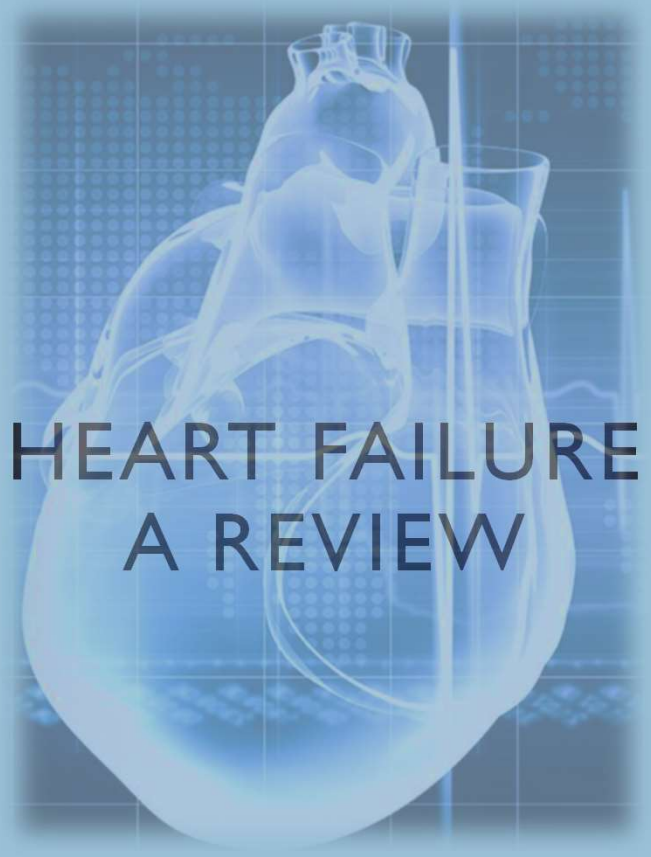


Heart One Associates

Heart One
ASSOCIATES

ACUTE CORONARY SYNDROME

Rajkumar Sugumaran, MD
Interventional Cardiologist
Heart One Associates

PENNY NICKEL

- 45 YEAR OLD FEMALE
- ONE WEEK OF WORSENING FATIGUE,
- SOB AND CP

PMH
HTN
DM
DYSLIPIDEMIA
GERD
HYPOTHYROID

SURGICAL HISTORY
TAH WITH BSO (Endometriosis)
Thyroidectomy (benign nodule)
Appendectomy
Cholecystectomy
Skin cancer excisions (BCC)

FAMILY HISTORY

Father: first MI at 45, 3V CABG/PCI
Mother: had MI prior to 50 y/o
Brother: PE and DVT
MGM: died from aneurysm (details uncertain)

MEDICATIONS

Metformin 500 mg BID
Lisinopril 20 mg
HCTZ 50 mg daily
Levothyroxine 125 mg daily
Omeprazole 20 mg daily
Aleve as needed
Ibuprofen as needed

- SOCIAL HISTORY
- She works as a professor at local state University, teaches history.
- Tobacco: Never
- Vaping: none, never
- ETOH: 1 glass of wine with dinner
- Drugs: CBD oil at night for sleep

SYMPTOMS

- She has to walk up hill to her class every day and usually has no problem. Also parks far away. When not at work, she exercises doing Zumba about 4 days a week
- About two weeks ago, I noticed when walking up my normal hill at work, I had some burning in my chest, some SOB. Initially the symptoms improved almost immediately when I stopped. I figured it was a cold or heart burn or something.
- Over the past week, the symptoms have started sooner and are taking longer to resolve after stopping (resting)
- She had to stop doing Zumba d/t symptoms while exercising…thought she was coming down with something.
- "I tried TUMS a couple of times, it did not make a difference. I have also been using NSAIDS the past couple of weeks, it doesn't seem to be helping.."
- Of note: She returned three weeks ago from visiting her sibling in Europe.

