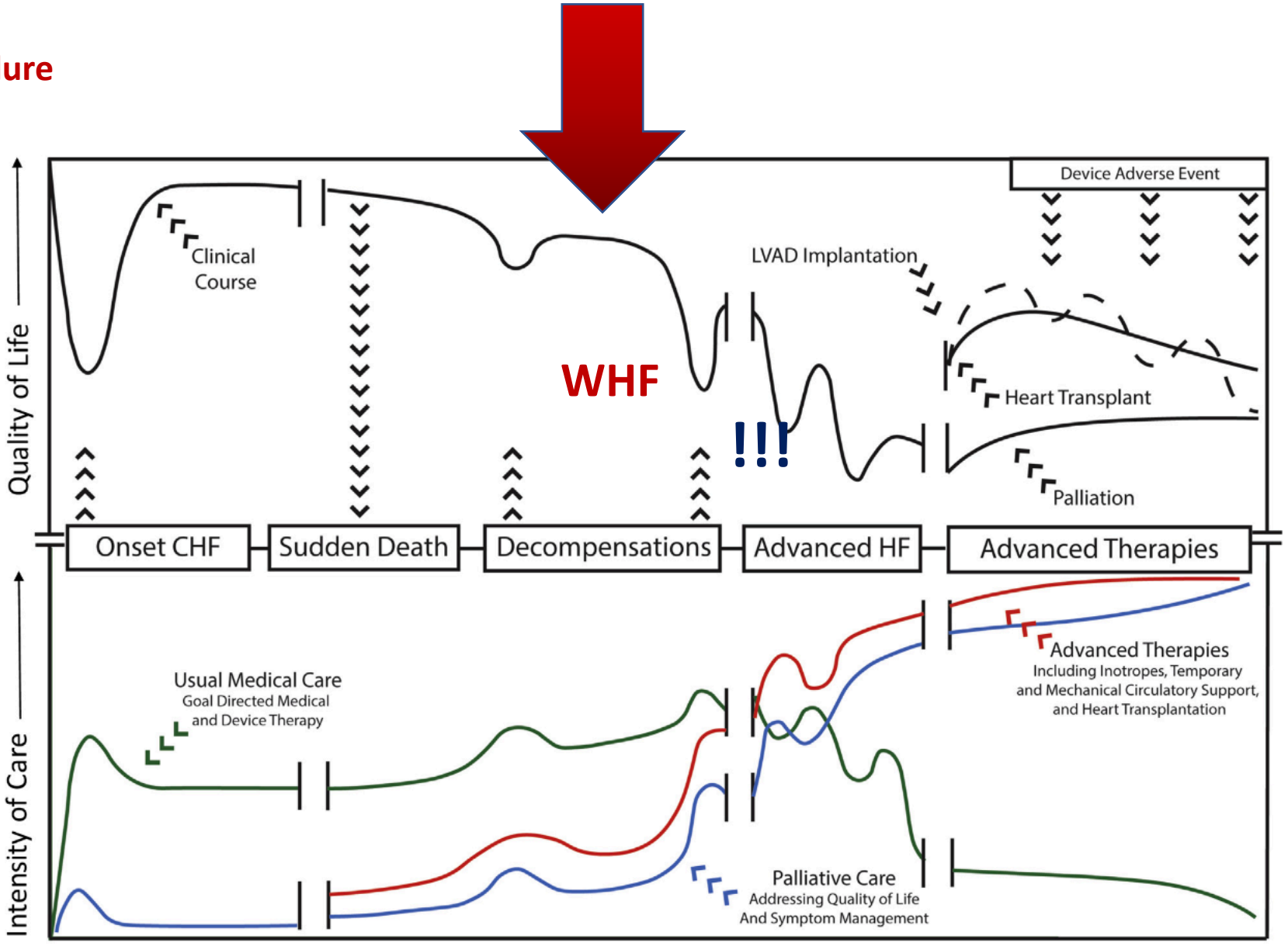
 # 1: uygun hasta kim?

 # 2: implantasyon için uygun zaman ?

ESC Guideline 2021

Worsening heart failure

I NEED HELP



Truby LK. JACC Heart Failure 2020;8(7):523-536

JACC 2023;81:413-424

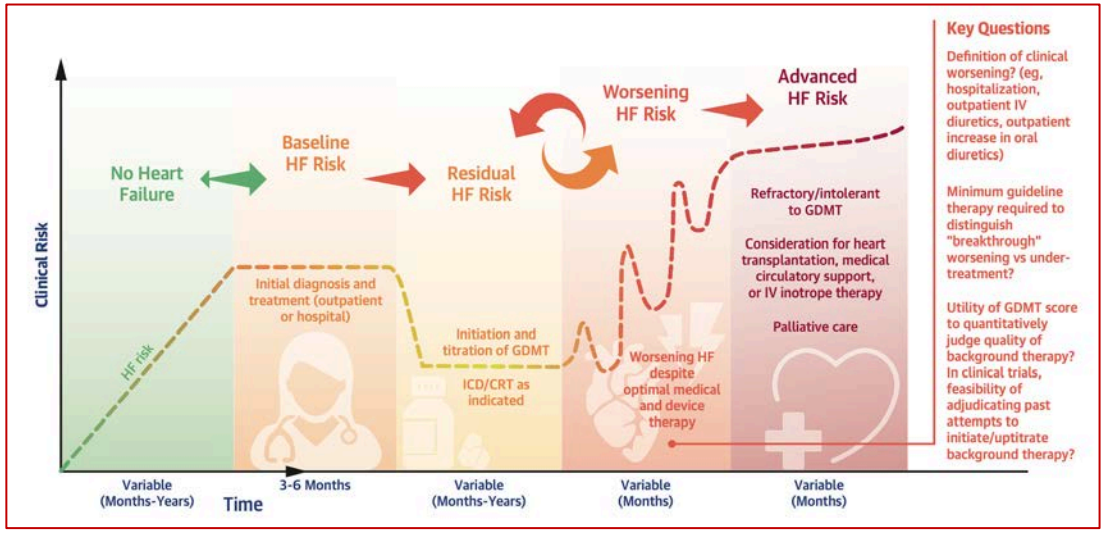
JACC REVIEW TOPIC OF THE WEEK

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week

Stephen J. Greene, MD,[a,b] Johann Bauersachs, MD,[c] Jasper J. Brugts, MD, MSc, PhD,[d] Justin A. Ezekowitz, MBBCh, MSc,[e] Carolyn S.P. Lam, MBBS, PhD,[f] Lars H. Lund, MD, PhD,[g] Piotr Ponikowski, MD, PhD,[h] Adriaan A. Voors, MD, PhD,[i] Faiez Zannad, MD, PhD,[j,k] Shelley Zieroth, MD,[l] Javed Butler, MD, MPH, MBA[m,n]

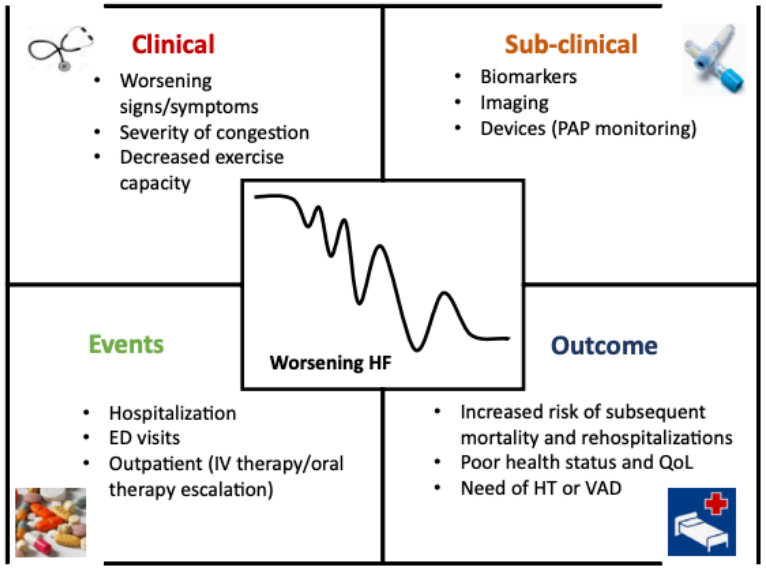
Current Definition:
- Deterioration of HF signs and symptoms in a patient with chronic HF, despite previous stable background therapy
- Requires urgent escalation of therapy, including hospitalization, ED visit, or outpatient IV diuretic therapy, ± outpatient oral therapy*



ESC European Society of Cardiology
European Journal of Heart Failure (2023)
doi:10.1002/ejhf.2874

POSITION PAPER

Worsening of chronic heart failure: definition, epidemiology, management and prevention. A clinical consensus statement by the Heart Failure Association of the European Society of Cardiology



Circulation

ORIGINAL RESEARCH ARTICLE

Effect of Dapagliflozin on Outpatient Worsening of Patients With Heart Failure and Reduced Ejection Fraction

A Prespecified Analysis of DAPA-HF

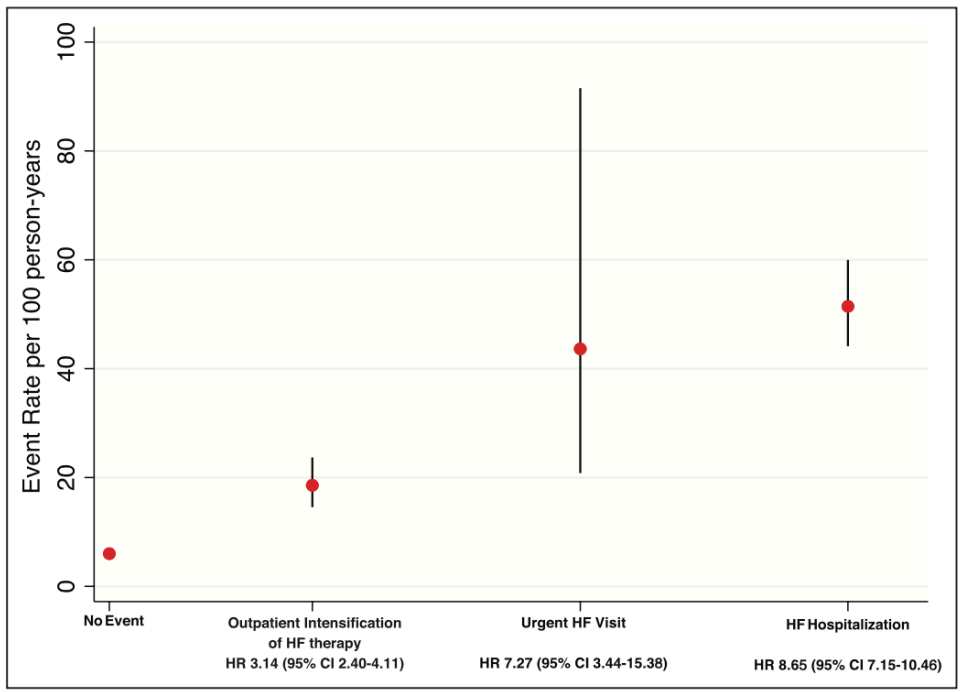


Figure 3. Rate and risk of all-cause mortality after a first nonfatal heart failure worsening event.
The risk of each death from any cause relative to patient not experiencing an event after a first nonfatal heart failure worsening event is calculated by using Cox regression models with the event entered in the model as a time-updated covariate. HF indicates heart failure; and HR, hazard ratio.

