Banner
University Medicine

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Clinical Associate Professor of Medicine
University of Arizona College of Medicine
Director, Center for Advanced Heart Disease
Banner University Medical Center
Phoenix, AZ

MEDICAL THERAPY FOR ADVANCED HEART FAILURE
Disclosure

None

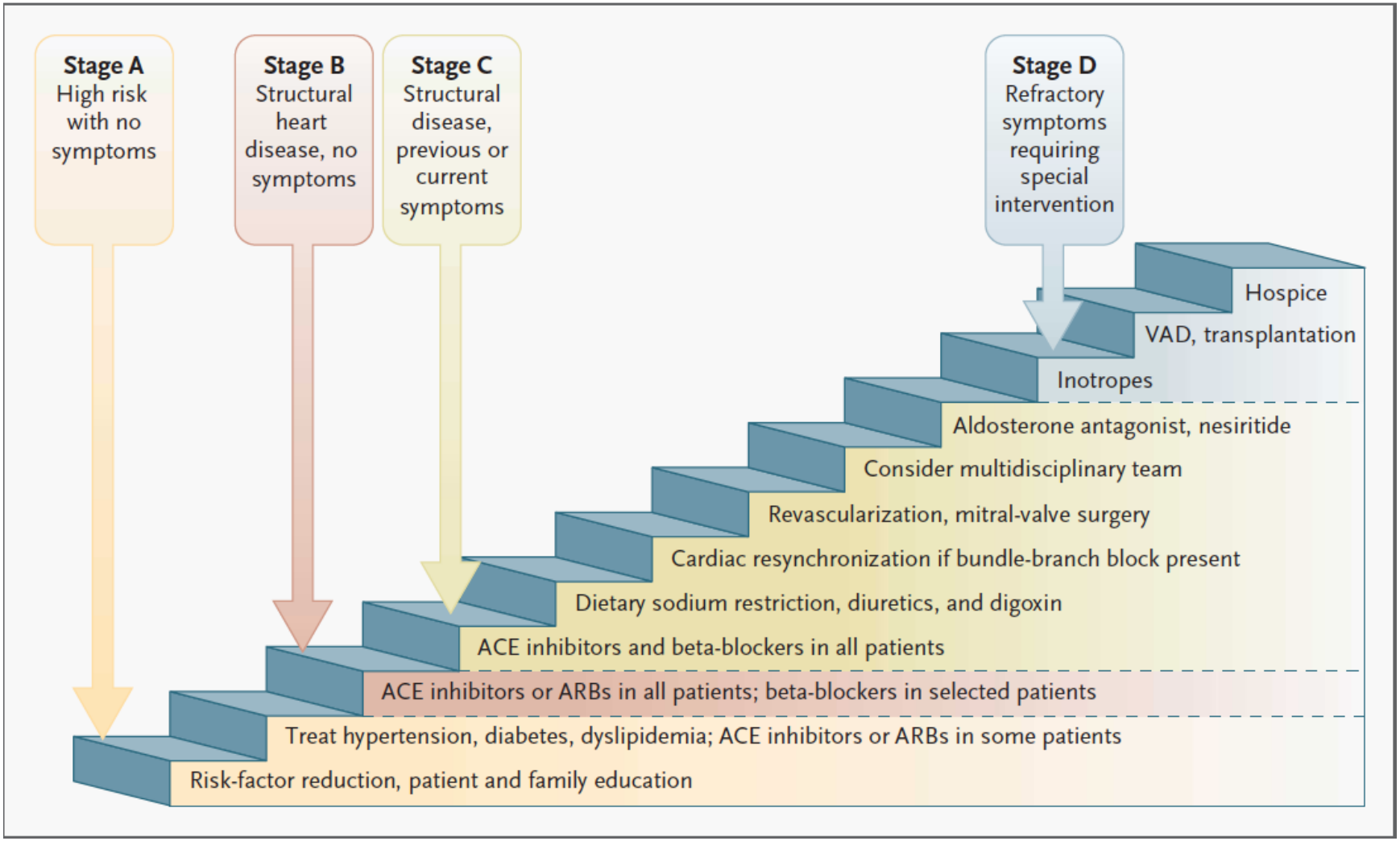
Banner
University Medicine

MEDICAL THERAPY FOR ADVANCED HEART FAILURE
Overview / concepts

- Recognizing transition to advanced heart failure from chronic heart failure.
- Current status of medical therapy for heart failure – medications, effectiveness and performance.
- Calibrating medical therapy for stage “C” ambulatory and hospitalized patients with heart failure.
- When to refer to a disease management program.