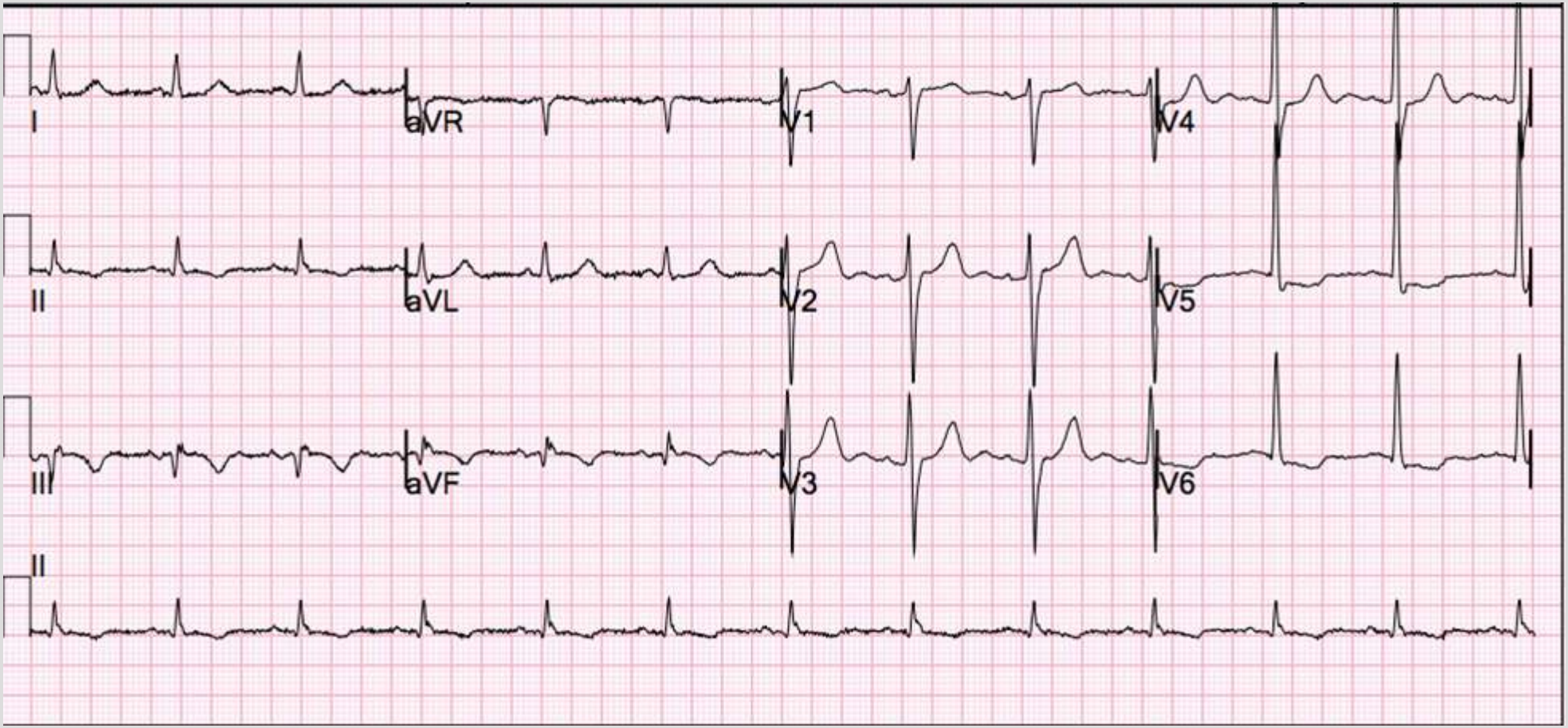
ED

Last night, I woke up at 3 AM with burning in my chest that would not go away. After about 45 minutes I told my husband to bring me in….

ED

- Pulse: 65
- BP: 125/66
- Weight: 150#
- Height: 65 inches
- Temp: 97.2
- RR: 14
- s/p ASA, Morphine and one NTG, almost virtually at the same time. Her symptoms resolved. She does not know which made her better.