Circulation 2020;142:1623-1632

‘I Need Help’ – Markers of Advanced Heart Failure

I	**I**notropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
N	**N**YHA class/ natriuretic peptide	Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP
E	**E**nd-organ dysfunction	Worsening renal or liver dysfunction in the setting of heart failure
E	**E**jection fraction	Very low ejection fraction <20%
D	**D**efibrillator shocks	Recurrent appropriate defibrillator shocks
H	**H**ospitalizations	More than 1 hospitalization with heart failure in the last 12 months
E	**E**dema/escalating diuretics	Persisting fluid overload and/or increasing diuretic requirement
L	**L**ow blood pressure	Consistently low BP with systolic <90 to 100 mmHg
P	**P**rognostic medication	Inability to up-titrate (or need to decrease/cease) ACEI, beta-blockers, ARNIs, or MRAs

HFA Position Paper 2018

Hasta *refere etmek* için önerilen klinik, laboratuvar, ve ekokardiyografik kriterler

Klinik bulgu

-Son 1 yılda >1 hosp.
-NYHA III – IV
-OMT ilaçlarına intol.
-Artan diüretik ihtiyacı
-sKB ≤ 90 mmHg
-6DYT < 300 m
-KPET yapamama
-CRT nonresponder
-Kaşeksi, istem dışı kilo kaybı
-KCCQ
-MLHFQ

Laboratuar

-eGFR < 45 mL/dk
-S Krtn > 160 mmol/L
-K > 5.2/ K < 3.5 mmol/l
-Hiponatremi
-Hb < 12 g/L
-NTproBNP ≥ 1000µg/mL
-bozuk KCFT
-düşük albumin

Görüntüleme

-LVEF ≤ % 30
-geniş alanı içeren akinezi, anevrizma
-modere-ciddi MY
-RV disfonksiyonu
-PAB ≥ 50 mmHg
-modere-ciddi TY
-derecelendirmesi güç AS
-dilate VCİ

Risk Skoru

-MAGGIC 1 yıl sağkalım ≤ %80
-SFHM 1 yıl sağkalım ≤ % 80

HFA Position Paper 2018

İleri evre kalp yetersizliği için ESC-HFA'nın yeni tanımı

All the following criteria must be present despite optimal guideline-directed treatment:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by a reduced LVEF ≤30%, isolated RV failure (e.g. ARVC) or non-operable severe valve abnormalities or congenital abnormalities or persistently high (or increasing) BNP or NT-proBNP values and data of severe diastolic dysfunction or LV structural abnormalities according to the ESC definition of HFpEF and HFmrEF.[9]
3. Episodes of pulmonary or systemic congestion requiring high-dose intravenous diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.
4. Severe impairment of exercise capacity with inability to exercise or low 6MWTD (<300 m) or pVO_2 (<12–14 mL/kg/min), estimated to be of cardiac origin.

In addition to the above, extra-cardiac organ dysfunction due to heart failure (e.g. cardiac cachexia, liver, or kidney dysfunction) or type 2 pulmonary hypertension may be present, but are not required.

Criteria 1 and 4 can be met in patients who have cardiac dysfunction (as described in criterion #2), but who also have substantial limitation due to other conditions (e.g. severe pulmonary disease, non-cardiac cirrhosis, or most commonly by renal disease with mixed aetiology). These patients still have limited quality of life and survival due to advanced disease and warrant the same intensity of evaluation as someone in whom the only disease is cardiac, but the therapeutic options for these patients are usually more limited.

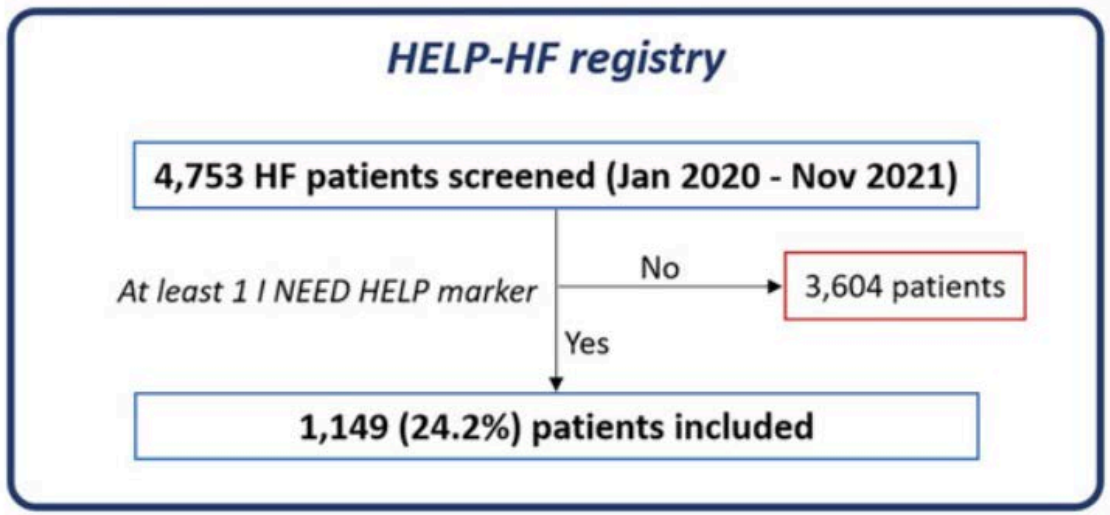
HFA Position Paper 2018

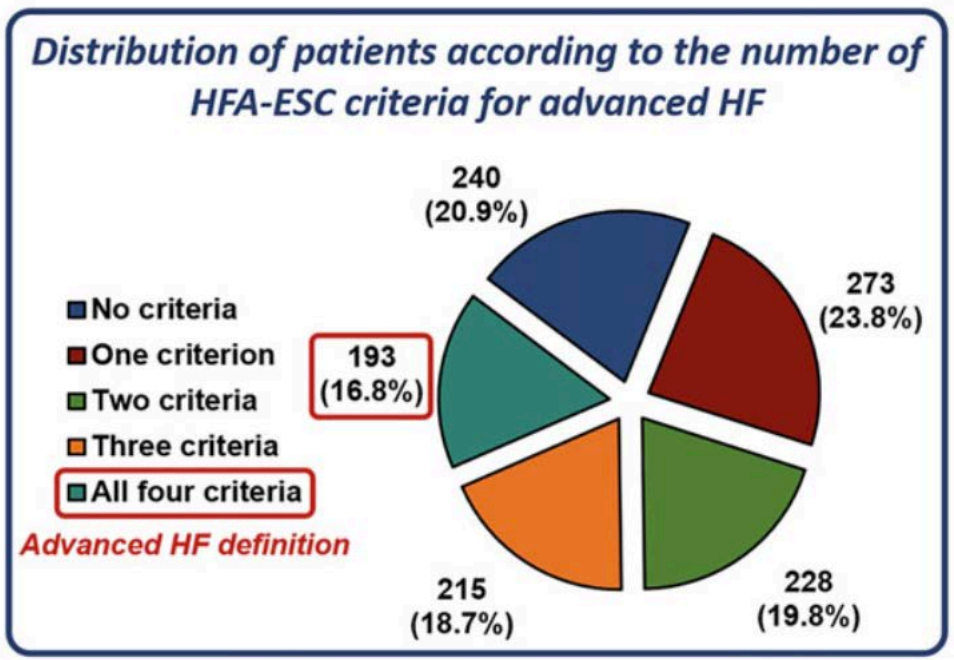
ESC European Society of Cardiology

European Journal of Heart Failure (2022) **24**, 1493–1503
doi:10.1002/ejhf.2561

RESEARCH ARTICLE

Prognostic impact of the updated 2018 HFA-ESC definition of advanced heart failure: results from the HELP-HF registry





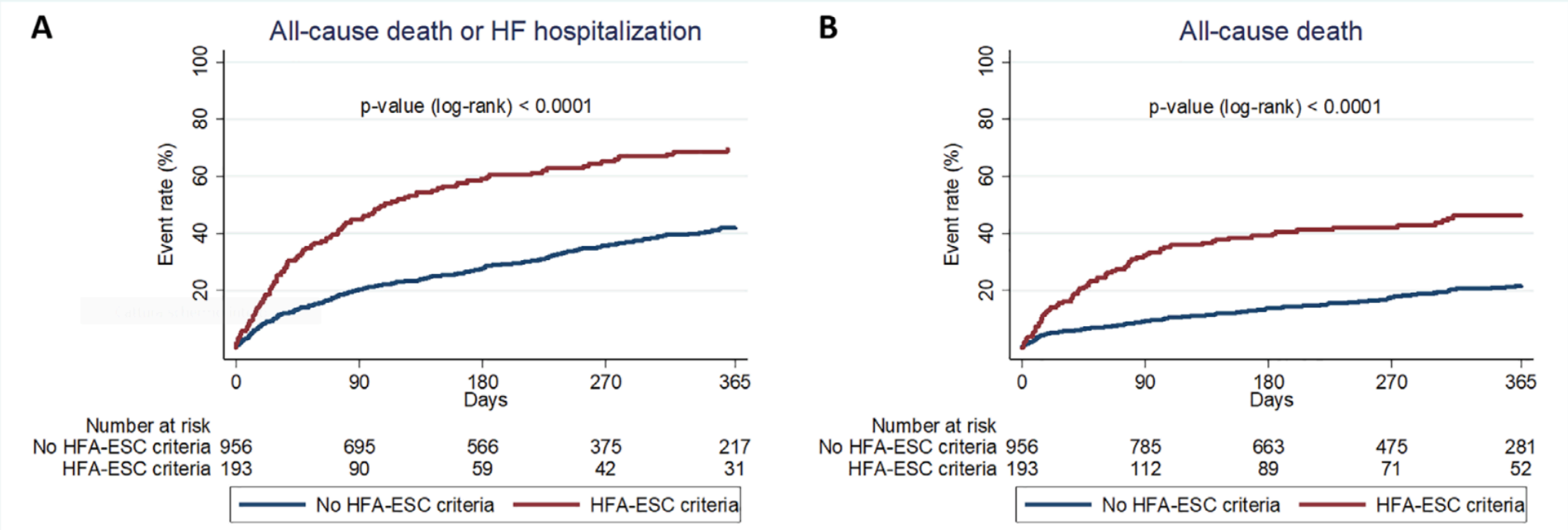


Figure 1 Primary composite endpoint and all-cause mortality at 1 year in patients with versus without advanced heart failure (HF) definition according to the 2018 Heart Failure Association of the European Society of Cardiology (HFA-ESC) criteria. The figure shows Kaplan–Meier curves for 1-year primary composite endpoint of all-cause mortality or HF hospitalization (*A*) and Kaplan–Meier curves for 1-year all-cause mortality (*B*) in patients with versus without advanced HF definition according to the 2018 HFA-ESC criteria (i.e. meeting vs. not meeting all four 2018 HFA-ESC criteria).