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

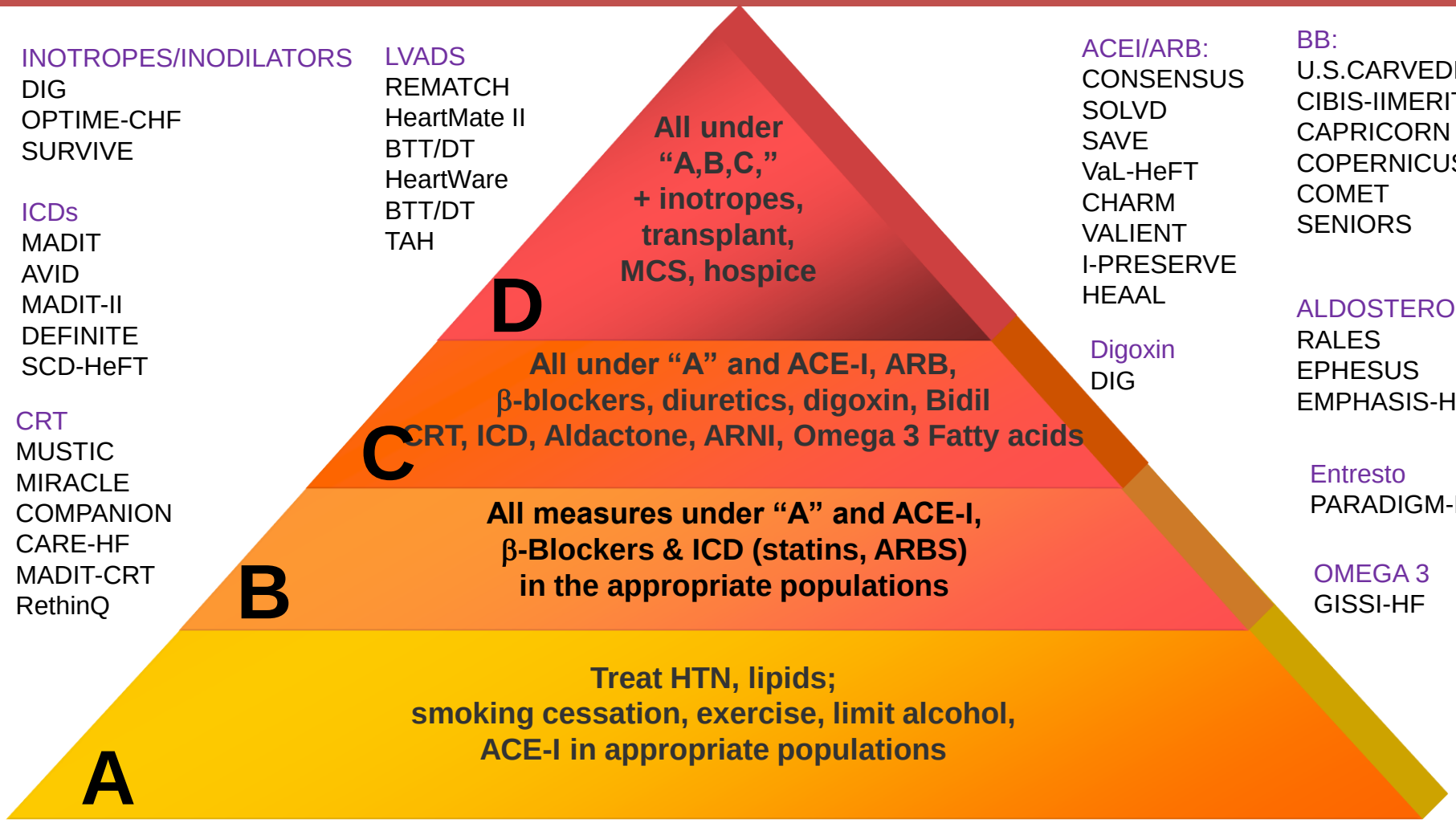
CHRONIC HF VERSUS ADVANCED HF



Jessup, *NEJM* 2003; 348:20

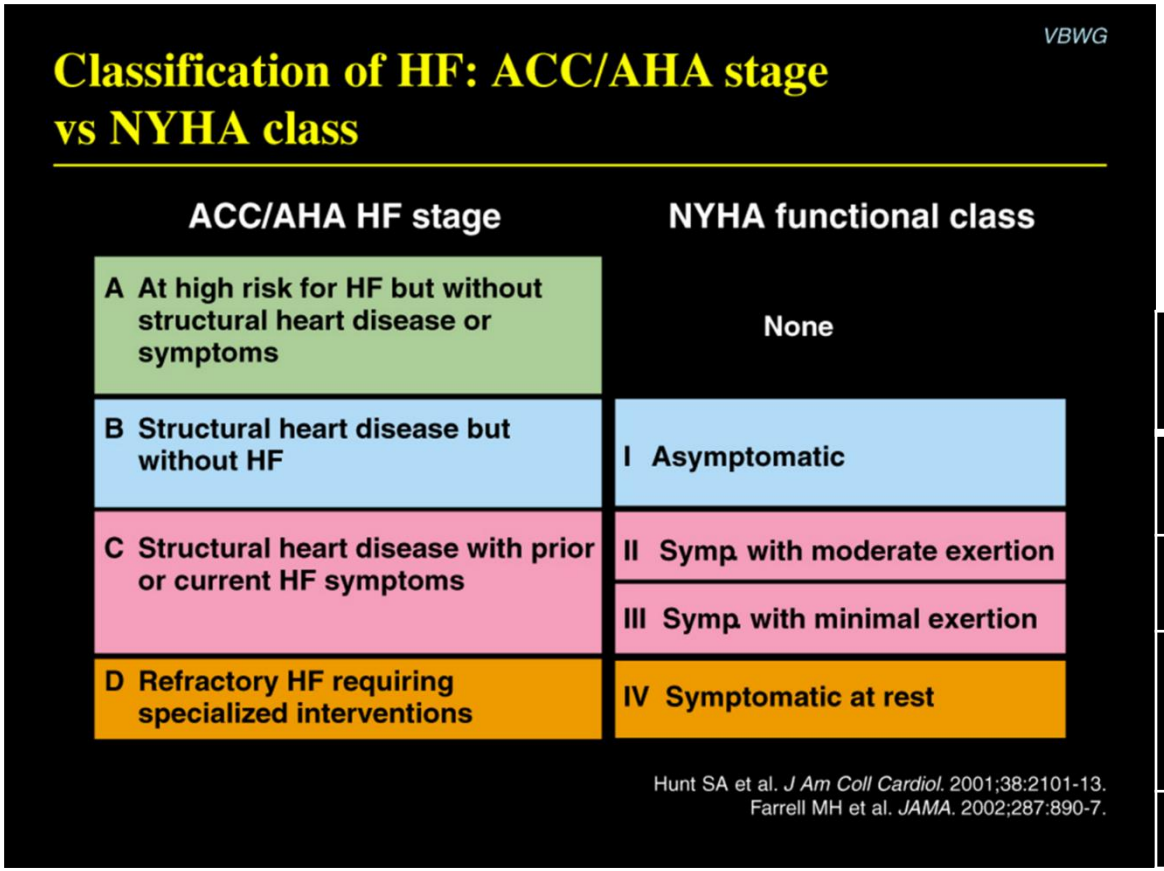
ACC/AHA Practice Guidelines

Pyramid Approach to HF Therapy



Yancy C W et al. Circulation. 2013;128:e240-e327

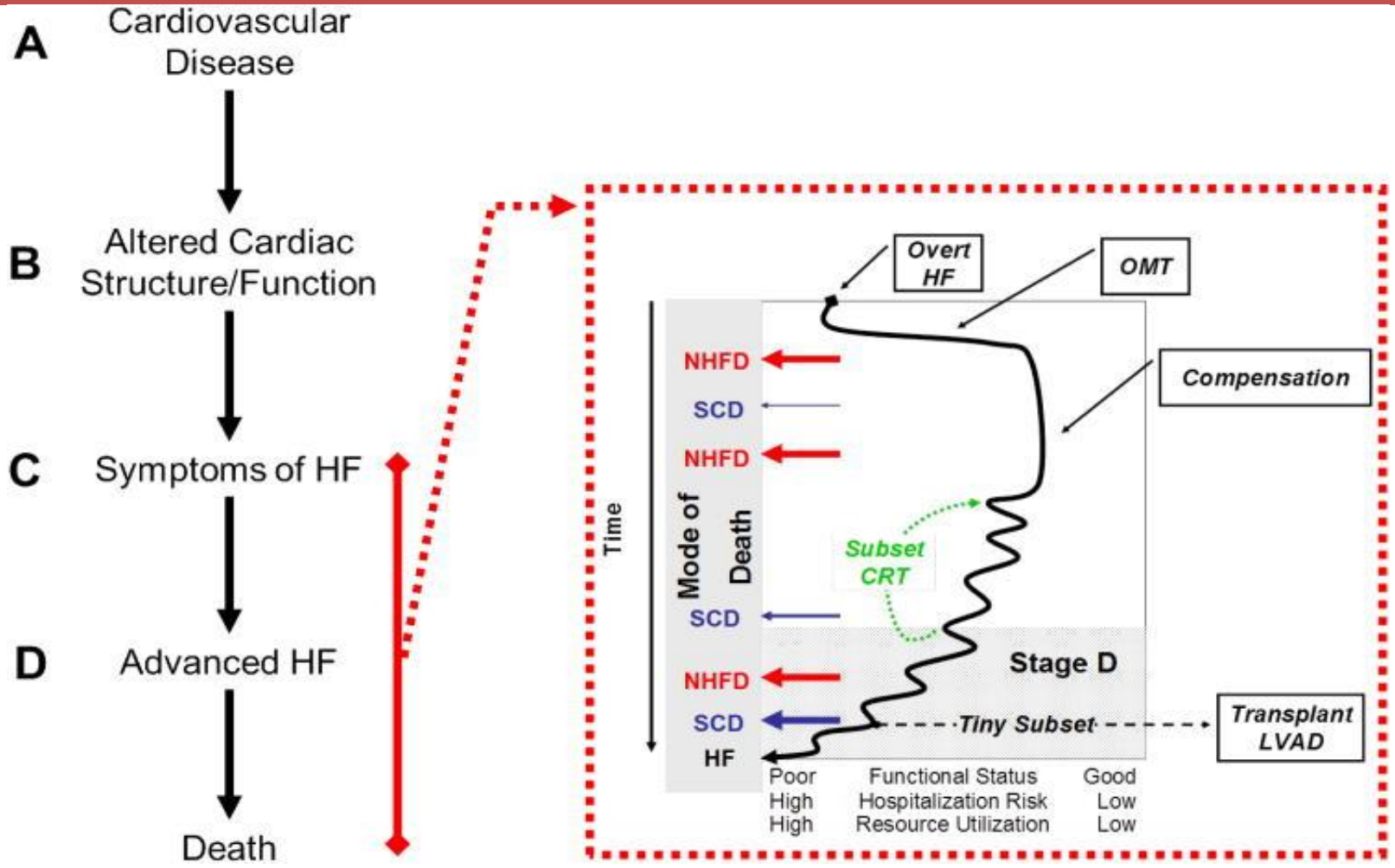
Clinical Class remains the #1 predictor of mortality in Heart failure



Hospital Admission	Annual Mortality
Rare	<10%
≤ 1	10-15%
2 – 4	20%
>4	35-50%

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

CHRONIC HF VERSUS ADVANCED HF



Congest Heart Fail. 2011 Jul-Aug;17(4):160-8. doi: 10.1111/j.1751-7133.2011.00246.x. Epub 2011 Jul 21.

ACE inhibitor, ARB or ARNI use is indicated in the following HF population;

A. ACC stage C heart failure patients
B. ACC stage B heart failure patients
C. ACC stage A patients with hypertension
D. All of the above

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

ADVANCED HF AND INTERMACS PROFILES

Inotrope/MCS/TX

Medical therapy

INTERMACS PROFILE-LEVEL	NYHA	Official Shorthand	Modifier options
INTERMACS 1	D - IV	"Crash and burn"	± Arrhythmia, ± Temporary Circ Support
INTERMACS 2	D - IV	"Sliding fast" despite inotropic support	± Arr, TCS
INTERMACS 3	D - IV	Stable but inotropic therapy-dependent, In hosp or home	± Arr ± Frequent Flyer
INTERMACS 4	D, Amb.IV	Resting symptoms on oral therapy at home.	± Arr ± FF
INTERMACS 5	D, Amb.IV	"Housebound", Comfortable at rest, symptoms with minimal daily activity	± Arr ± FF
INTERMACS 6	D, Amb.IV	"Walking wounded"- ADL possible but meaningful activity limited	± Arr ± FF
INTERMACS 7	C,D III, IIIB	Advanced Class III	± Arr

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Patient example

- 54 year old man referred as outpatient with 4 years of HF from DCM. NYHA III-IV, 3 ADHF admissions in 9 months
- Echo EF 15%, EDD 7.4, Mod MR, Mod TR, Mod RV dysfunction
- Cr 1.6, Na 136

- Physical Exam:

Comfortable at rest. BP 100/75, HR 94, JVD 12, clear lungs, +S3, +S4 , P2, Palpable liver, Cool ext. 2+ bilateral edema

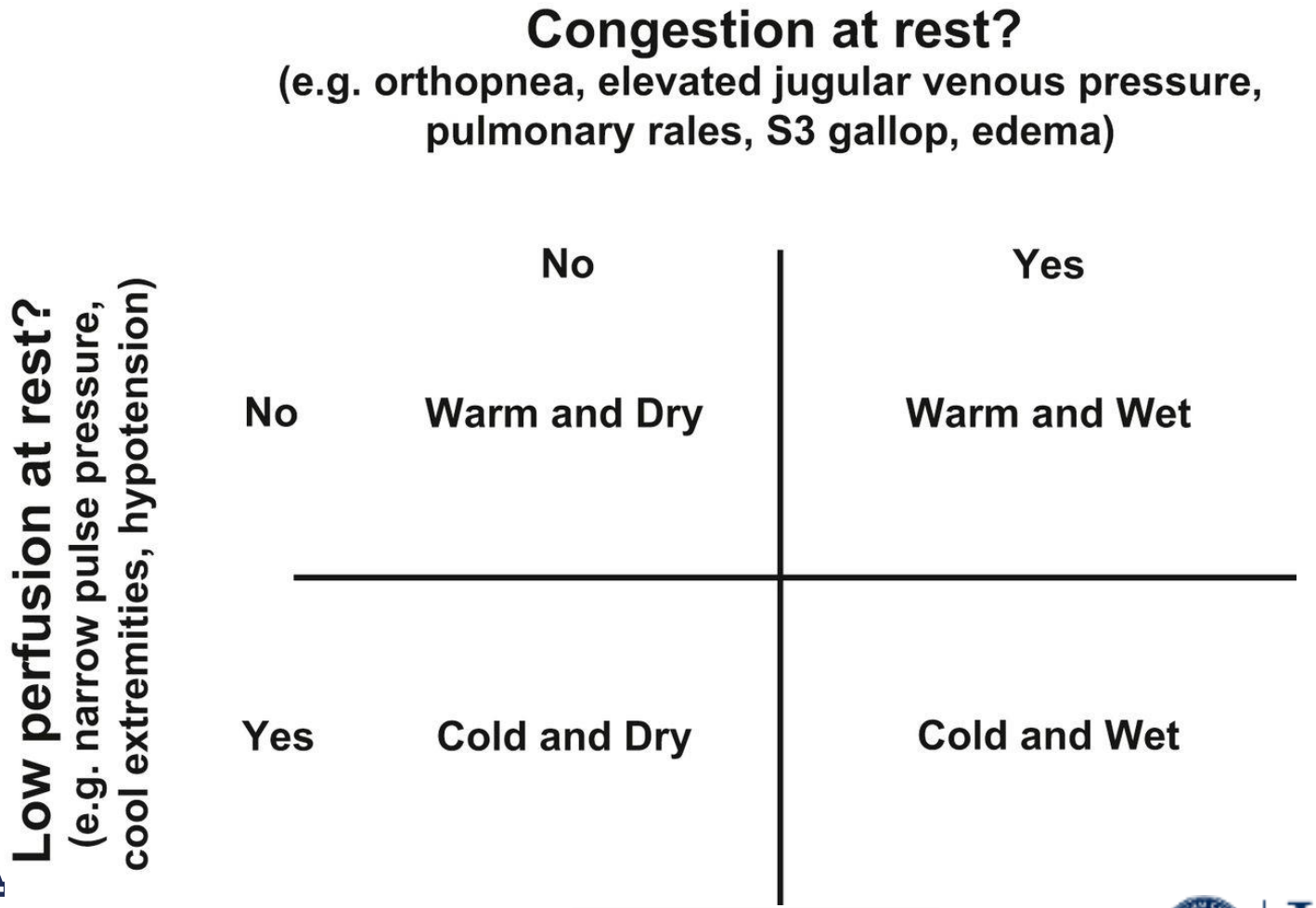
- Meds:

Carvedilol, Lisinopril, Aldactone, Digoxin, Lasix

6MWD = 265 meters

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

What clinical hemodynamic profile?



Profile?