"WHAT DOES HER ECG LOOK LIKE?



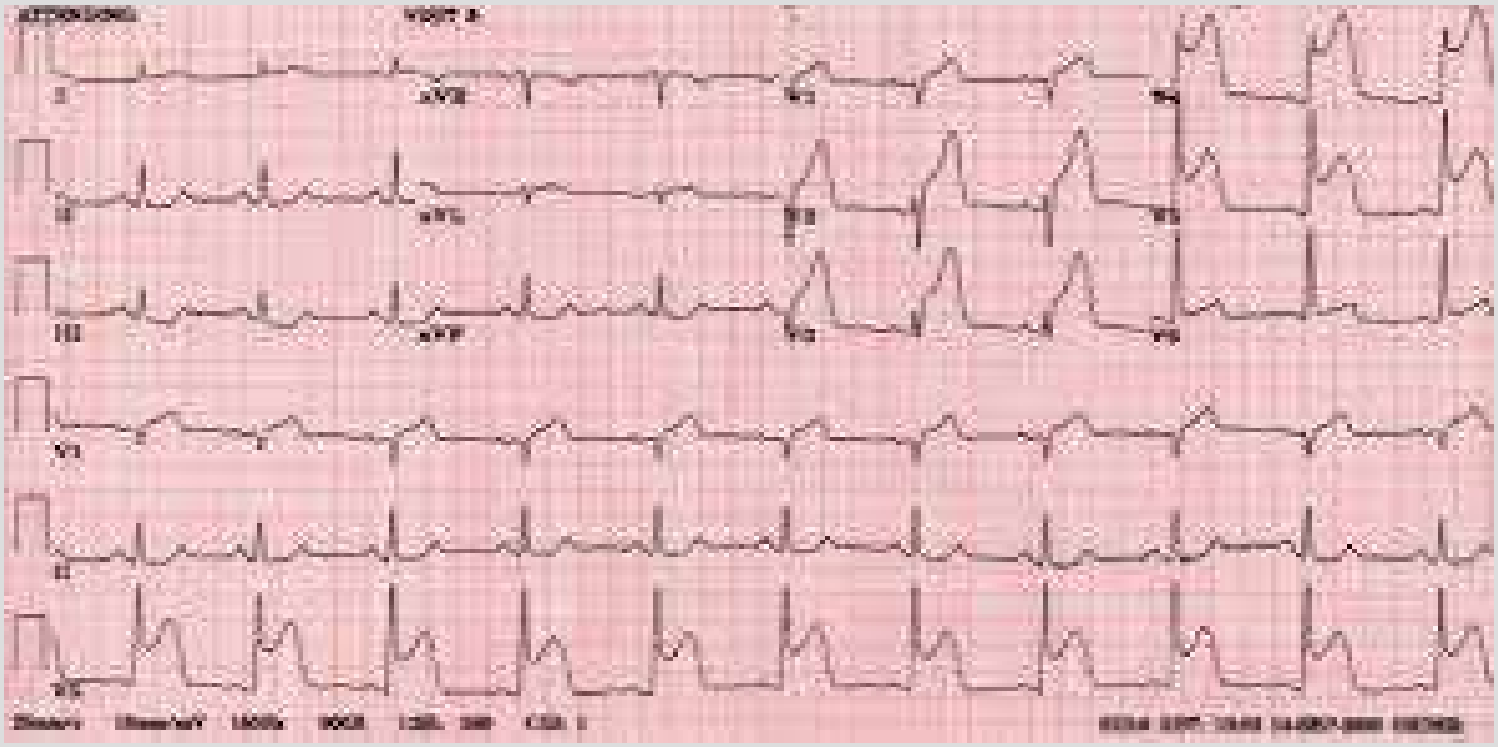
LABS/IMAGING

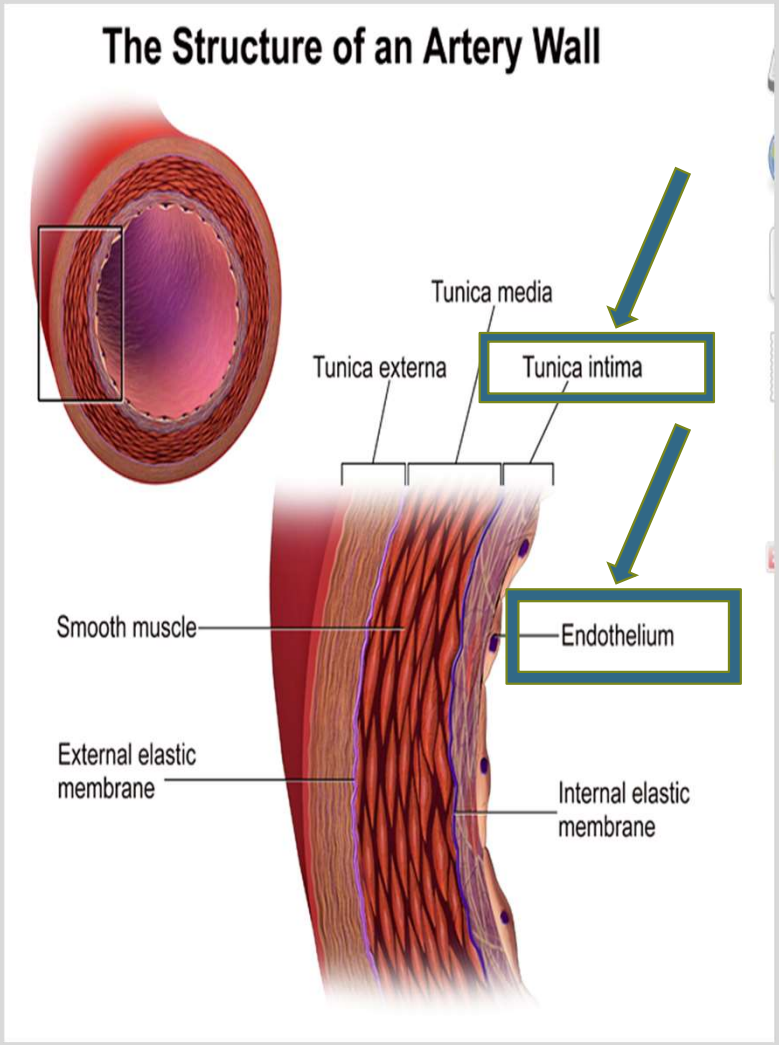
- TROPONIN I : 0.03→0.18→ 0.43→ 2.25
- High sensitivity: 30=> 180=> 430=> 2250
- BNP: 745