Table 3 Impact of each 2018 HFA-ESC criterion of advanced heart failure on clinical outcomes

	All-cause death or HF hospitalization (primary endpoint)		All-cause death		First HF hospitalization	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	SHR (95% CI)	*p*-value
Criterion 1 (severe/persistent symptoms)						
Univariable analysis	1.64 (1.38–1.96)	**<0.001**	2.03 (1.59–2.59)	**<0.001**	1.40 (1.12–1.75)	**0.003**
Multivariable analysis	1.44 (1.17–1.77)[a]	**0.001**	1.69 (1.27–2.25)[b]	**<0.001**	1.25 (0.97–1.62)[c]	0.089
Criterion 2 (severe cardiac dysfunction)						
Univariable analysis	1.23 (1.03–1.47)	**0.025**	1.46 (1.14–1.88)	**0.003**	1.12 (0.89–1.40)	0.342
Multivariable analysis	1.18 (0.97–1.43)[a]	0.098	1.36 (1.03–1.79)[b]	**0.032**	1.10 (0.85–1.41)[c]	0.486
Criterion 3 (>1 unplanned visit/hospitalization in the last year for episodes of congestion, LCOS or arrhythmias)						
Univariable analysis	1.54 (1.31–1.81)	**<0.001**	1.70 (1.37–2.12)	**<0.001**	1.34 (1.07–1.68)	**0.010**
Multivariable analysis	1.55 (1.28–1.87)[a]	**<0.001**	1.55 (1.19–2.01)[b]	**0.001**	1.33 (1.05–1.67)[c]	**0.018**
Criterion 4 (inability to exercise or low 6MWTD)						
Univariable analysis	1.76 (1.48–2.11)	**<0.001**	2.38 (1.86–3.05)	**<0.001**	1.37 (1.09–1.71)	**0.006**
Multivariable analysis	1.58 (1.29–1.92)[a]	**<0.001**	2.03 (1.54–2.68)[b]	**<0.001**	1.24 (0.97–1.59)[c]	0.088

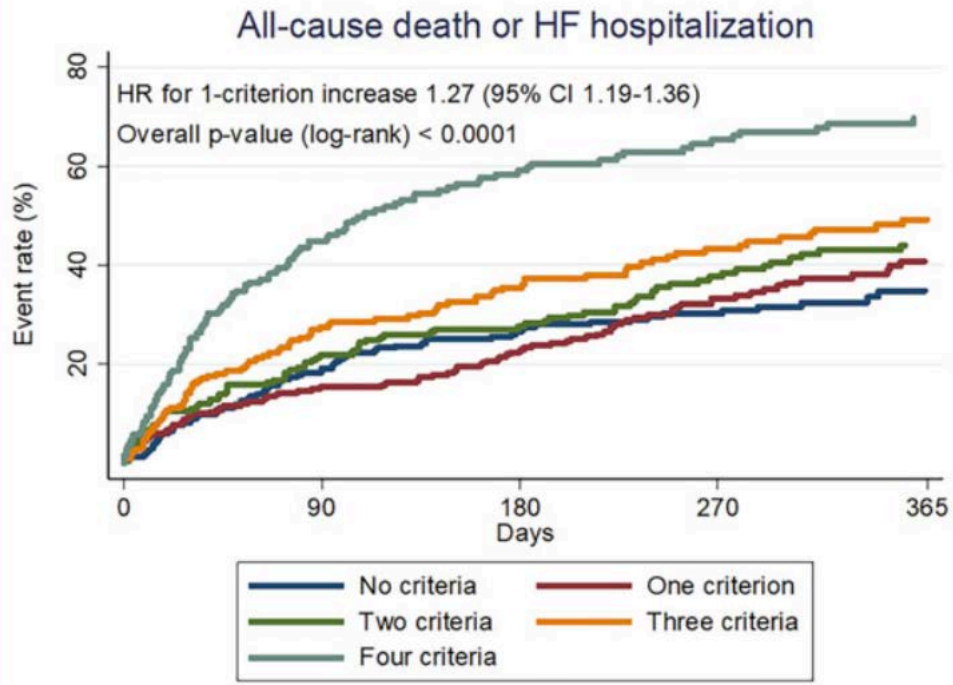
6MWTD, 6-min walking test distance; CI, confidence interval; HFA-ESC, Heart Failure Association of the European Society of Cardiology; HF, heart failure; HR, hazard ratio; LCOS, low cardiac output syndrome; SHR, subhazard ratio.

[a]Adjusted for age, sex, inpatient versus outpatient status, peripheral artery disease, prior stroke or transient ischaemic attack, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, New York Heart Association class III–IV, systolic blood pressure and estimated glomerular filtration rate.

[b]Adjusted for age, sex, inpatient versus outpatient status, peripheral artery disease, prior stroke or transient ischaemic attack, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, New York Heart Association class III–IV, systolic blood pressure, heart rate and estimated glomerular filtration rate.

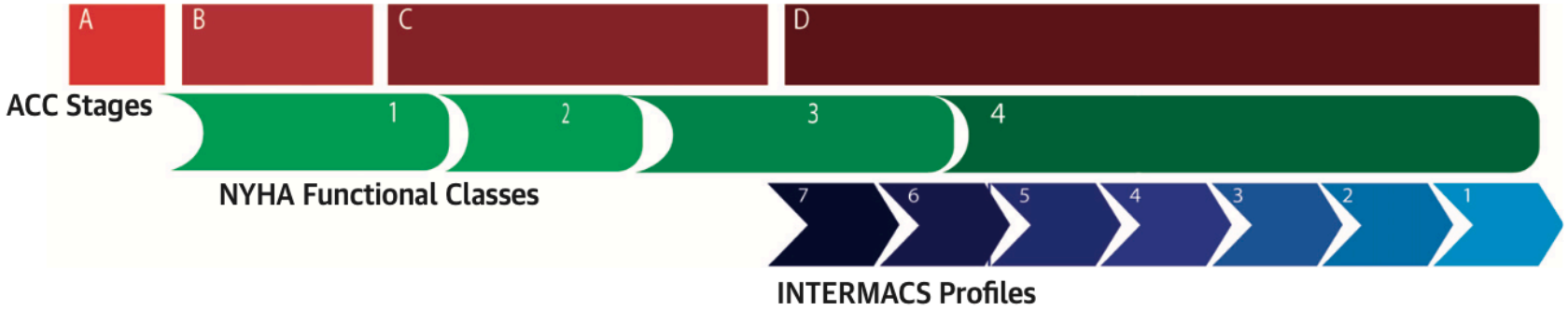
[c]Adjusted for age, sex, history of atrial fibrillation, prior myocardial infarction, chronic obstructive pulmonary disease, New York Heart Association class III–IV, left ventricular ejection fraction <40% and estimated glomerular filtration rate.

Prognostic impact of the HFA-ESC advanced HF definition on the primary composite endpoint



	1-year KM rate	Adjusted HR (95% CI)	p-value
No criteria	34.8%	*Reference*	*Reference*
One criterion	40.4%	1.09 (0.80-1.48)	0.582
Two criteria	44.2%	1.25 (0.92-1.71)	0.160
Three criteria	49.1%	1.40 (1.02-1.91)	**0.038**
Four criteria	69.3%	2.40 (1.74-3.30)	**<0.001**

INTERMACS SINIFLAMASI



UPDATES IN CARDIOLOGY
JOURNAL OF THE TURKISH SOCIETY OF CARDIOLOGY
KARDİYOLOJİ GÜNCELLEMELERİ
TÜRK KARDİYOLOJİ DERNEĞİ DERGİSİ

INTERMACS	1	2	3	4	5	6	7
	Kardiyojenik şok	Giderek kötüleşme	Stabil ama inotrop bağımlı	İstirahatte yakınmalar	Egzersiz entoleransı	Egzersiz kısıtlaması	İleri evre KY
	"Umutsuzlar"	"İnotropa rağmen kötüye gidenler"	"İnotrop bağımlı stabiller"	"Bir ayağı hastanede olanlar"	"Eve bağımlılar"	"Zor yürüyenler"	"Belirsizler"
Hastanın tanımı	İnotrop tedavi ve mekanik destek cihazlarına rağmen hayatı tehdit edici organ perfüzyon bozukluğu mevcuttur	İnotrop tedavi ile KB korunsa da, böbrek işlevleri, beslenme ve konjesyon bulgularında ilerleyici kötüleşme mevcuttur	Düşük-orta doz inotrop tedavi ile stabil olmakla birlikte, tedavi kesilmesiyle böbrek işlevleri, beslenme ve konjesyon bulgularında kötüleşme olur	İnotrop tedaviye ara verilebilse de, tekrarlayan belirti ve bulgularla sık hastaye başvurur	İstirahatte yakınmasız olmakla birlikte, efor yapamaz ve KY belirti ve bulguları kısmen devam etmektedir	Çabuk yorulmakla birlikte, hafif eforu yapabilir ve istirahatte konjesyon bulguları yoktur	Fonksiyonel kapasitesi NYHA III'dür ve yakın zamanda KY bulgu ve belirtileri tekrarlamamıştır
ACC/AHA sınıflaması	Evre D			Evre C			
NYHA sınıflaması[1]	IV			Ambulatuvar IV	Ambulatuvar IV	IIIB	IIIA

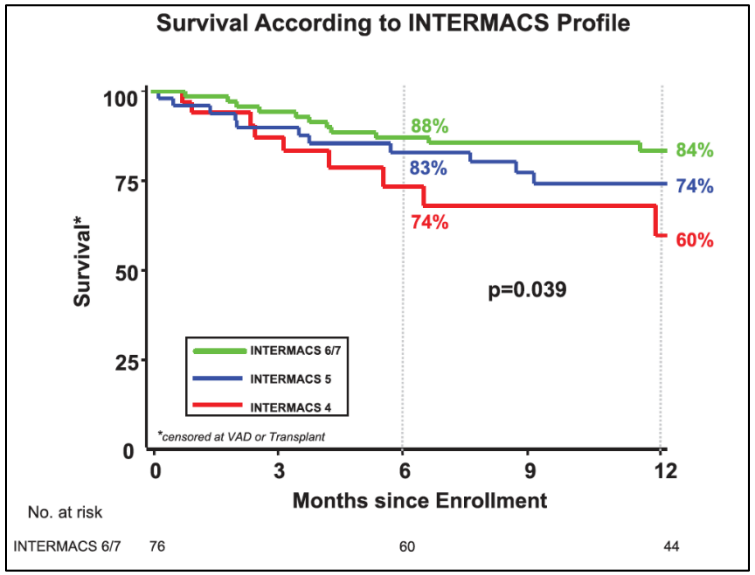
'ileri kalp yetersizliği rehberi'
TKD Arşivi 2018 suppl