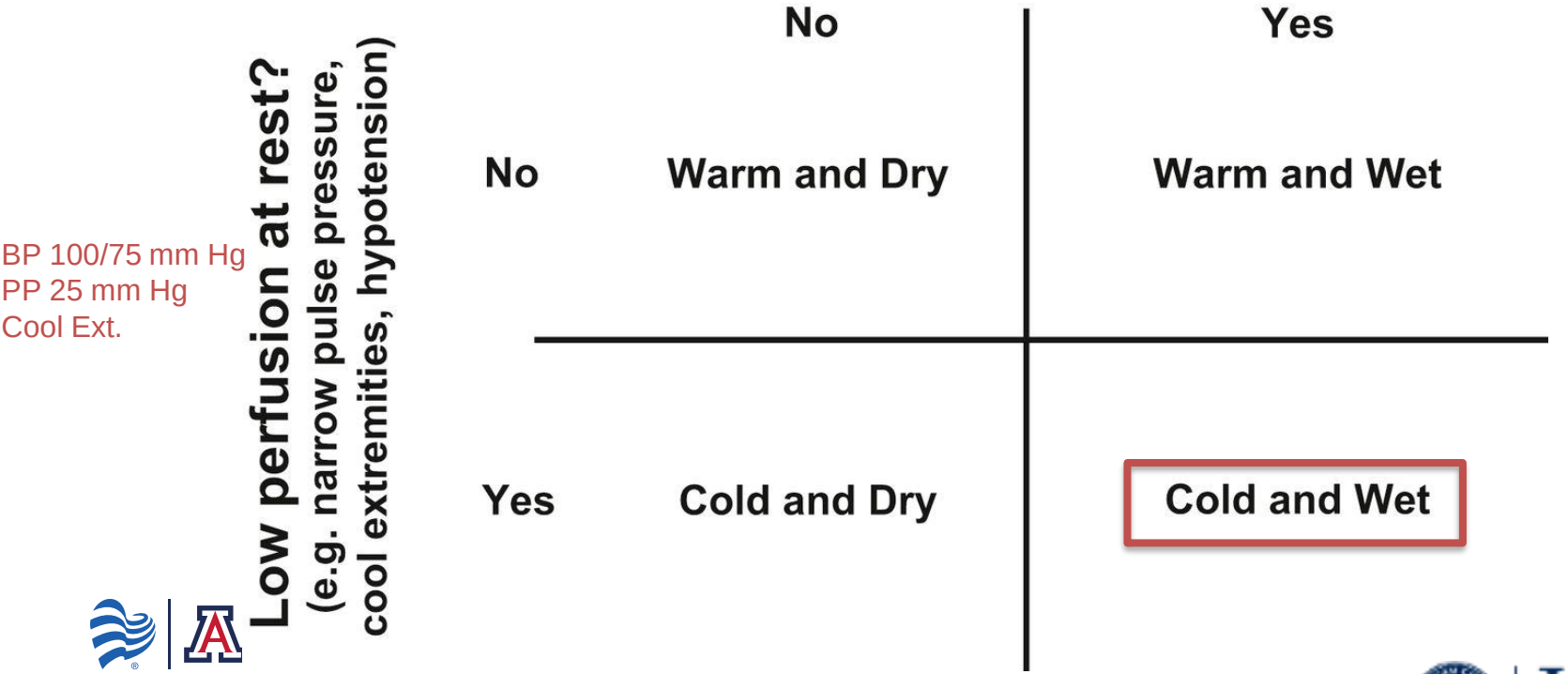
Banner University Medicine

JACC

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

What clinical hemodynamic profile?

JVD 12
S3
2+ Edema



BP 100/75 mm Hg
PP 25 mm Hg
Cool Ext.

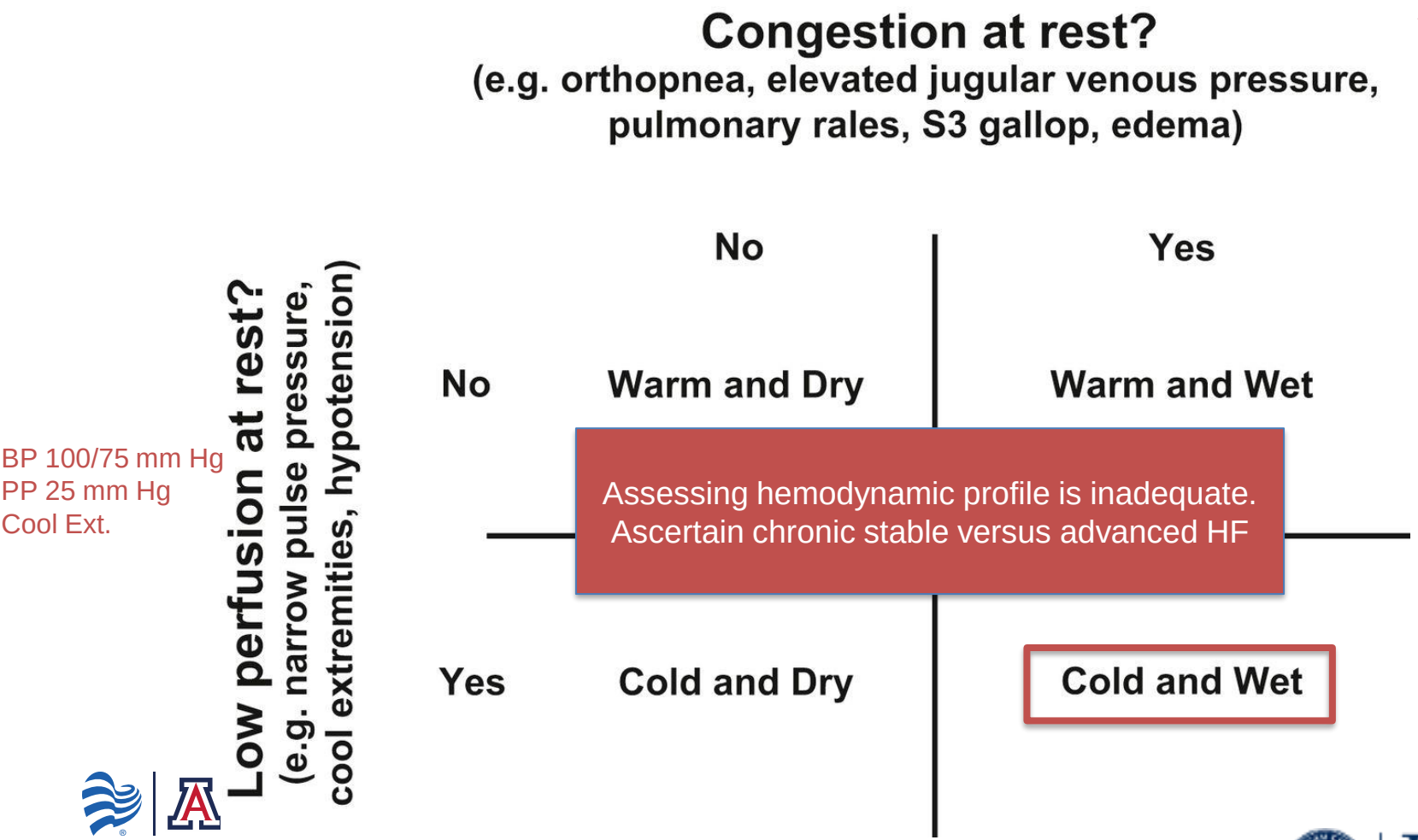
Banner
University Medicine

JACC

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

What clinical hemodynamic profile?

JVD 12
S3
2+ Edema



BP 100/75 mm Hg
PP 25 mm Hg
Cool Ext.

Banner
University Medicine

JACC

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

CHRONIC HF VERSUS ADVANCED HF - ESC GUIDELINES

1. ***NYHA Class III-IV Symptoms***
2. ***Episodes of volume overload and/or peripheral hypo-perfusion***
3. ***Objective evidence of severe cardiac dysfunction***
(EF<30%, Doppler Pseudonormal or Restrictive filling pattern, PCWP>16mmHg or RAP >12 mmHg)
4. ***Severely impaired functional capacity***
(Inability to exercise, 6MWD<300m, Peak VO2<12-14 ml/kg/min)
5. ***HF Hospitalizations***
(≥1 in past 6 months)
6. ***Above occurring despite attempts to optimize diuretics, RAAS antagonists, BB, CRT or in the setting of intolerance to OMT***

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

DOES THIS PATIENT MEET CRITERIA FOR ADVANCED HF?

- 54 year old man referred as outpatient with 4 years of HF from DCM. NYHA III-IV, 3 ADHF admissions in 9 months
- Echo EF 15%, EDD 7.4, Mod MR, Mod TR, Mod RV dysfunction
- Cr 1.6, Na 136

- Physical Exam:

Comfortable at rest. BP 100/75, HR 94, JVD 12, clear lungs, +S3, +S4 , P2, Palpable liver, Cool ext. 2+ bilateral edema

- Meds:

Carvedilol, Lisinopril, Aldactone, Digoxin, Lasix

6MWD = 265 meters

Advanced HF?

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

DOES THIS PATIENT MEET CRITERIA FOR ADVANCED HF?

- 54 year old man referred as outpatient with 4 years of HF from DCM. NYHA III-IV, 3 ADHF admissions in 9 months [1] [5]
- Echo EF 15%, EDD 7.4, Mod MR, Mod TR, Mod RV dysfunction [3]
- Cr 1.6, Na 136

- Physical Exam:

Comfortable at rest. BP 100/75, HR 94, JVD 12, clear lungs, +S3, +S4 , P2, Palpable liver, Cool ext. 2+ bilateral edema [2]

- Meds:

Carvedilol, Lisinopril, Aldactone, Digoxin, Lasix [6]

6MWD = 265 meters [4]

WHAT CONSITITUES CLASSIFICATION OF APATIENT INTO COLD AND WET HEMODYNAMIC PROFILE?