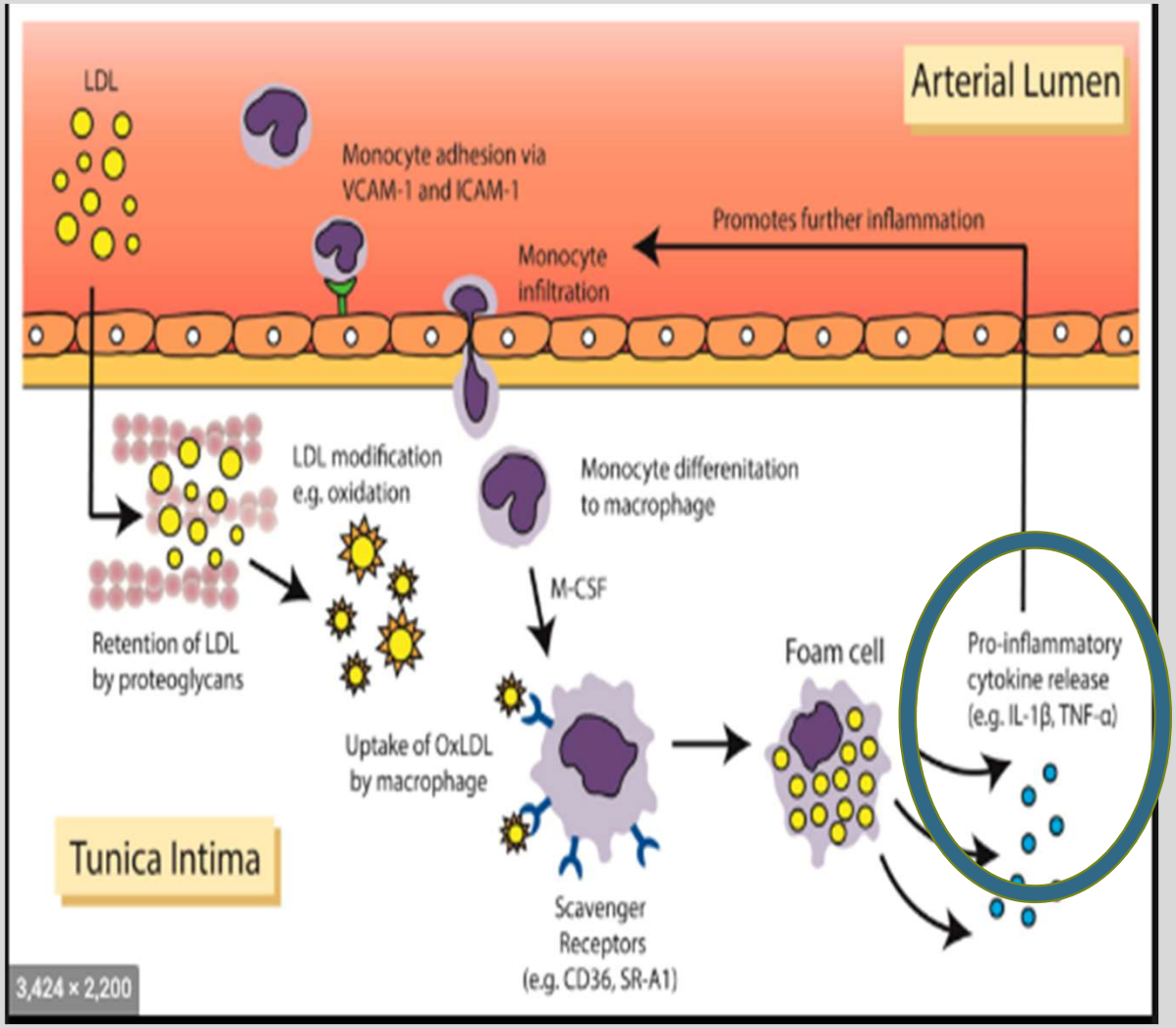
- HGB: 12.8
- Platelet: 344
- Creatinine: 2.1, GFR 28
- K: 3.2
- Mg: 1.6