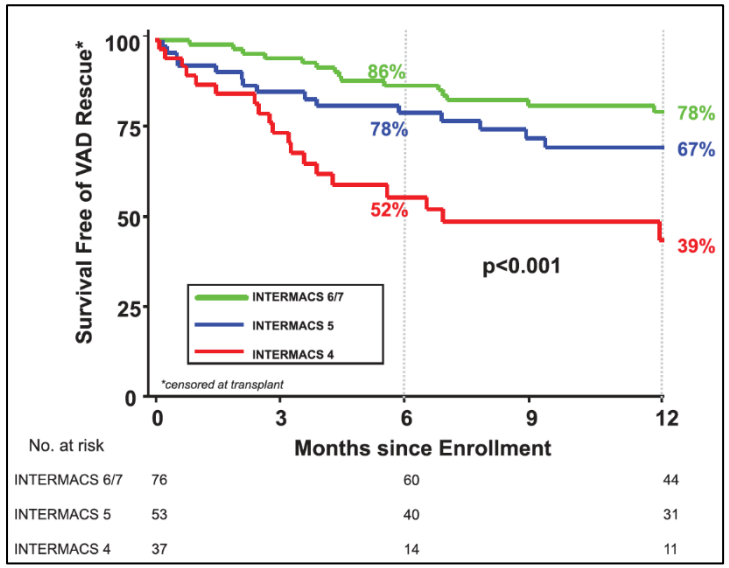
INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) Profiling Identifies Ambulatory Patients at High Risk on Medical Therapy After Hospitalizations for Heart Failure

Stewart GC, Circ Heart Fail 2016

%47 OMT ile hayatta
%23 ölüm
%15 LT-LVAD
%15 Tx

Profile	Shorthand	Definition
4 22%	Resting symptoms	At home on oral therapy but with frequent symptoms of congestion at rest or with any activities of daily living
5 32%	Exertion intolerant	Comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound, but without overt congestion
6 34%	Exertion limited	Comfortable at rest without evidence of fluid overload and able to do some mild activities of daily living, but gets fatigued within a few minutes of any meaningful exertion
7 12%	Advanced NHYA class III	Clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent





INTERMACS 4: % 48 ölüm ve ya 'rescue' LVAD @ 6 ay
INTERMACS 5: % 22 ölüm ve ya 'rescue' LVAD @ 6 ay

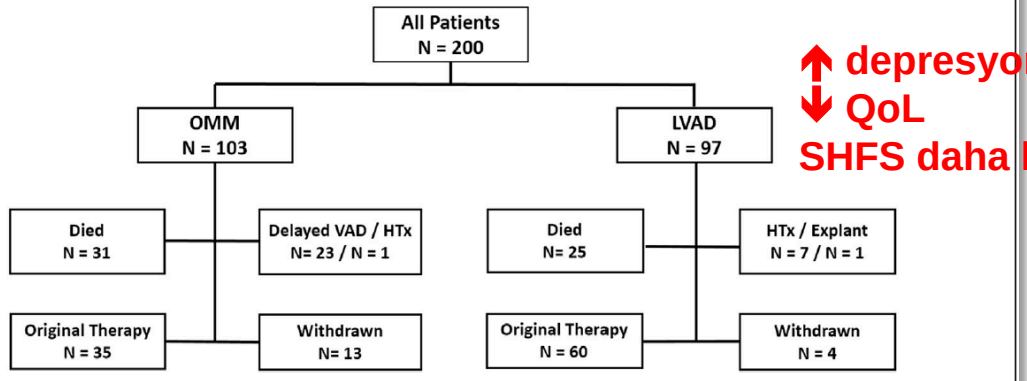
Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients

The ROADMAP Study 2-Year Results

Starling RC et al. JACC Heart Failure 2017

NYHA IIIB/IV
6 DYT < 300 m
≥ 1 hospitalizasyon
LVEF < %25
OMT

FIGURE 1 Roadmap Study Patients at 2 Years



HTx = heart transplantation; LVAD = left ventricular assist device; OMM = optimal medical management; VAD = ventricular assist device.

↑ depresyon
↓ QoL
SHFS daha kötü

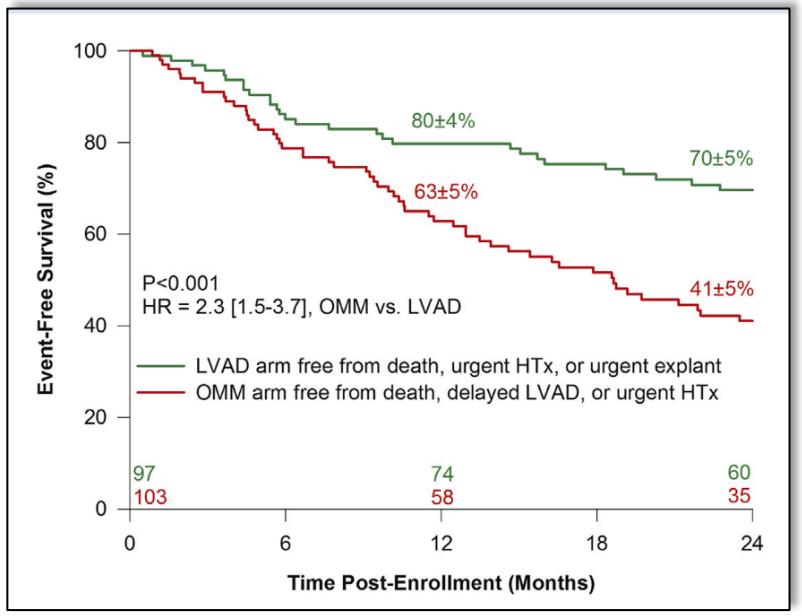
Primer sonlanım: sağ kalım ve 6 DYT'de > 75 m değişim

Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients

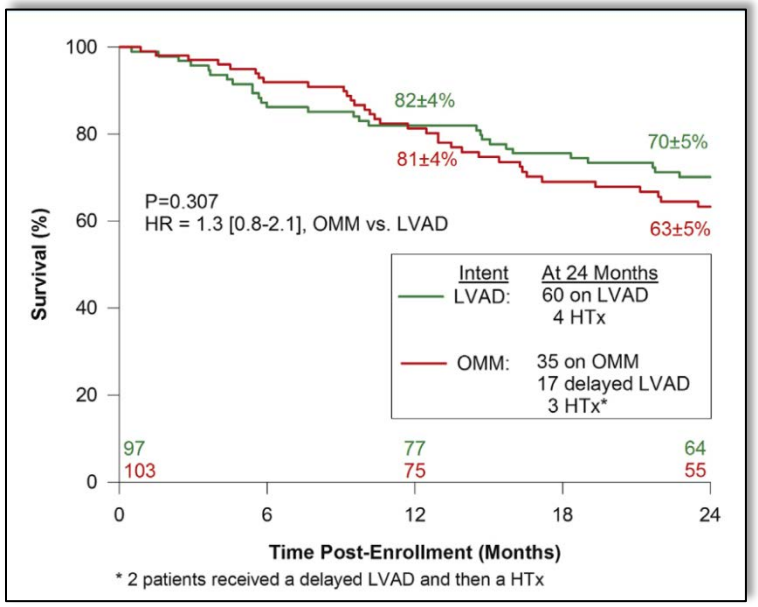
The ROADMAP Study 2-Year Results

Esteep JD et al. JACC 2015;66:1747
Starling RC et al. JACC Heart Failure 2017

survival as-treated



intention to treat



LVAD populasyonunda sağ kaılım ve 1. ve 2. yıllarda 6 DYT daha iyi
LVAD tedavisi ile hayat kalitesi ve depresif semptomlar daha iyi

Left ventricular assist devices versus medical management in ambulatory heart failure patients: An analysis of INTERMACS Profiles 4 and 5 to 7 from the ROADMAP study

Shah KB et al. JHLT 2018;37:706-714

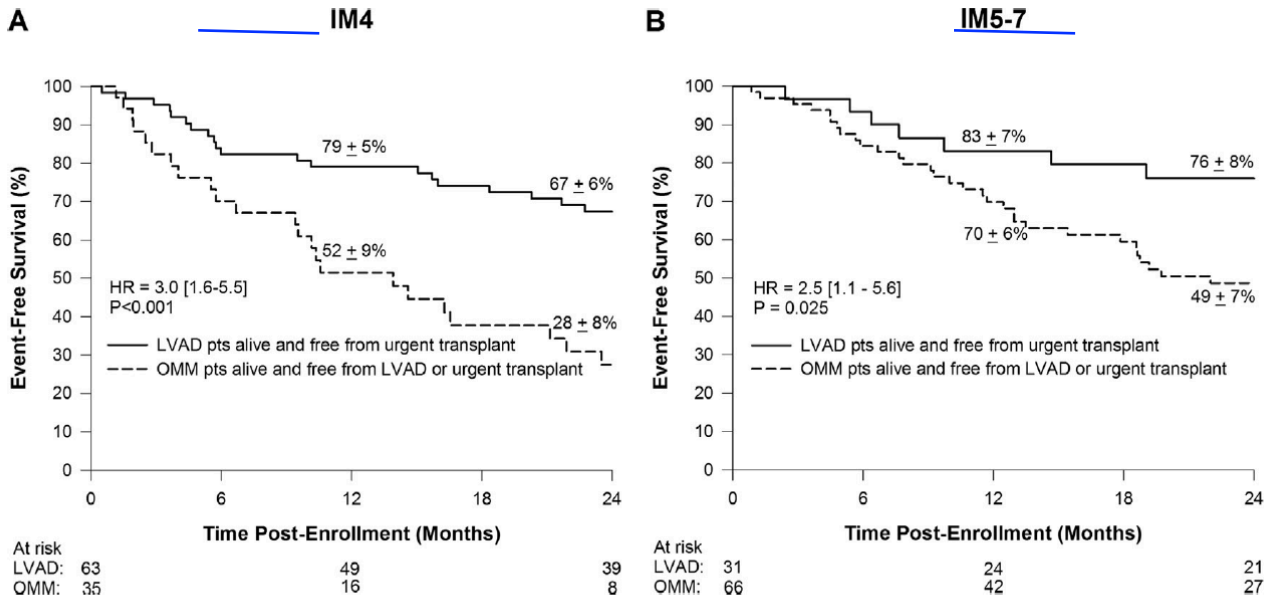


Figure 3 Survival as-treated on original therapy in INTERMACS Profile 4 (IM 4) and Profile 5 to 7 (IM 5-7) patients.