A. Hypotension, warm extremities with JVP of 8 cm.

B. Cold extremities, narrow pulse pressure, elevated JVP and rales.

C. Normotension, peripheral edema and rales along with elevated JVP.

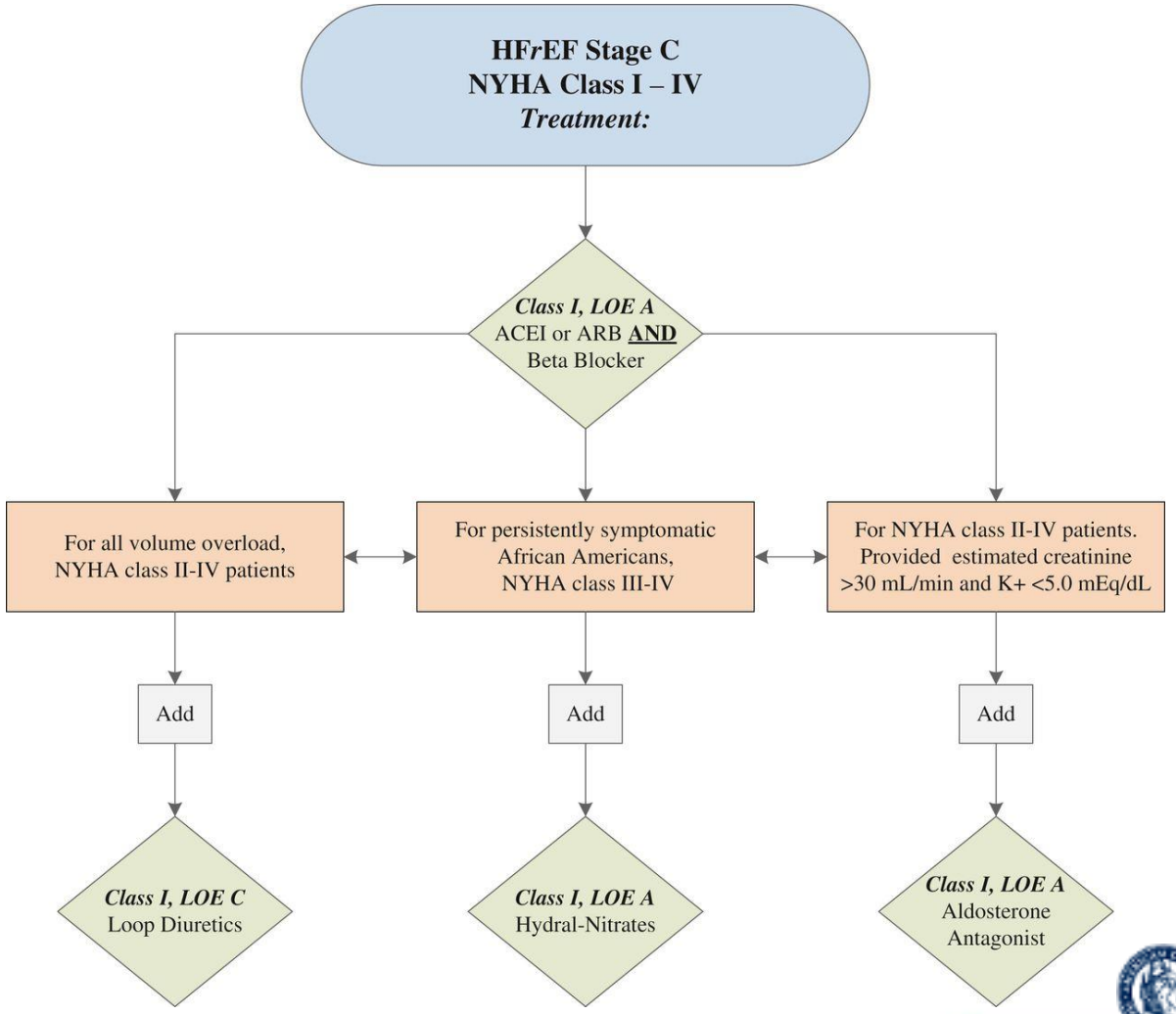
D. Hypertension, rales, lower extremity edema and shortness of breath.

MEDICAL THERAPY FOR ADVANCED HEART FAILURE
Overview / concepts

- Recognizing transition to advanced heart failure from chronic heart failure.
- Current status of medical therapy for heart failure – medications, effectiveness and performance.
- Calibrating medical therapy for stage “C” ambulatory and hospitalized patients with heart failure.
- When to refer to a disease management program.

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Stage “C” - 2013



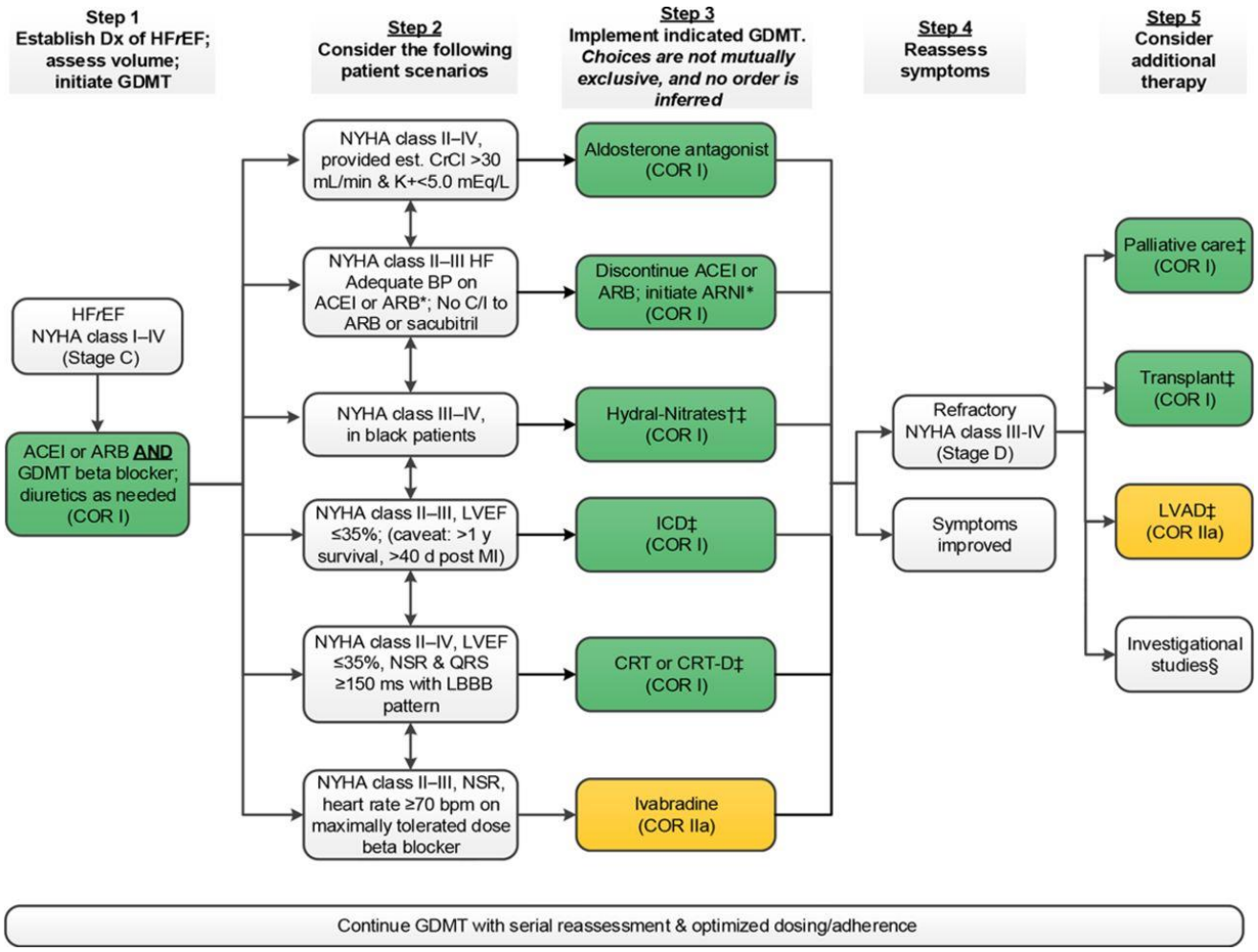
Banner University Medicine

JACC

Clyde W. Yancy et al. JACC 2013;62:e147-e239

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Stage “C” - 2017



2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America, Volume: 136, Issue: 6, Pages: e137-e161, DOI: (10.1161/CIR.0000000000000509)

Banner University Medicine

JACC

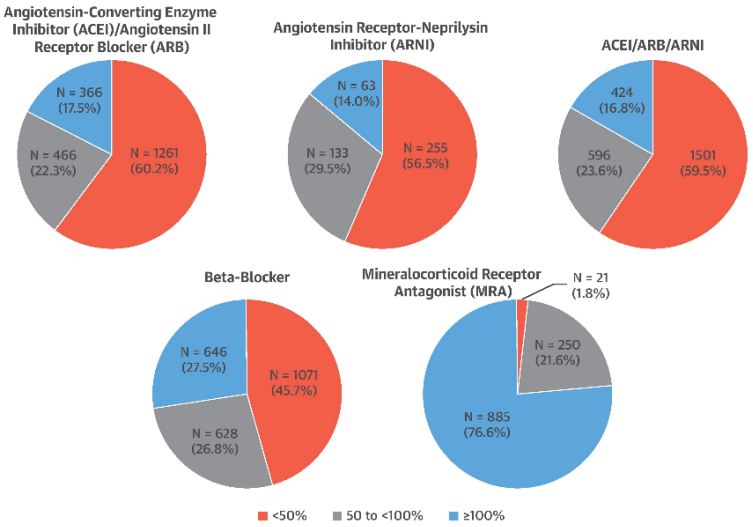
MEDICAL THERAPY FOR ADVANCED HEART FAILURE
What do we know from CHAMP HF registry?

CENTRAL ILLUSTRATION: Use and Dosing of Guideline-Directed Medical Therapy Among Patients With Chronic HFrEF in Contemporary U.S. Outpatient Practice

A

	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

B



Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351-66.

Banner University Medicine

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

CHAMP HF (2018)

- ACEI/ARB/ARNI Target dose = 16.7%
- BB Target dose = 27.5%
- MRA Target dose = 76.6%
- Eligible patients simultaneously receiving any dose of all 3 medications = <25%

IMPROVE HF (2010)

- ACEI/ARB Target dose = 36.1%
- BB Target dose = 20.5%
- MRA Target dose = 74.4%

Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351-66

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

US Performance in 2018 (CHAMP HF) and comparison to prior registries (IMPROVE HF)

CHAMP HF

- ACEI/ARB/ARNI
  Target dose = 16.7%
- BB Target dose = 27.5%
- MRA Target dose = 76.6%
- Eligible patients simultaneously receiving any dose of all 3 medications = <25%

IMPROVE HF

- ACEI/ARB
  Target dose = 36.1%
- BB Target dose = 20.5%
- MRA Target dose =74.4%