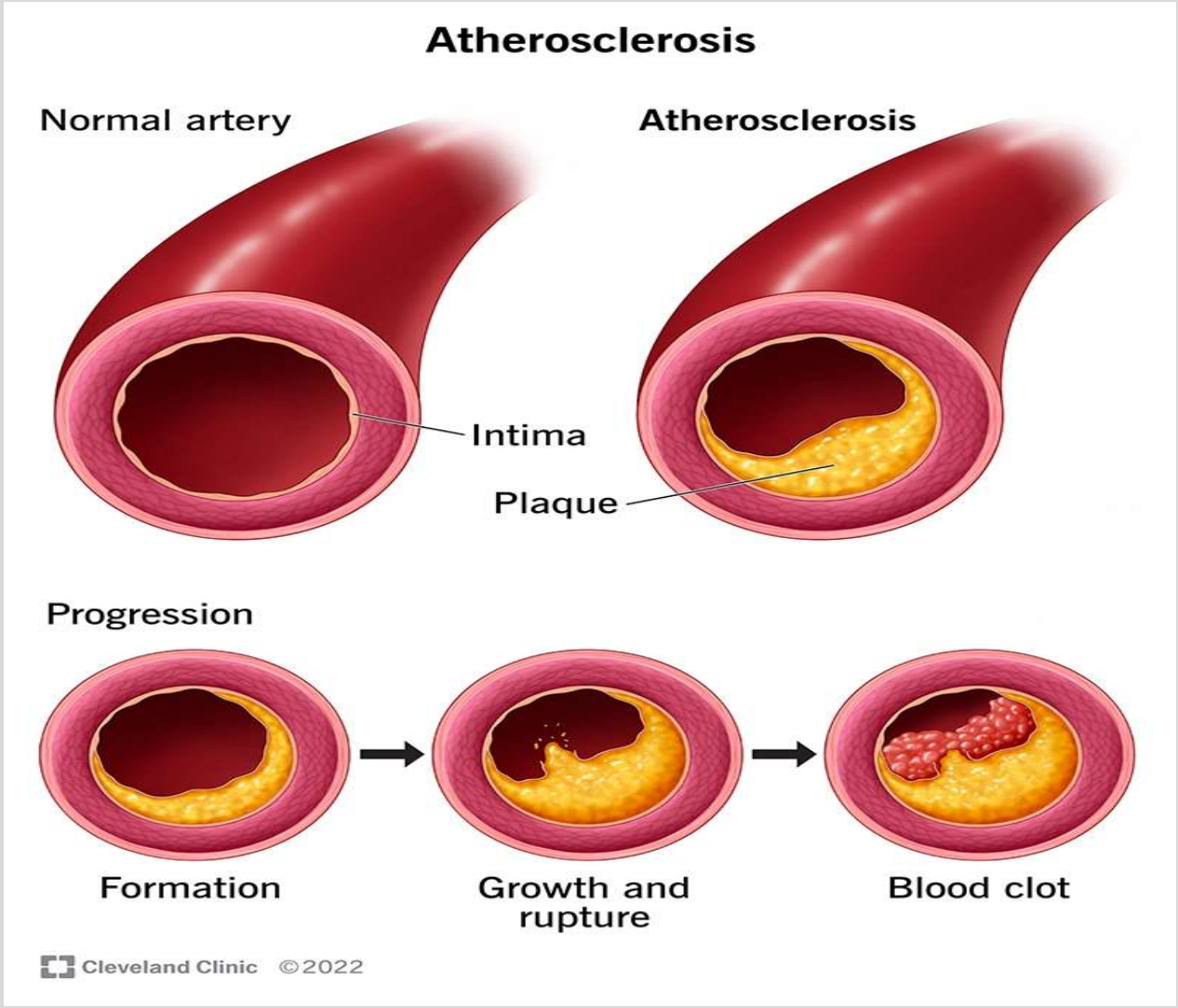
- CTA: NO PE

LATER THAT NIGHT, SHE DEVELOPED RECURRENT CP
HER SBP IS NOW IN 70S
HERE IS HER ECG…




The Structure of an Artery Wall
Tunica media
Tunica externa
Tunica intima
Smooth muscle
Endothelium
External elastic membrane
Internal elastic membrane