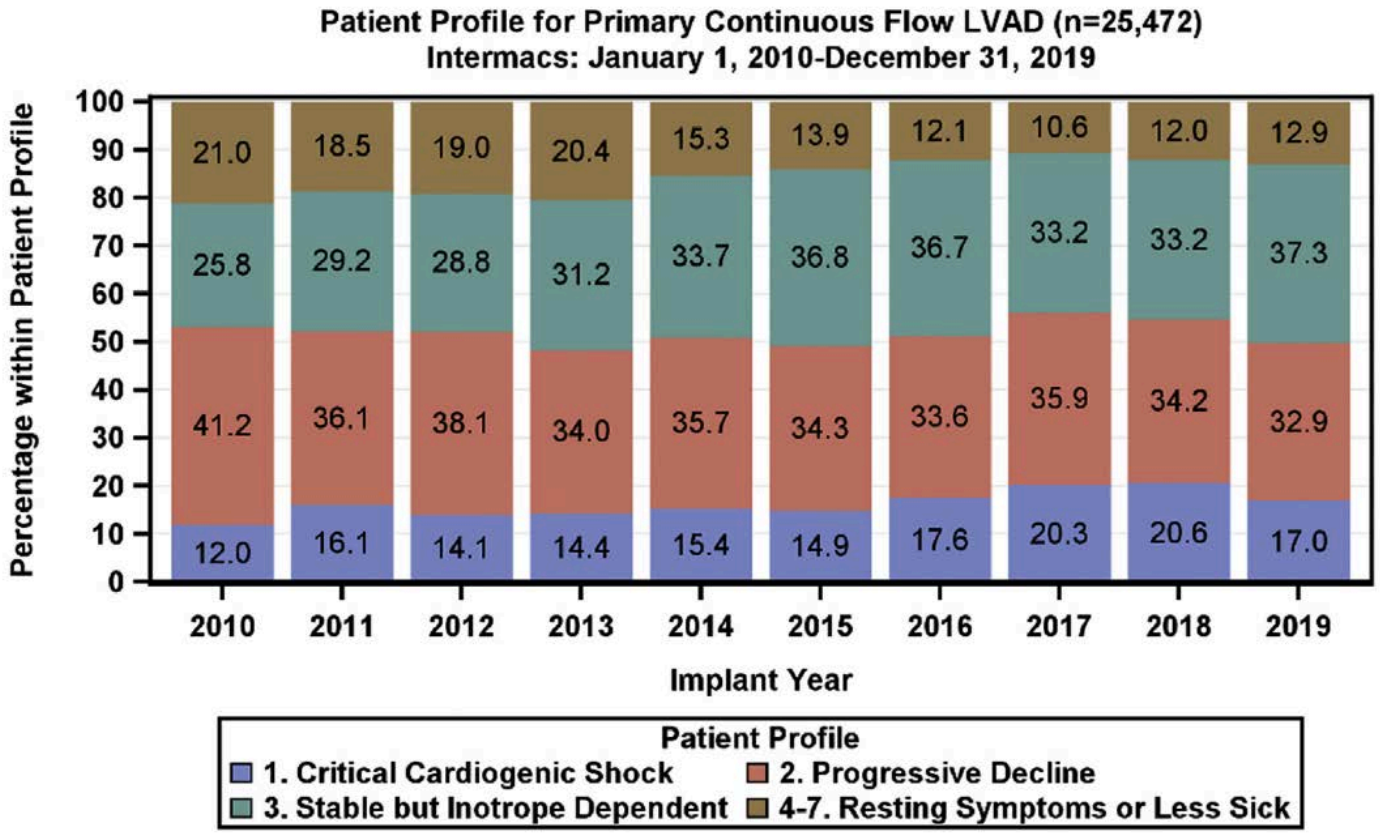
LVAD tedavisinin IM 4 olan hastalarda anlamlı olarak sağ kalımı etkilemiştir
OMT: yalnız %23 hasta 2 yılın sonunda hayatta kalmıştır (% 40 ölüm, %26% LVAD imp, %11 izlem yok)
LVAD: LVAD, IM4 hastalarında transplantasyona köprüleme amaçlı düşünülmelidir
IM 5-7 hastaları çok yakın takip edilmelidir

Uzun dönem MDC: LVAD

THE SOCIETY OF THORACIC SURGEONS INTERMACS ANNUAL REPORT

The Society of Thoracic Surgeons Intermacs 2020 Annual Report

Ezequiel J. Molina, MD, Palak Shah, MD, MS, Michael S. Kiernan, MD, MS, William K. Cornwell III, MD, MSCS, Hannah Copeland, MD, Koji Takeda, MD, PhD, Felix G. Fernandez, MD, Vinay Badhwar, MD, Robert H. Habib, PhD, Jeffrey P. Jacobs, MD, Devin Koehl, MSDS, James K. Kirklin, MD, Francis D. Pagani, MD, PhD, and Jennifer A. Cowger, MD, MS



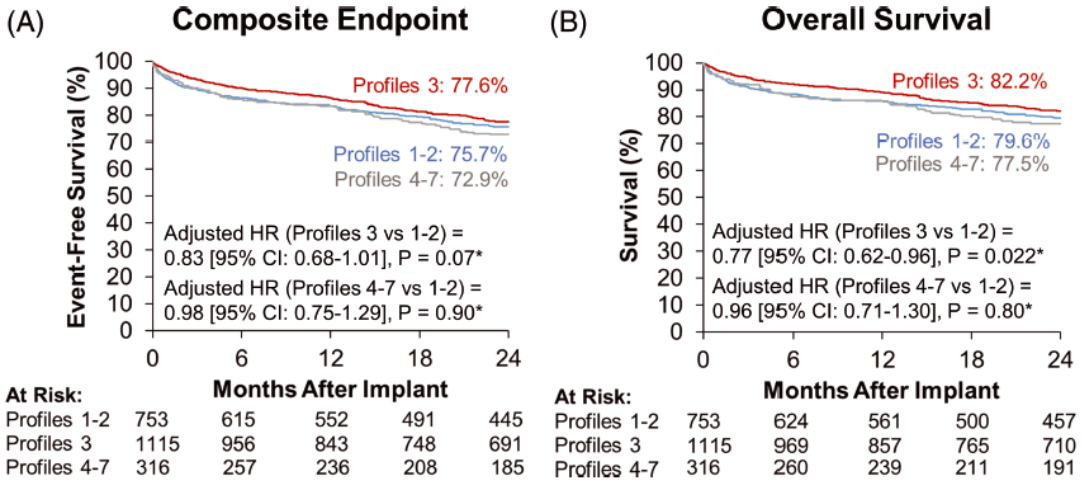
profiles 4-7 were less common in the more recent era

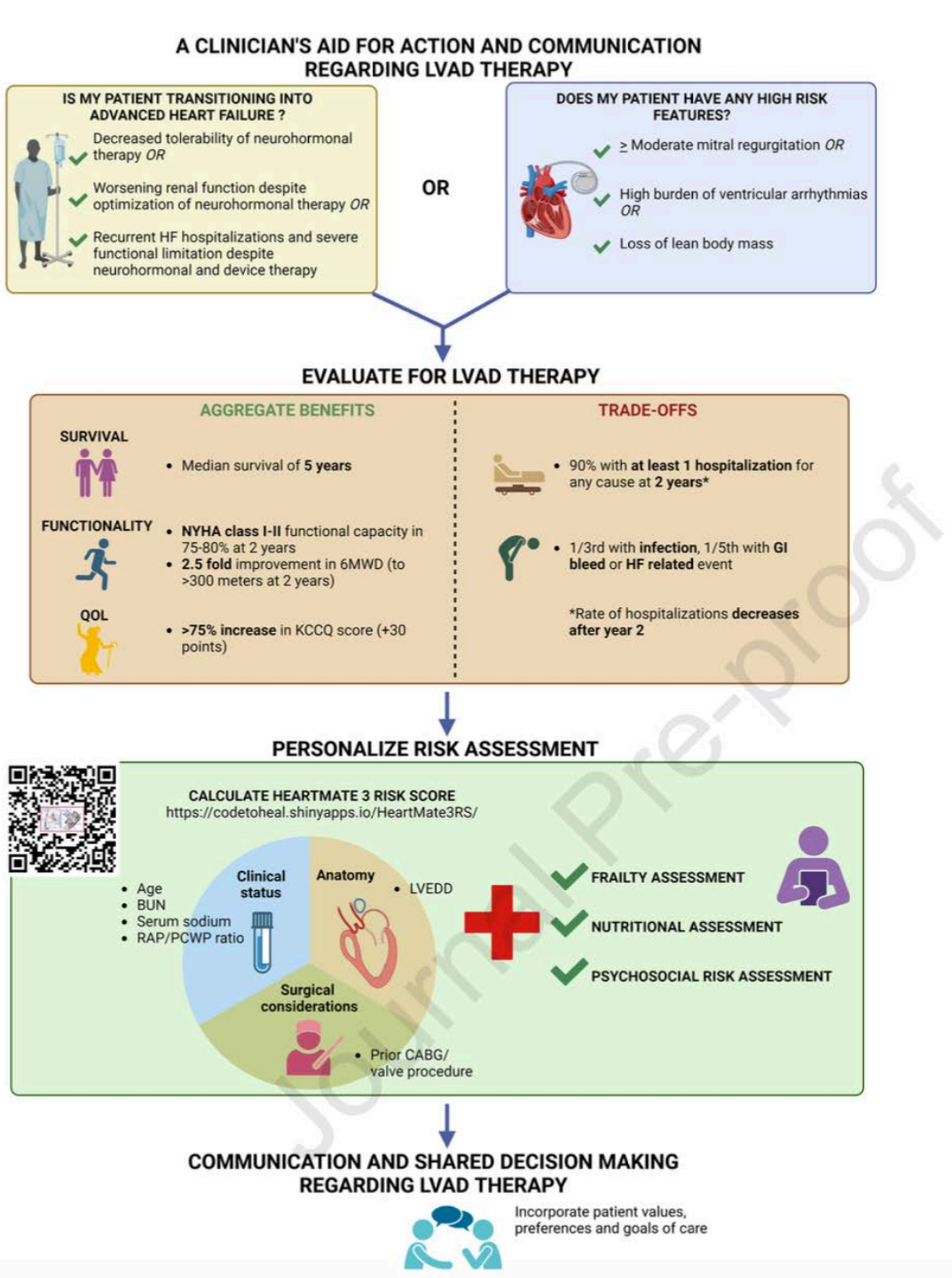
ESC European Society of Cardiology
European Journal of Heart Failure (2021) 23, 1392–1400
doi:10.1002/ejhf.2211

RESEARCH ARTICLE

Primary results of long-term outcomes in the MOMENTUM 3 pivotal trial and continued access protocol study phase: a study of 2200 HeartMate 3 left ventricular assist device implants