Factors reported to prevent GDMT in CHAMP HF

- Low BP
- Higher NYHA class
- CKD
- Hospitalization for HF

Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351-66

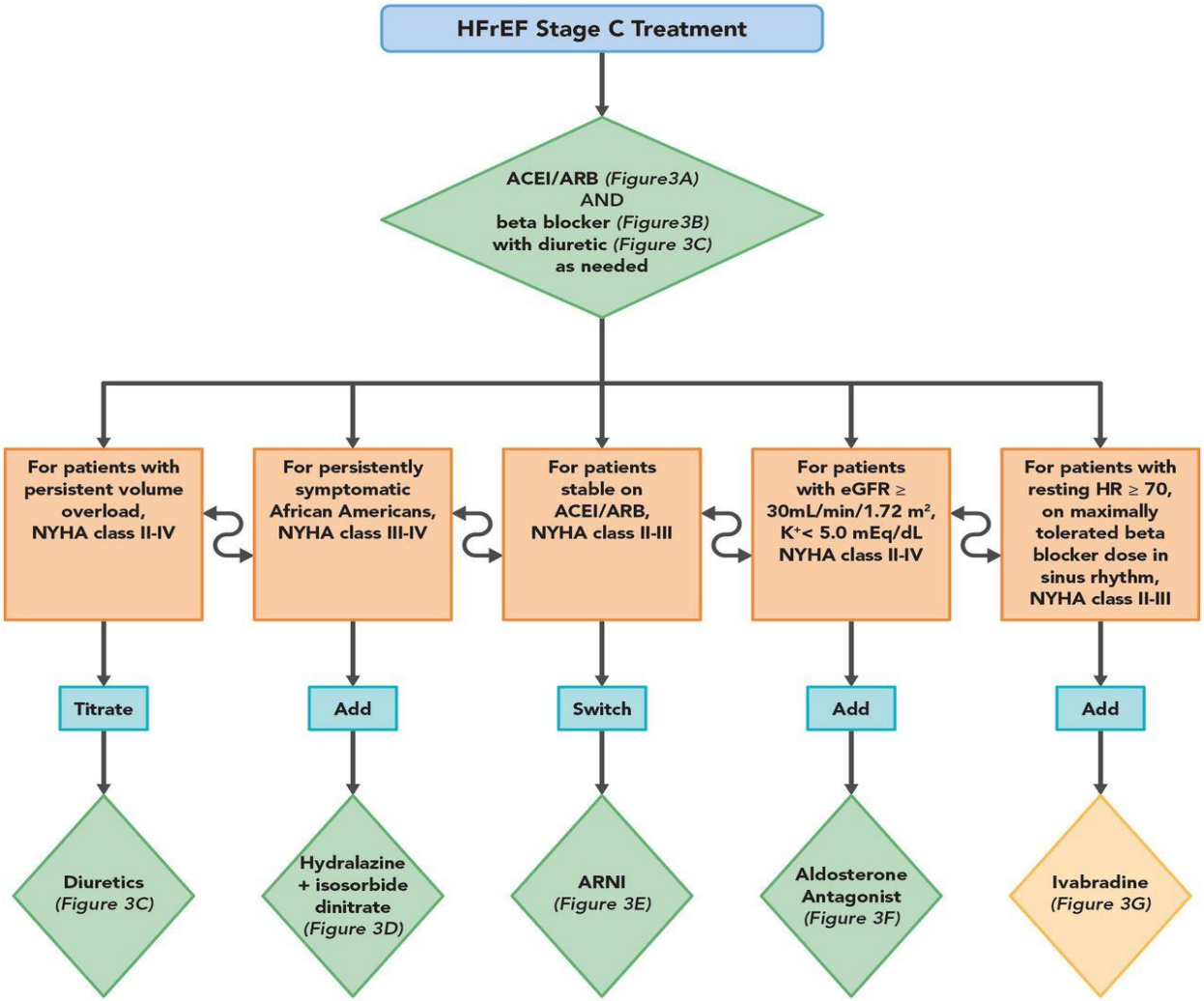
MEDICAL THERAPY FOR ADVANCED HEART FAILURE
Overview / concepts

- Recognizing transition to advanced heart failure from chronic heart failure.
- Current status of medical therapy for heart failure – medications, effectiveness and performance.
- Calibrating medical therapy for stage “C” ambulatory and hospitalized patients with heart failure.
- When to refer to a disease management program.