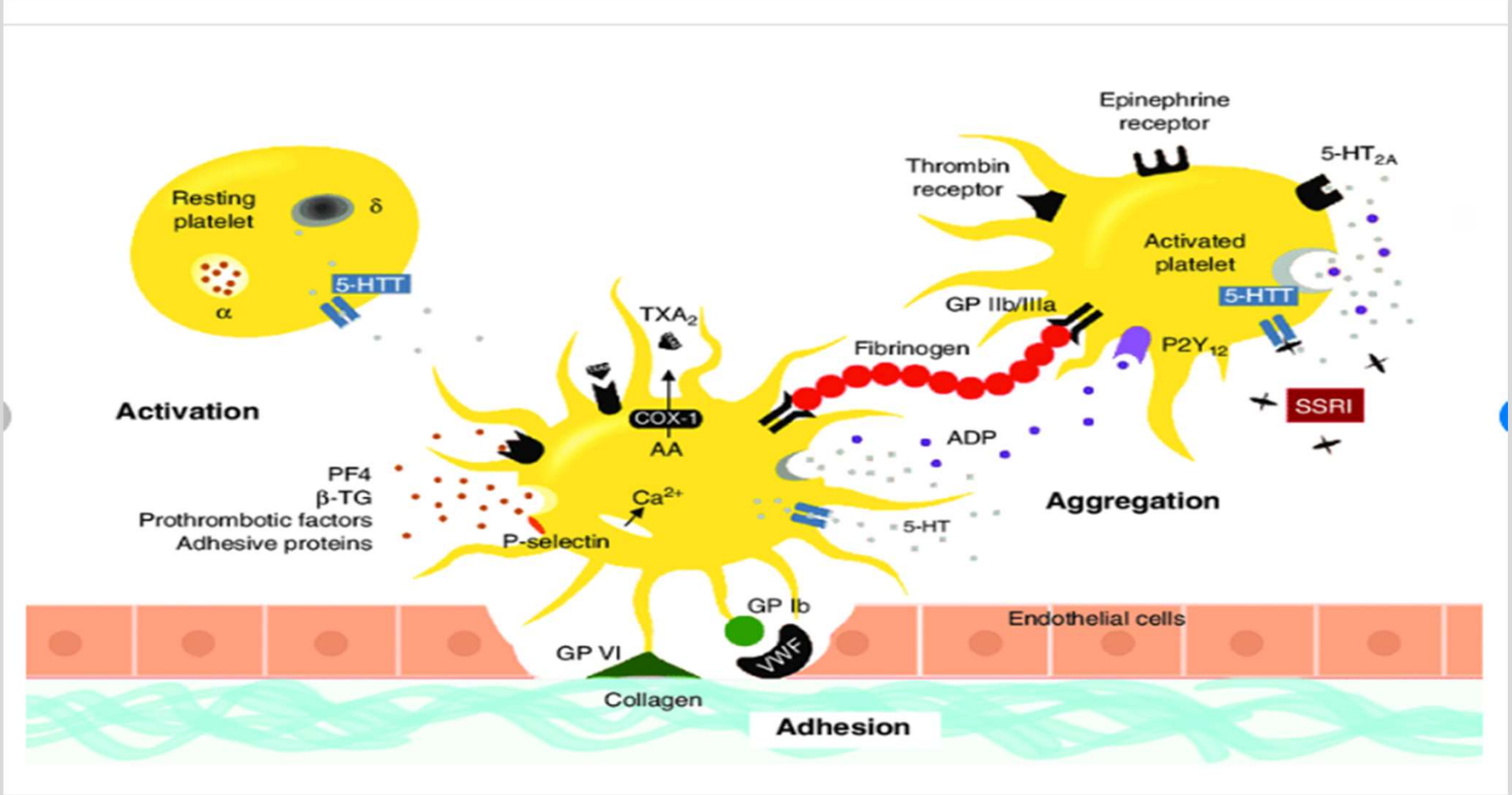

LDL
Arterial Lumen
Monocyte adhesion via VCAM-1 and ICAM-1
Promotes further inflammation
Monocyte infiltration
LDL modification e.g. oxidation
Monocyte differenitation to macrophage
M-CSF
Retention of LDL by proteoglycans
Foam cell
Pro-inflammatory cytokine release (e.g. IL-1β, TNF-α)
Uptake of OxLDL by macrophage
Tunica Intima
Scavenger Receptors (e.g. CD36, SR-A1)
3,424 × 2,200


Atherosclerosis
Normal artery
Atherosclerosis
Intima
Plaque
Progression
Formation
Growth and rupture
Blood clot
Cleveland Clinic ©2022