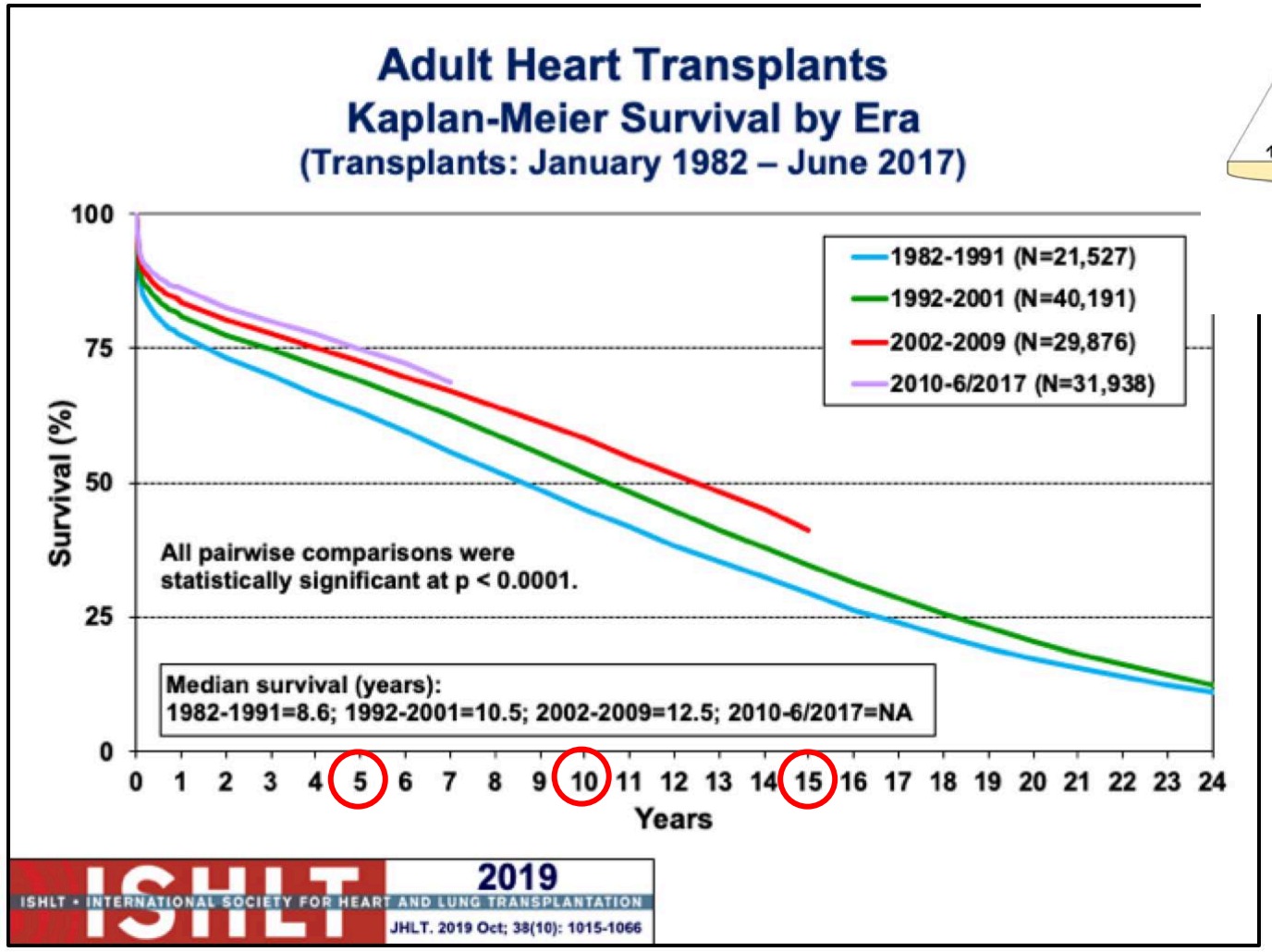
INTERMACS profile	pivotal cohort (n=515)	CAP cohort (n=1685)	p-value
1	11 (2.1%)	69 (4.1%)	0.036
2	156 (30.4%)	517 (31.0%)	0.79
3	272 (52.9%)	843 (50.5%)	0.33
4–7	75 (14.6%)	241 (14.3%)	0.88

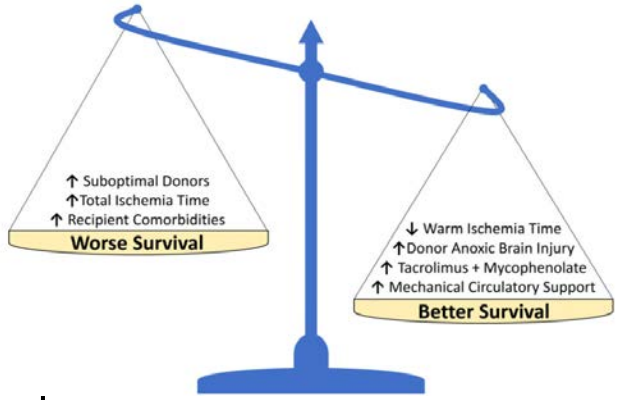




Mehra M, et al. doi.org/10.1016/j.jchf.2023.05.013

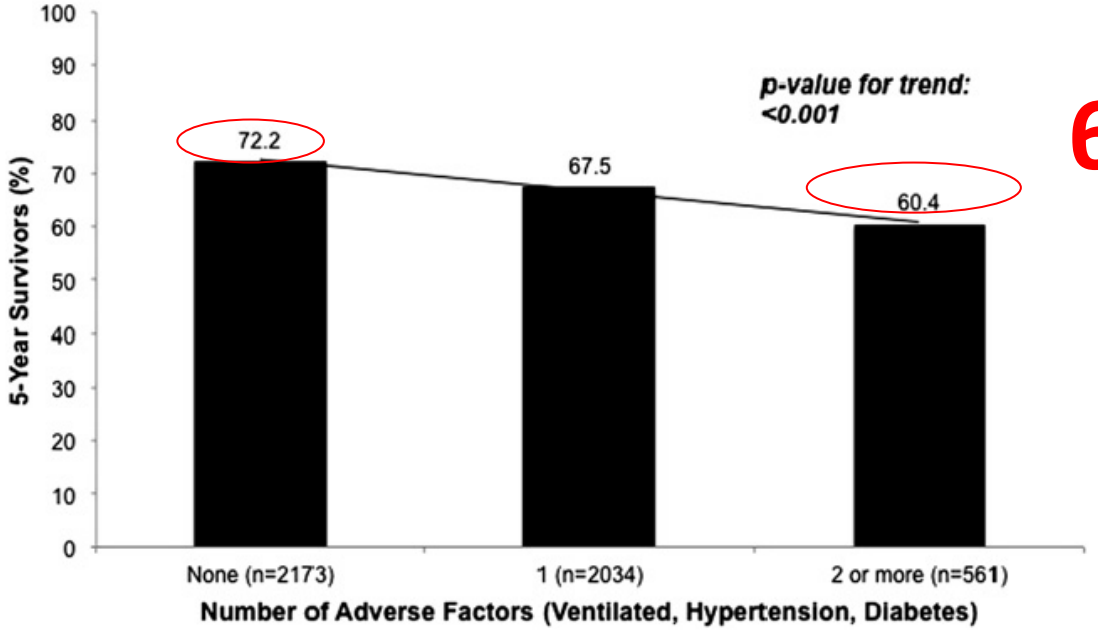
Kalp Transplantasyonu ve Sağ kalım





Eur Heart J. 2021;42:4944-46

Kalp Transplantasyonu ve Sağ kalım



60.4 %

Proportion of 5-year survivors by number of adverse risk factors
(mechanical ventilation, hypertension, diabetes)

Kilic et al. Factors associated with 5-year survival in older heart transplant recipients. *J Thorac Cardiovasc Surg* 2012;143:468-74

The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-eighth adult heart transplantation report — 2021; Focus on recipient characteristics

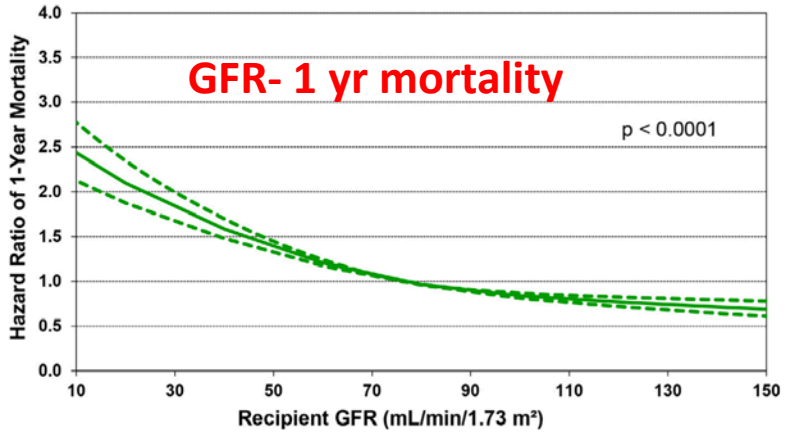


Figure 12 Multivariable hazard ratio plot for 1-year mortality with 95% confidence limits, by recipient glomerular filtration rate (GFR) (transplants: January 2000-June 2017; N = 67,223). GFR was estimated using the Cockcroft-Gault formula

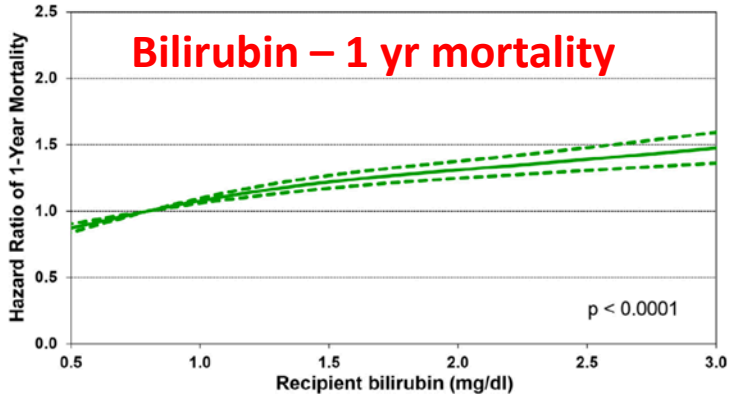
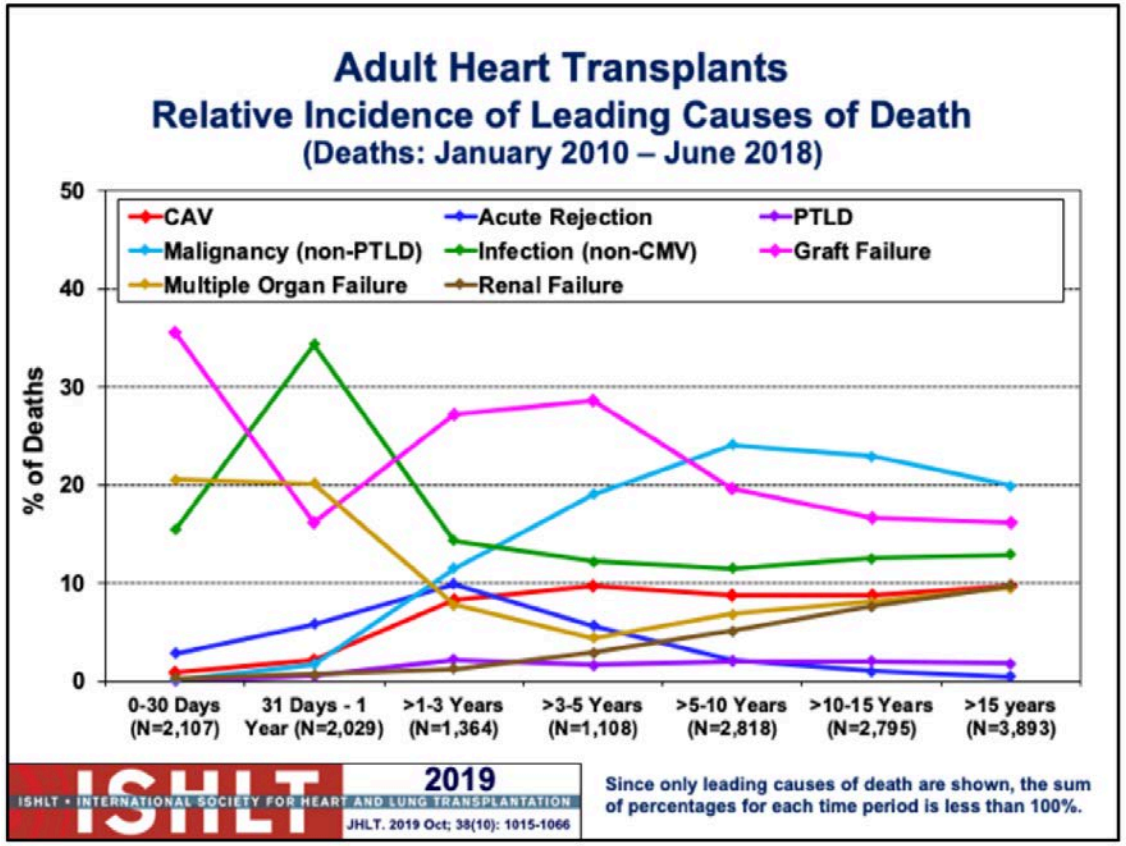