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient

Evidence

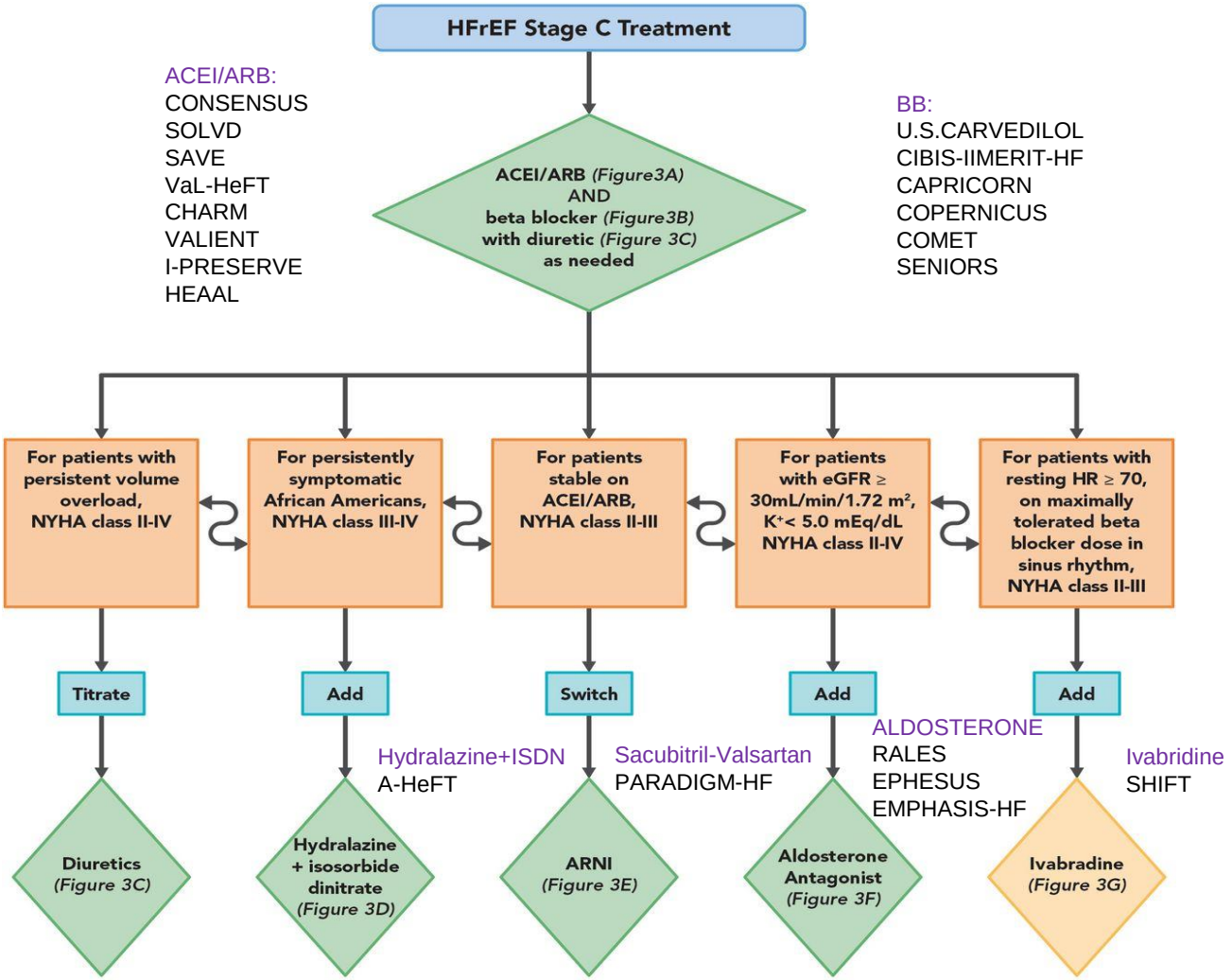


Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient

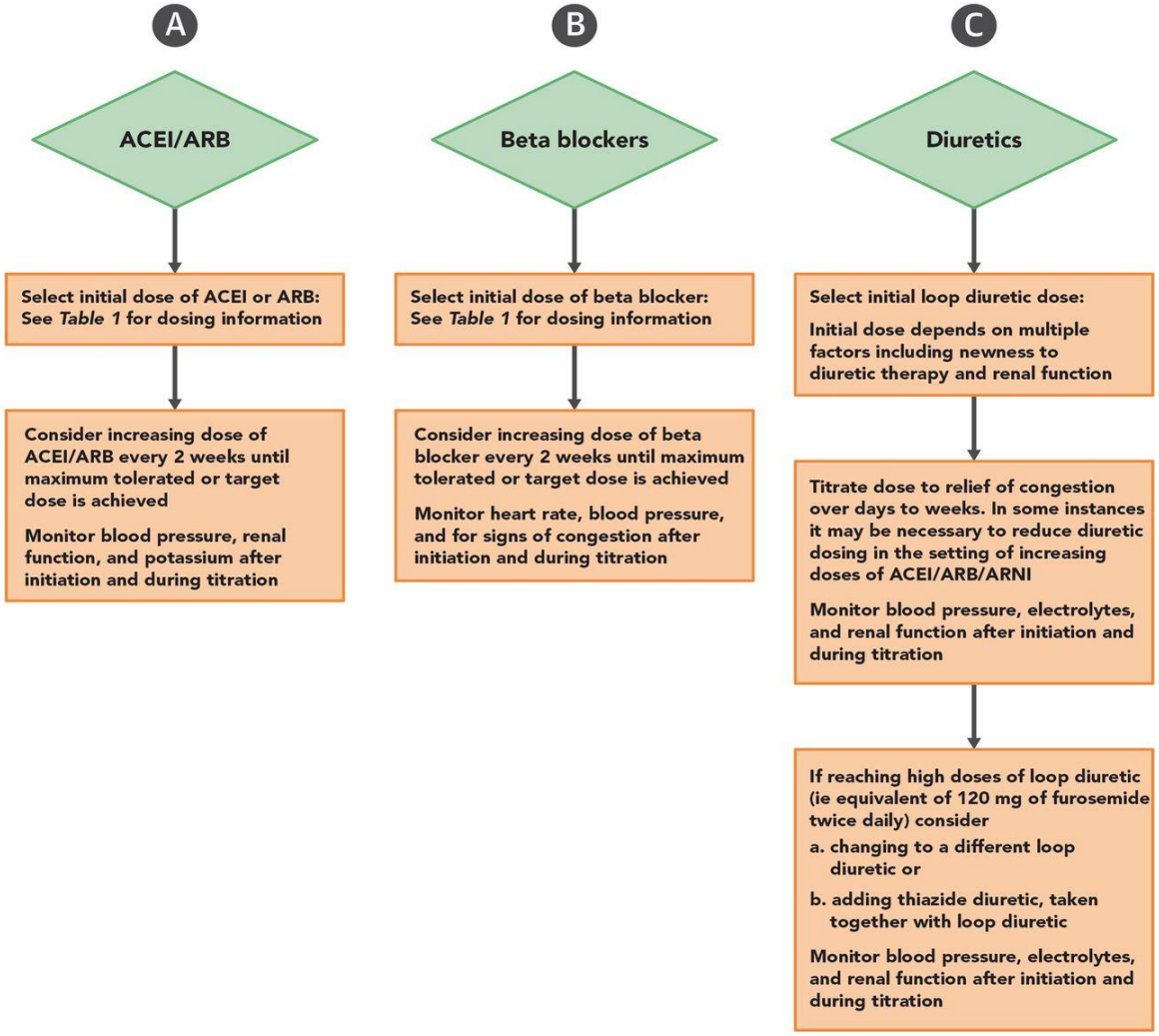


Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



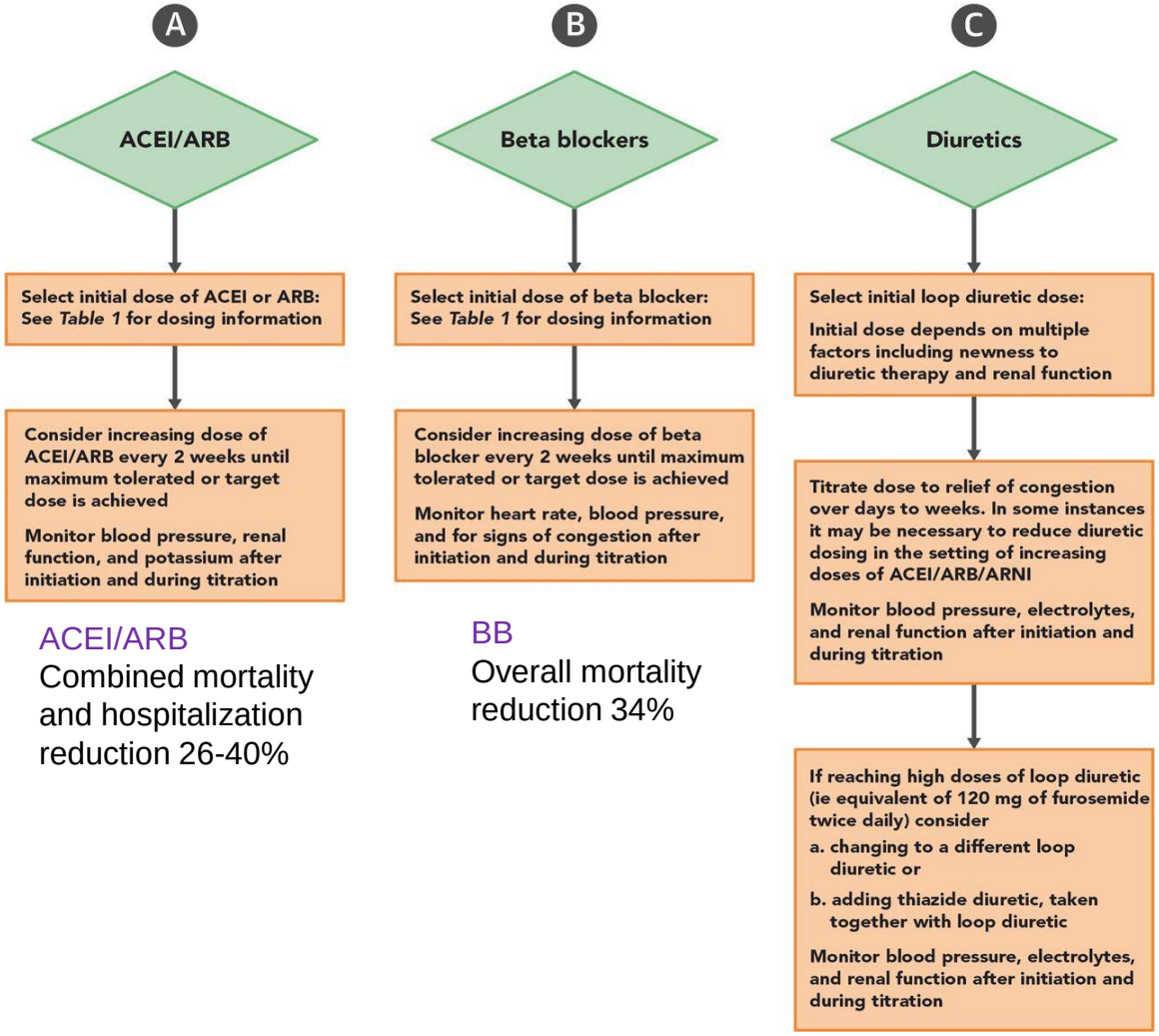
Benefit

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



ACEI/ARB
Combined mortality and hospitalization reduction 26-40%

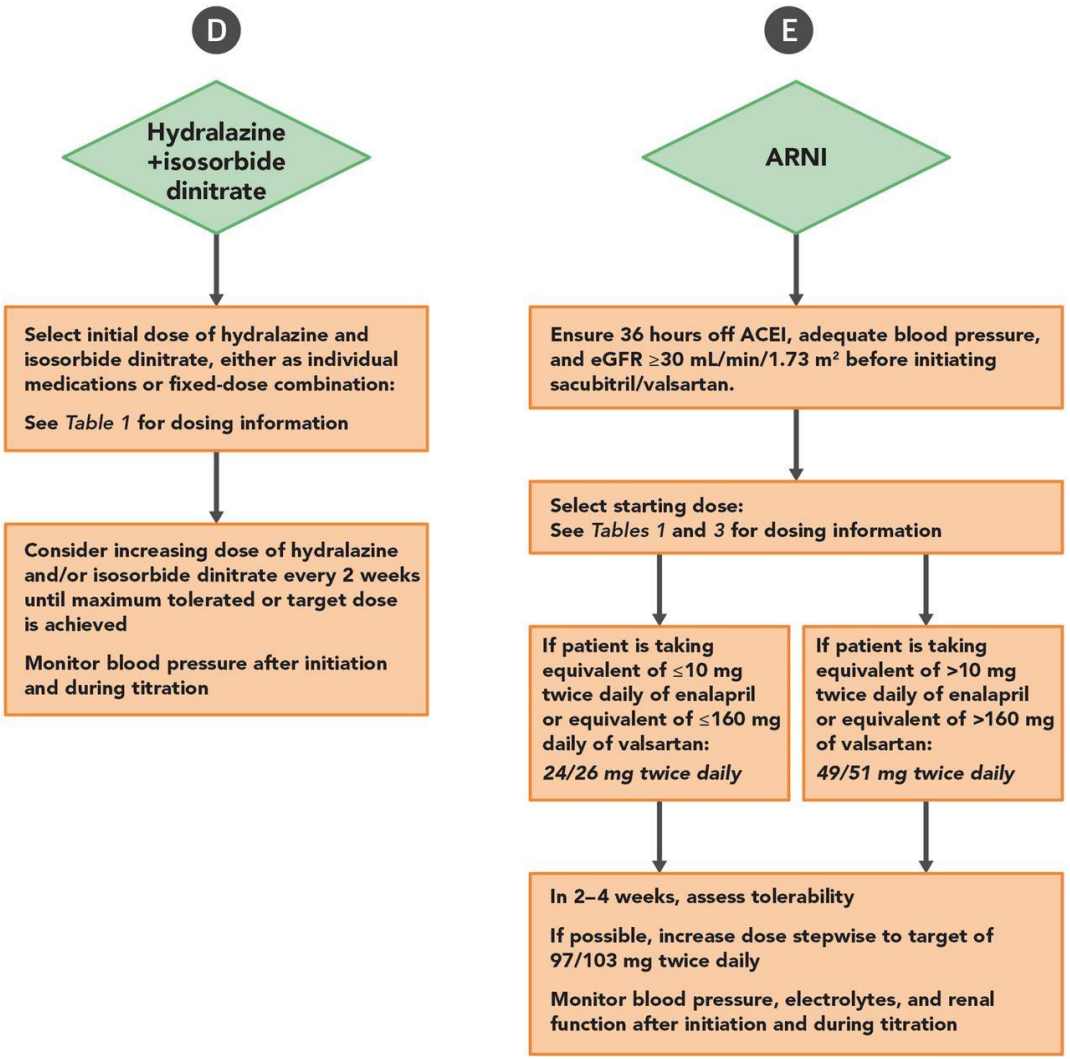
BB
Overall mortality reduction 34%

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



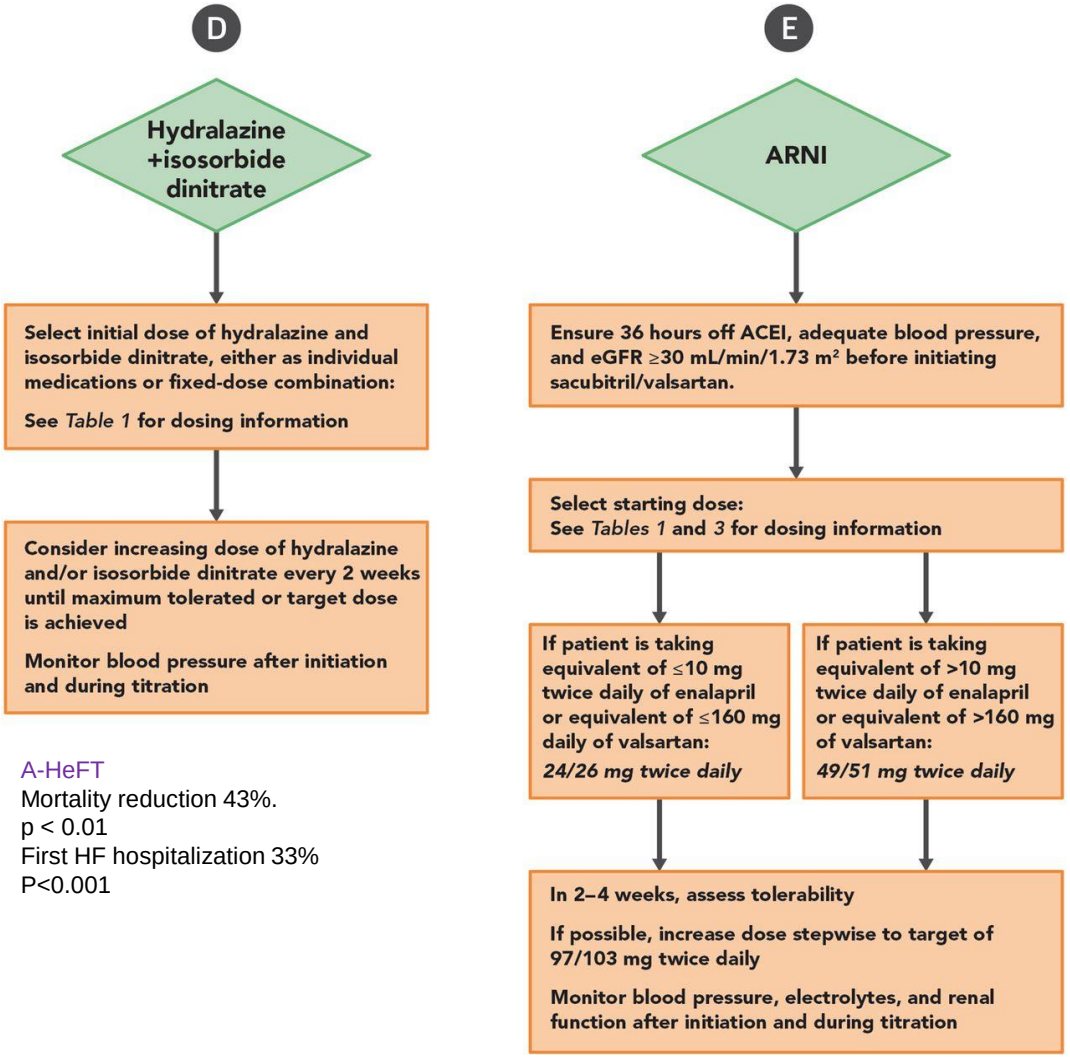
Benefit

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



A-HeFT
Mortality reduction 43%.
p < 0.01
First HF hospitalization 33%
P<0.001

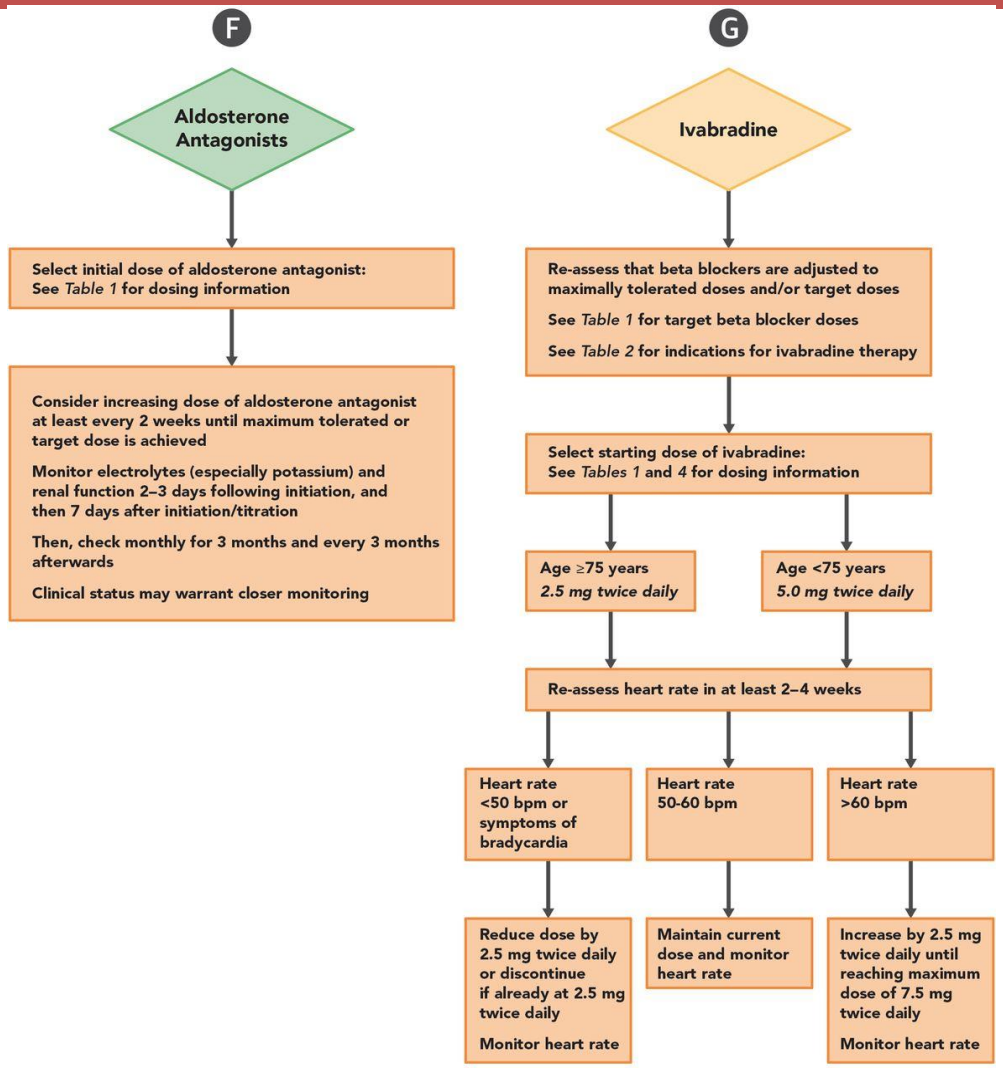
PARADIGM-HF
20% reduction in cardiovascular death or HF hospitalization.
P < 0.0001

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



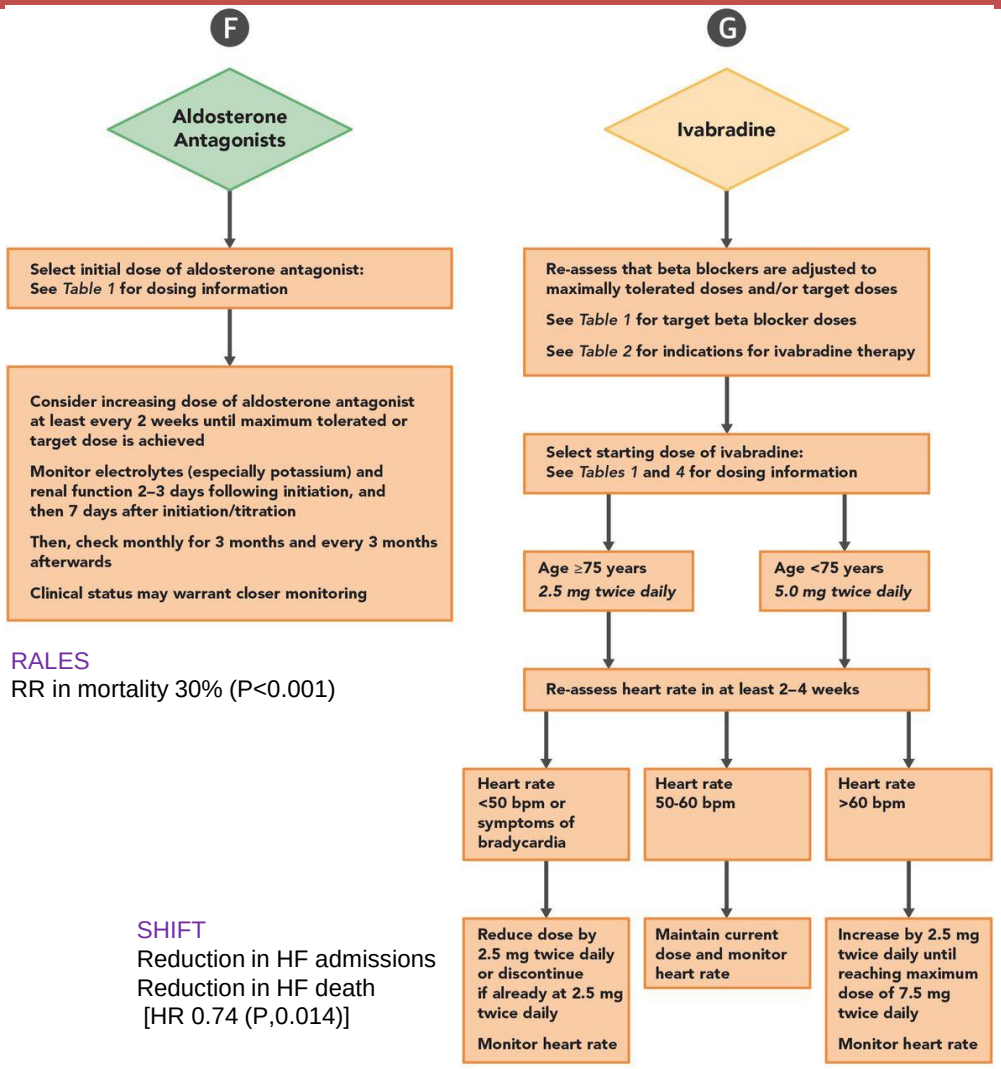
Benefit

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Ambulatory Patient



RALES
RR in mortality 30% (P<0.001)

SHIFT
Reduction in HF admissions
Reduction in HF death
[HR 0.74 (P,0.014)]

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Back to the hospitalized patient….

Right heart catheterization shows:

BP 95/65/75 mm Hg

RA 10 mm Hg

PA 65/24/35 mm Hg

PCWP 16 mm Hg

CO 3.5 L/min

SVR 1440 dynes/sec

PVR 435 dynes/sec (5.4WU)

- Acute testing was not successful - admitted to telemetry on IV Milrinone.
- No absolute contraindications for transplant.
- Develops VT and received ICD shock 3 times.
- Placed on IV Amiodarone, and given volume for hypotension.
- The following clinical picture ensues after 2 days despite maximal medical therapy….

Indicated?

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Back to the patient….

Right heart catheterization shows:

BP 95/65/75 mm Hg

RA 10 mm Hg

PA 65/24/35 mm Hg

PCWP 16 mm Hg

CO 3.5 L/min

SVR 1440 dynes/sec

PVR 435 dynes/sec (5.4WU)

- Acute testing was not successful - admitted to telemetry on IV Milrinone.
- No absolute contraindications for transplant.
- Develops VT and received ICD shock 3 times.
- Placed on IV Amiodarone, and given volume for hypotension.
- The following clinical picture ensues after 2 days despite maximal medical therapy….

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Hospitalized Patient

Recommendations	COR	LOE	References
Inotropic support			
Cardiogenic shock pending definitive therapy or resolution	I	C	N/A
BTT or MCS in stage D refractory to GDMT	IIa	B	647, 648
Short-term support for threatened end-organ dysfunction in hospitalized patients with stage D and severe HF/EF	IIb	B	592, 649, 650
Long-term support with continuous infusion palliative therapy in select stage D HF	IIb	B	651–653
Routine intravenous use, either continuous or intermittent, is potentially harmful in stage D HF	III: Harm	B	416, 654–659
Short-term intravenous use in hospitalized patients without evidence of shock or threatened end-organ performance is potentially harmful	III: Harm	B	592, 649, 650
MCS			