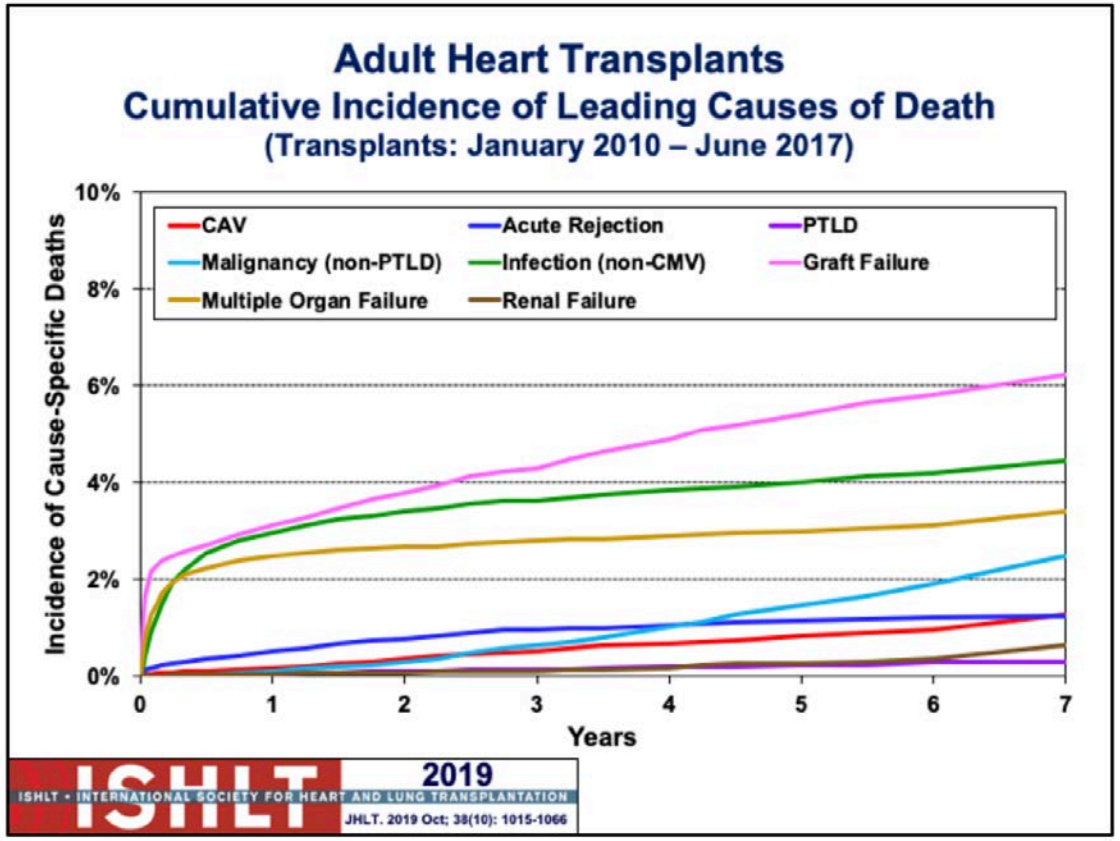
Figure 14 Multivariable hazard ratio plot for 1-year mortality with 95% confidence limits, by recipient bilirubin (transplants: January 2000-June 2017; N = 67,223)

J Heart Lung Transplant 2021;40:1035-1049

Kalp Transplantasyonu ve Mortalite



% ölüm

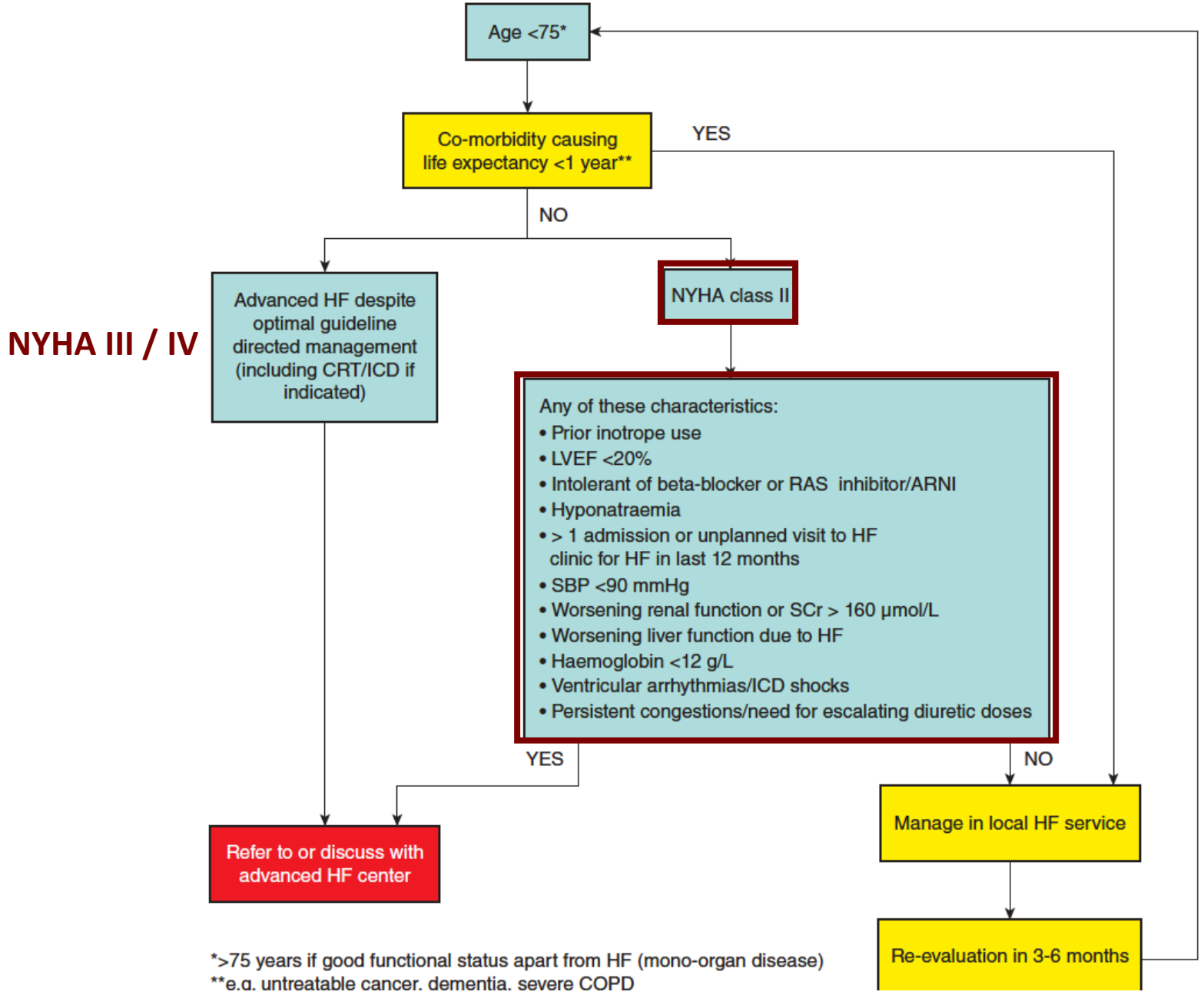


Ölüm nedenleri

Kime LVAD ? / Tx ?

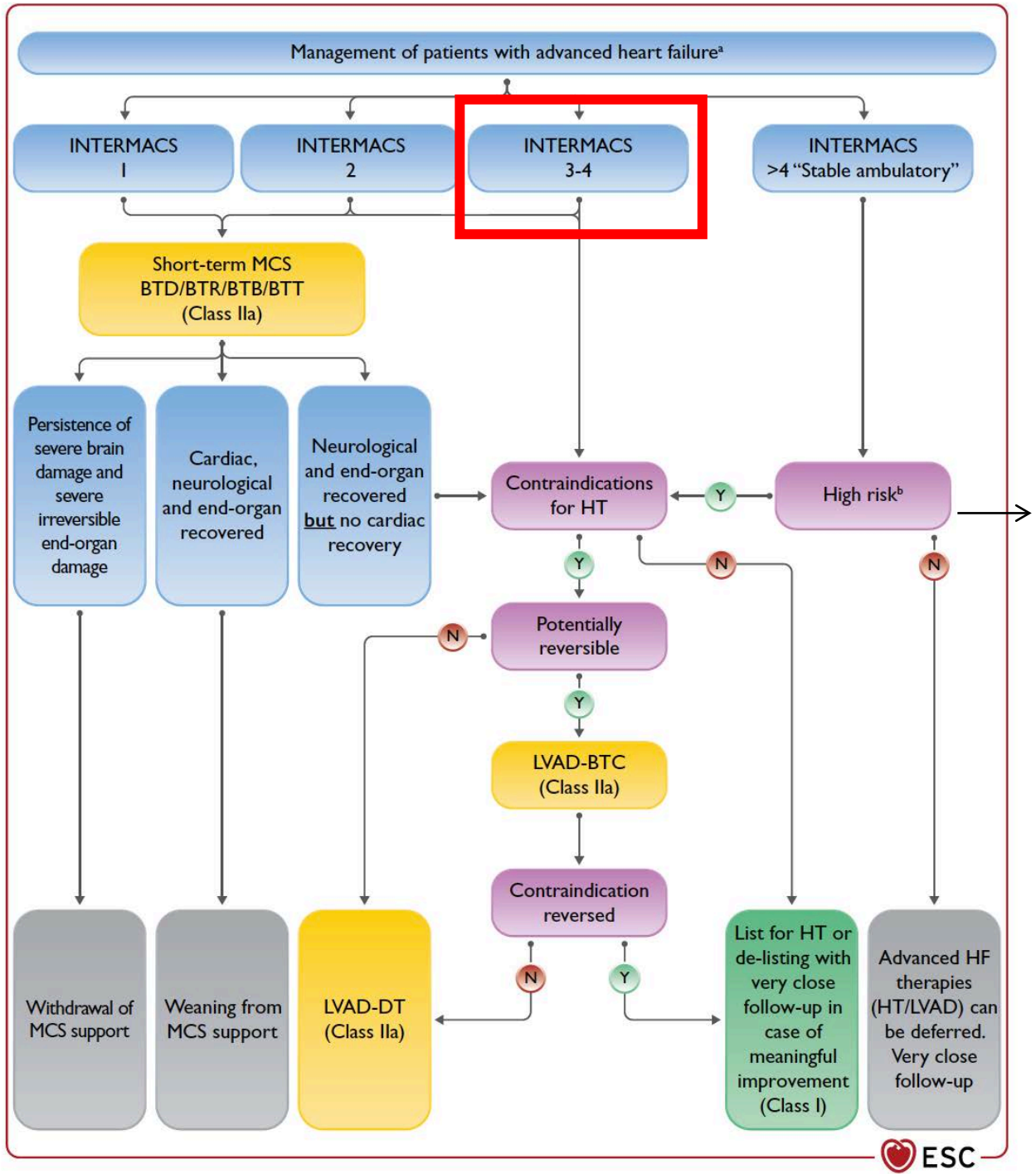
- **Biventriküler yetmezlik / RV tutan kardiyomiyopatiler**
- **Hipertrofik kmp**
- **Restriktif kmp**
- **Konjenital kalp hastalıkları**
- **Çoklu kapak hastalıkları**

İleri evre kalp yetersizliği hastasının yönlendirilmesi / refere etmek için zamanlama



HFA Position Paper 2018

ESC Kılavuz 2021

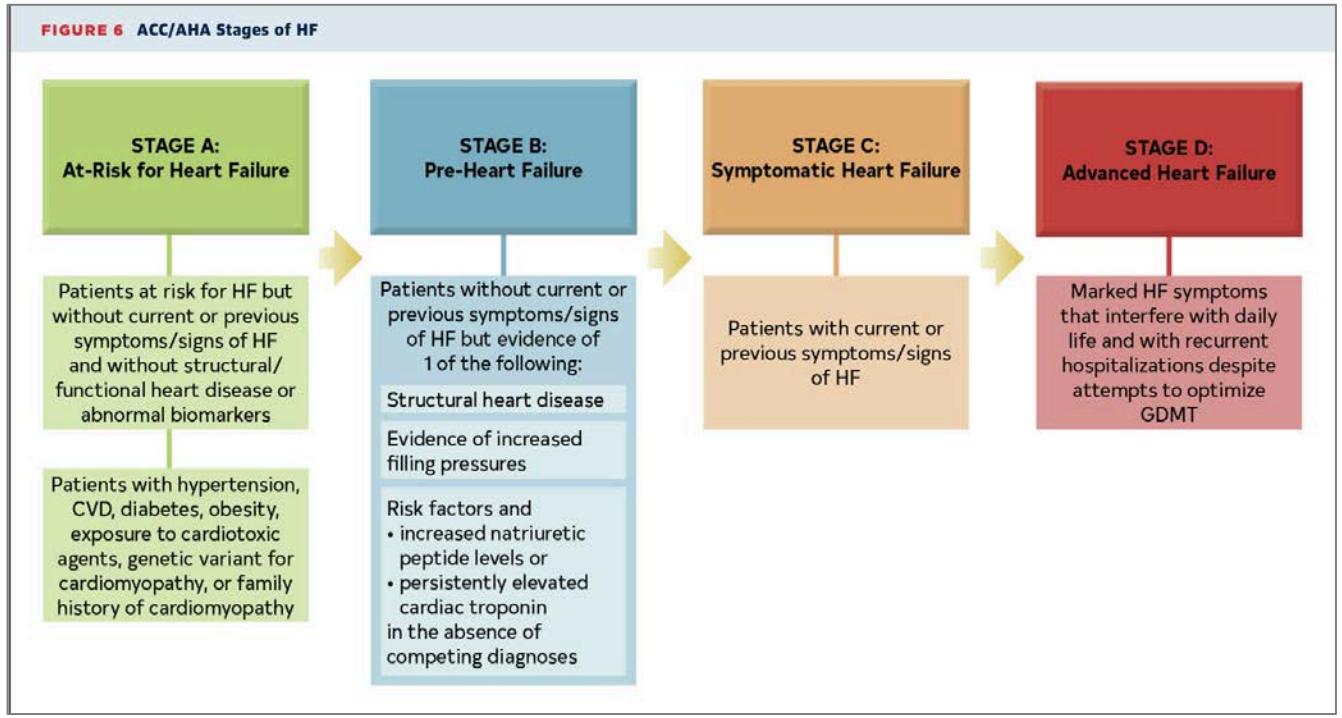


Tekrarlayan hospitalizasyon
Progresif son – organ hasarı
Refrakter konjesyon
pVO2 < 12 mL/min/kg
Sağ kalp yeterzisliği
Pulmoner Hipertansiyon

ESC Guideline 2021

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary

FIGURE 6 ACC/AHA Stages of HF

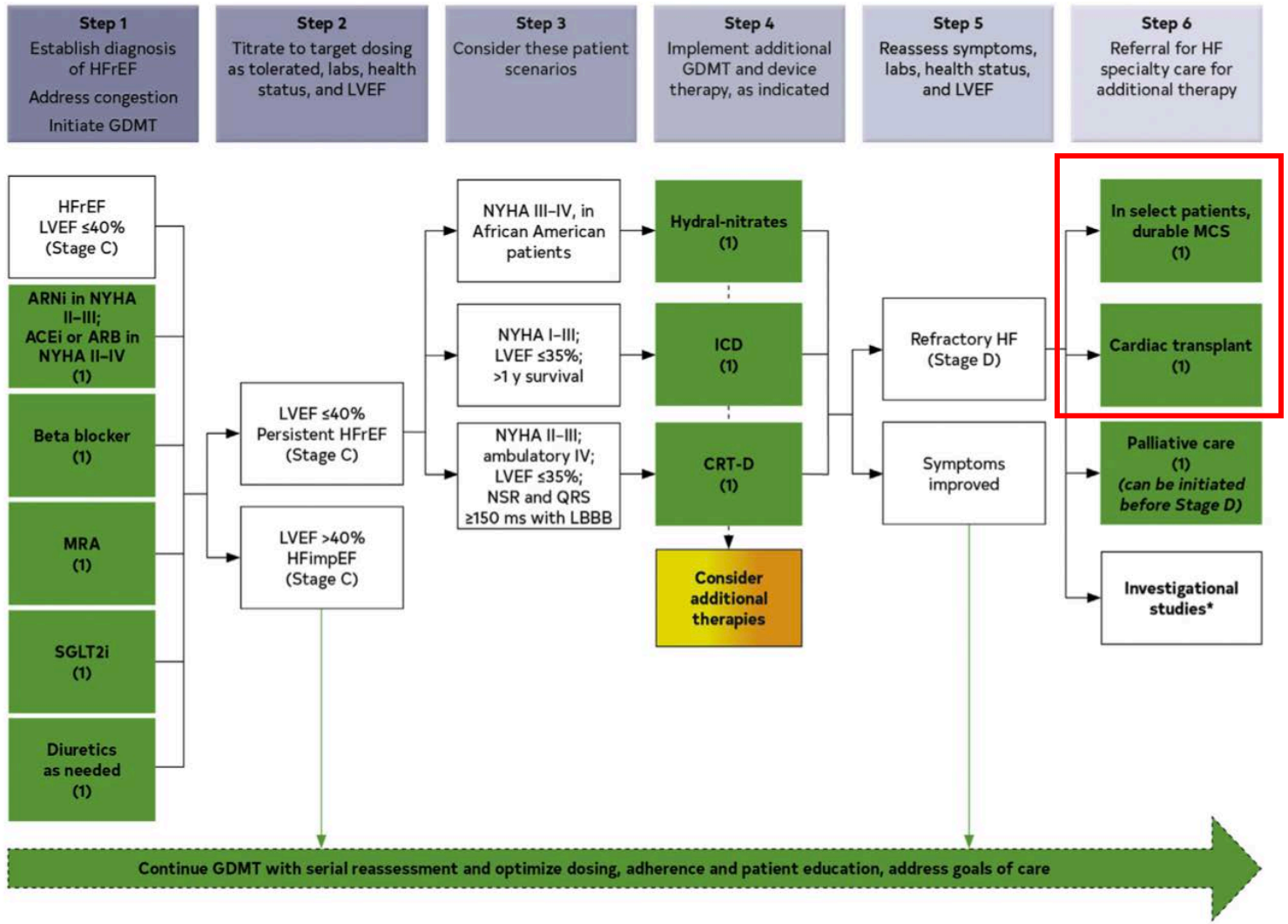


Recommendation for Specialty Referral for Advanced HF

COR	LOE	RECOMMENDATION
1	C-LD	1. In patients with advanced HF, when consistent with the patient's goals of care, timely referral for HF specialty care is recommended to review HF management and assess suitability for advanced HF therapies (e.g., left ventricular assist devices, cardiac transplantation, palliative care, and palliative inotropes) (105-110).

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary

FIGURE 1 Treatment of HFrEF Stages C and D



MDC endikasyonu

TABLE 19 Indications and Contraindications to Durable Mechanical Support (37)

Indications (combination of these):
■ Frequent hospitalizations for HF
■ NYHA class IIIb to IV functional limitations despite maximal therapy
■ Intolerance of neurohormonal antagonists
■ Increasing diuretic requirement
■ Symptomatic despite CRT
■ Inotrope dependence
■ Low peak VO_2 (<14–16)
■ End-organ dysfunction attributable to low cardiac output
Contraindications:
Absolute
■ Irreversible hepatic disease
■ Irreversible renal disease
■ Irreversible neurological disease
■ Medical nonadherence
■ Severe psychosocial limitations
Relative
■ Age >80 y for destination therapy
■ Obesity or malnutrition
■ Musculoskeletal disease that impairs rehabilitation
■ Active systemic infection or prolonged intubation
■ Untreated malignancy
■ Severe PVD
■ Active substance abuse
■ Impaired cognitive function
■ Unmanaged psychiatric disorder
■ Lack of social support

CRT indicates cardiac resynchronization therapy; HF, heart failure; NYHA, New York Heart Association; VO_2, oxygen consumption; and PVD, peripheral vascular disease.

İleri evre KY hastaları....

 # 1: uygun hasta kim?
 # 2: implantasyon / tx için uygun zaman ?

- Ambulatuar ileri evre KY hastasında mortalite ve morbidite yüksektir
- IM 4 – 5 hastalarının da sağkalımı kötüdür, mortalite ve morbidite yüksektir. LVAD tedavisinden yarar görmektedirler
- IM 4 – 5 hastalarının hayat kalitesi kötüdür, LVAD tedavisi ile hayat kalitesi artmaktadır
- IM 6 - 7 hastaları medical tedavi ile izlenmelidir ancak ÇOK YAKIN takipte olmalıdırlar
- Progresif son organ disfonksiyonu ileri ever KY hastasında kalp tx / LVAD sonrası mortalite ve morbiditeyi arttırır
- Biventriküler yetmezliği / sağ ventriküler yetmezliği olan hastalarda kalp tx planlanabilir