MCS is beneficial in carefully selected* patients with stage D HF in whom definitive management (eg, cardiac transplantation) is anticipated or planned	IIa	B	660–667
Nondurable MCS is reasonable as a "bridge to recovery" or "bridge to decision" for carefully selected* patients with HF and acute profound disease	IIa	B	668–671
Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HF/EF	IIa	B	672–675
Cardiac transplantation			
Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management	I	C	680

*Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy include patients with LVEF <25% and NYHA class III–IV functional status despite GDMT, including, when indicated, CRT, with either high predicted 1- to 2-year mortality (eg, as suggested by markedly reduced peak oxygen consumption and clinical prognostic scores) or dependence on continuous parenteral inotropic support. Patient selection requires a multidisciplinary team of experienced advanced HF and transplantation cardiologists, cardiothoracic surgeons, nurses and ideally, social workers and palliative care clinicians.

BTT indicates bridge to transplant; COR, Class of Recommendation; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HF/EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; N/A, not applicable; and NYHA, New York Heart Association.

Yancy C W et al. Circulation. 2013;128:e240-e327

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Hospitalized Patient

Recommendations	COR	LOE	References
HF patients hospitalized with fluid overload should be treated with intravenous diuretics	I	B	737, 738
HF patients receiving loop diuretic therapy should receive an initial parenteral dose greater than or equal to their chronic oral daily dose; then dose should be serially adjusted	I	B	739
HF*r*EF patients requiring HF hospitalization on GDMT should continue GDMT except in cases of hemodynamic instability or where contraindicated	I	B	195, 735, 736
Initiation of beta-blocker therapy at a low dose is recommended after optimization of volume status and discontinuation of intravenous agents	I	B	195, 735, 736
Thrombosis/thromboembolism prophylaxis is recommended for patients hospitalized with HF	I	B	21, 770–774
Serum electrolytes, urea nitrogen, and creatinine should be measured during titration of HF medications, including diuretics	I	C	N/A
When diuresis is inadequate, it is reasonable to a. give higher doses of intravenous loop diuretics; or	IIa	B	38, 739
b. add a second diuretic (eg, thiazide)		B	740–743
Low-dose dopamine infusion may be considered with loop diuretics to improve diuresis	IIb	B	744, 745
Ultrafiltration may be considered for patients with obvious volume overload	IIb	B	752
Ultrafiltration may be considered for patients with refractory congestion	IIb	C	N/A
Intravenous nitroglycerin, nitroprusside, or nesiritide may be considered an adjuvant to diuretic therapy for stable patients with HF	IIb	A	760–763
In patients hospitalized with volume overload and severe hyponatremia, vasopressin antagonists may be considered	IIb	B	787, 788

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; and N/A, not available.

Yancy C W et al. Circulation. 2013;128:e240-e327

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

Back to the hospitalized patient….

- Patient on mechanical ventilator
- Vitals: BP 90/55, HR 104, JVD 12, clear lungs, +S3, +S4 , Palpable liver, Cool ext. 2+ edema
- Meds: Milrinone @ 0.5 mcg/kg/min, Amiodarone 0.5mg, Lasix
- Labs: Na+ - 132, Cr – 2.0, Bili – 2.4, Hgb – 10, WBC – 9, Platelets -155.
- Hemodynamics: CO -3.8, CI – 1.8, RA – 14, PCW – 18, SVR – 1108, PVR- 3.1

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

ADVANCED HF AND INTERMACS PROFILES: TRANSITION AMONG PROFILES – A COMMON OCCURRENCE

Inotrope/MCS/TX

Medical therapy

INTERMACS PROFILE-LEVEL	NYHA	Official Shorthand	Modifier options
INTERMACS 1	D - IV	"Crash and burn"	± Arrhythmia, ± Temporary Circ Support
INTERMACS 2	D - IV	"Sliding fast" despite inotropic support	± Arr, TCS
INTERMACS 3	D - IV	Stable but inotropic therapy-dependent, In hosp or home	± Arr ± Frequent Flyer
INTERMACS 4	D, Amb.IV	Resting symptoms on oral therapy at home.	± Arr ± FF
INTERMACS 5	D, Amb.IV	"Housebound", Comfortable at rest, symptoms with minimal daily activity	± Arr ± FF
INTERMACS 6	D, Amb.IV	"Walking wounded"- ADL possible but meaningful activity limited	± Arr ± FF
INTERMACS 7	C,D III, IIIB	Advanced Class III	± Arr

MEDICAL THERAPY FOR ADVANCED HEART FAILURE
Overview / concepts

- Recognizing transition to advanced heart failure from chronic heart failure.
- Current status of medical therapy for heart failure – medications, effectiveness and performance.
- Calibrating medical therapy for stage “C” ambulatory and hospitalized patients with heart failure.
- When to refer to a disease management program.

The determination of advanced heart failure includes consideration of following parameters despite optimal medical therapy except;

A. NYHA Class III-IV Symptoms

B. Objective evidence of severe cardiac dysfunction
(EF<30%, Doppler Pseudonormal or Restrictive filling pattern, PCWP>16mmHg or RAP >12 mmHg)

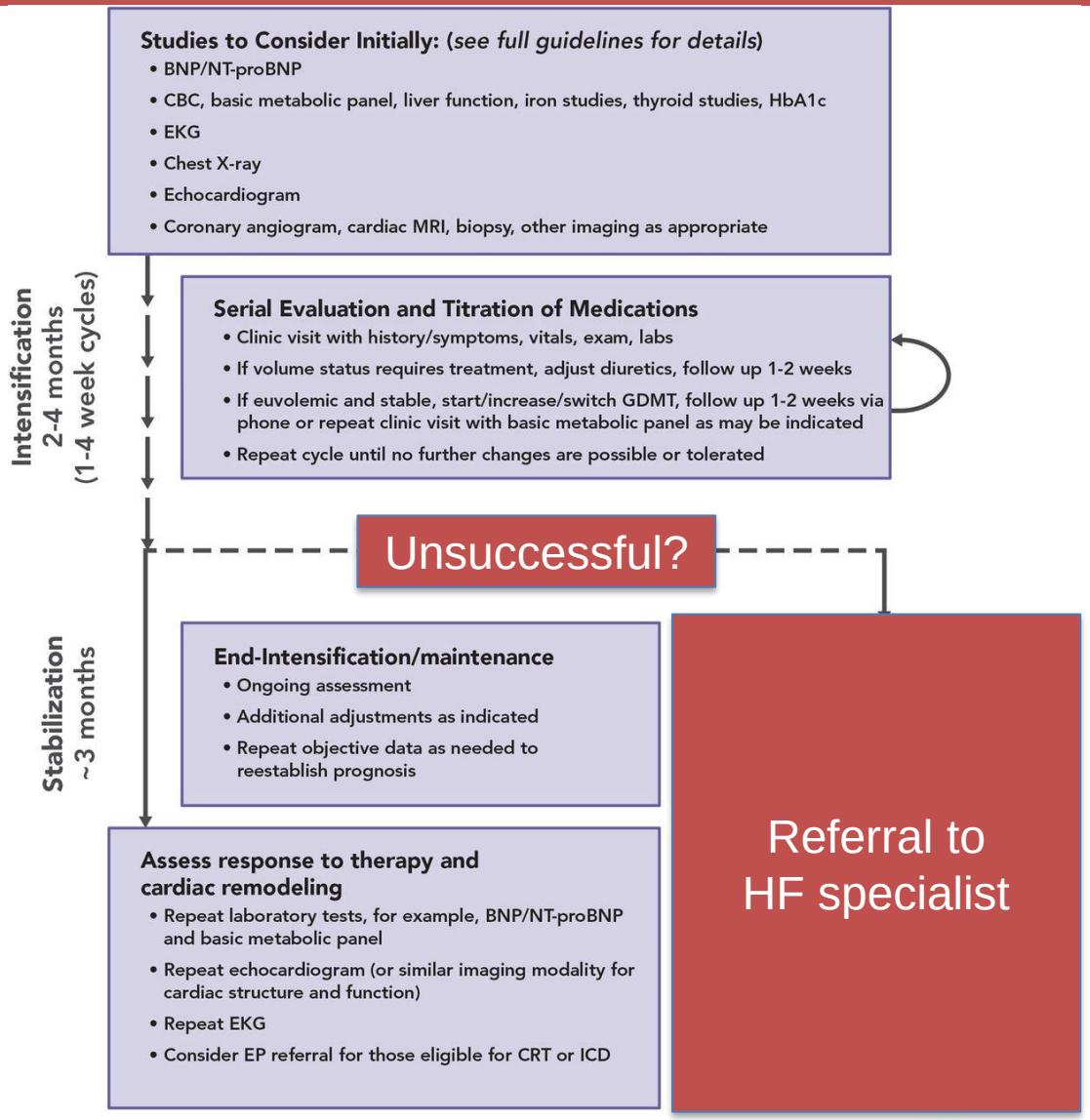
C. Severely impaired functional capacity
(Inability to exercise, 6MWD<300m, Peak VO2<12-14 ml/kg/min)

D. HF Hospitalizations
(≥1 in past 6 months)

E. Ventricular tachyarrhythmia successfully treated with antiarrhythmic and defibrillator

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

DURING CALIBRATED MEDICAL THERAPY…. DECIDING REFERRAL TO HF PROGRAM

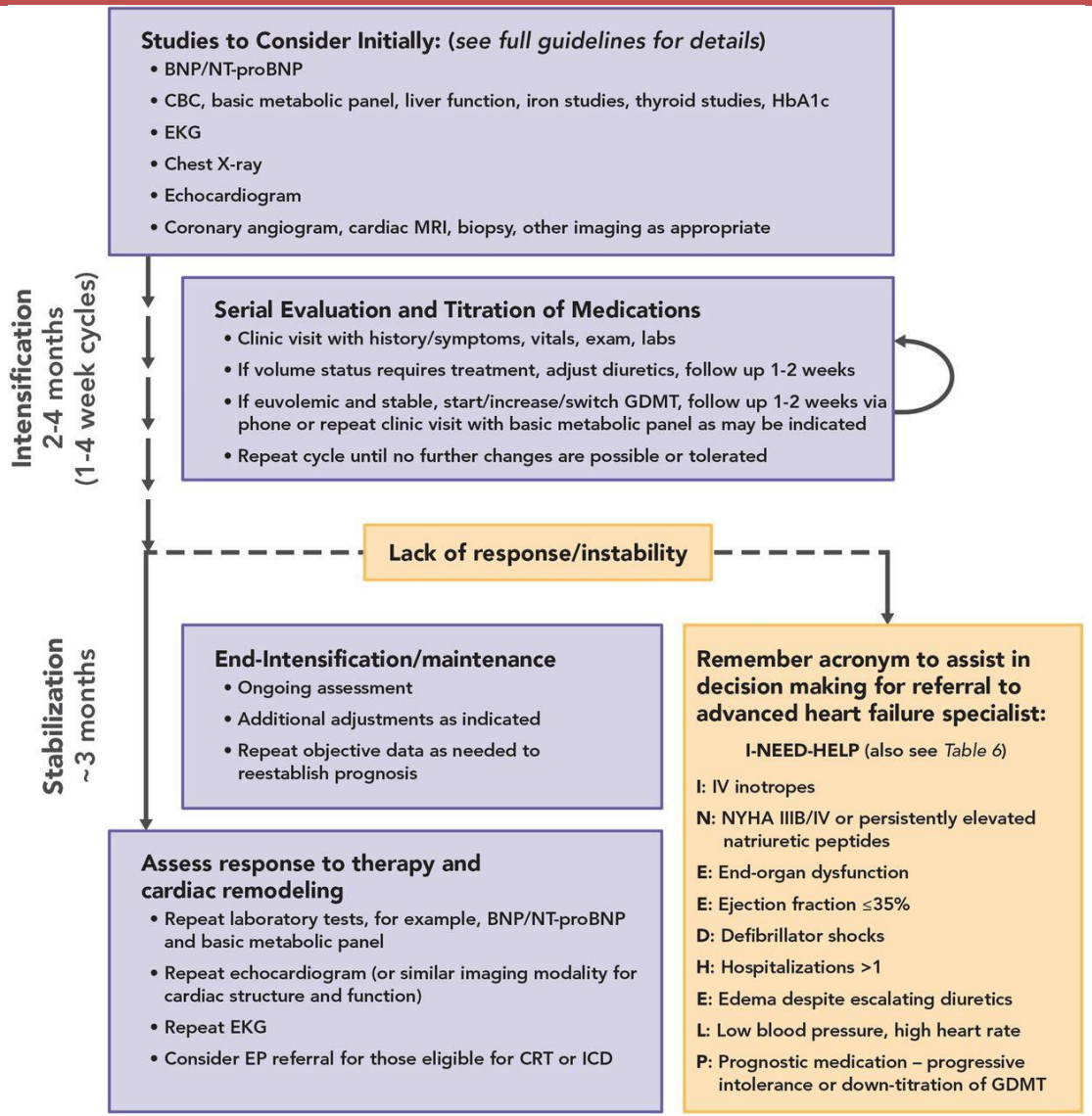


Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

Banner University Medicine

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

DURING CALIBRATED MEDICAL THERAPY…. DECIDING REFERRAL TO HF PROGRAM



Referral to
HF speciali

Banner University Medicine

Heart Failure Pathway Writing Committee et al. JACC 2017;j.jacc.2017.11.025

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE

MEDICAL THERAPY FOR ADVANCED HEART FAILURE