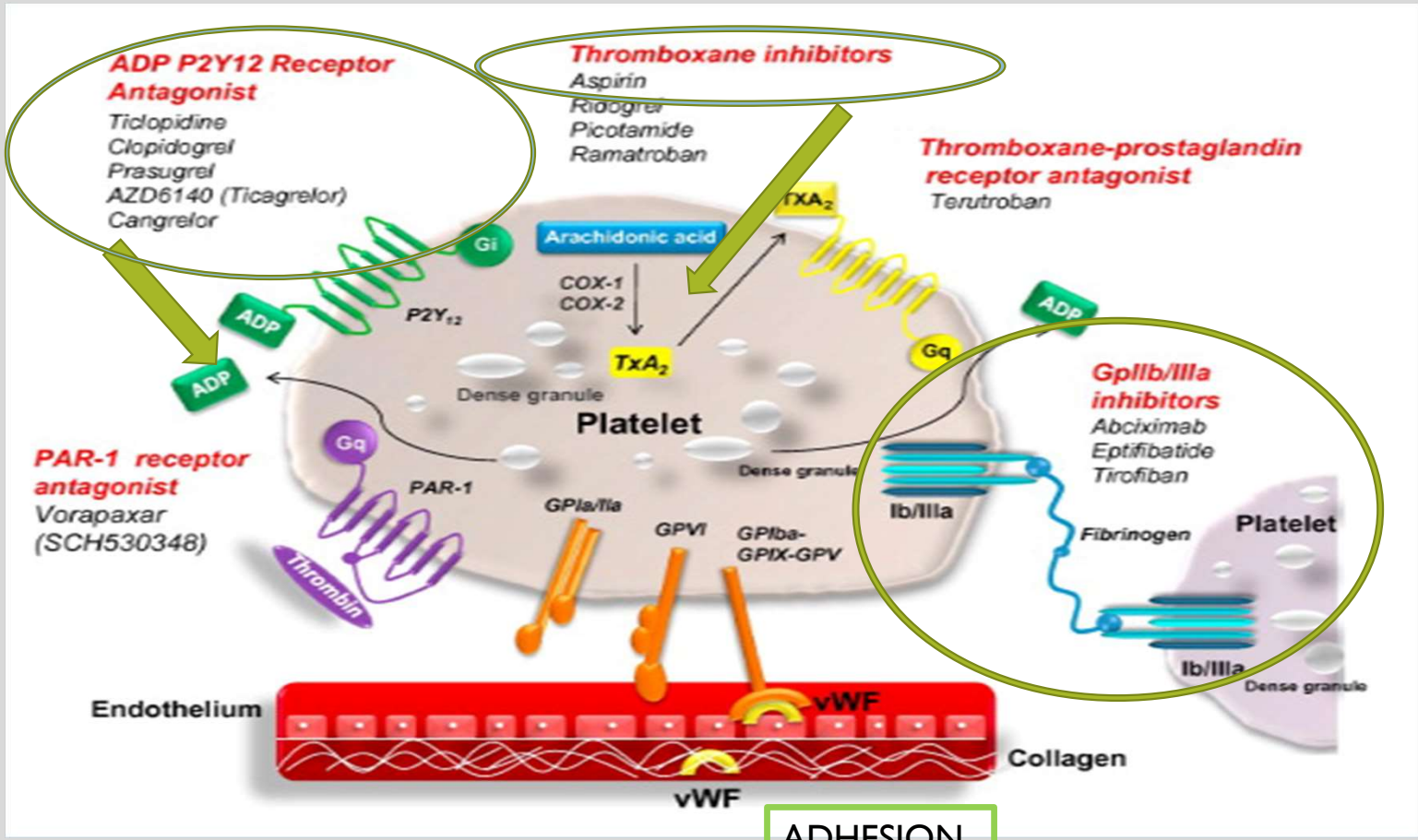
ACS PHYSIOLOGY
3 A'S

PLAQUE RUPTURE

ACS AND PLATELET



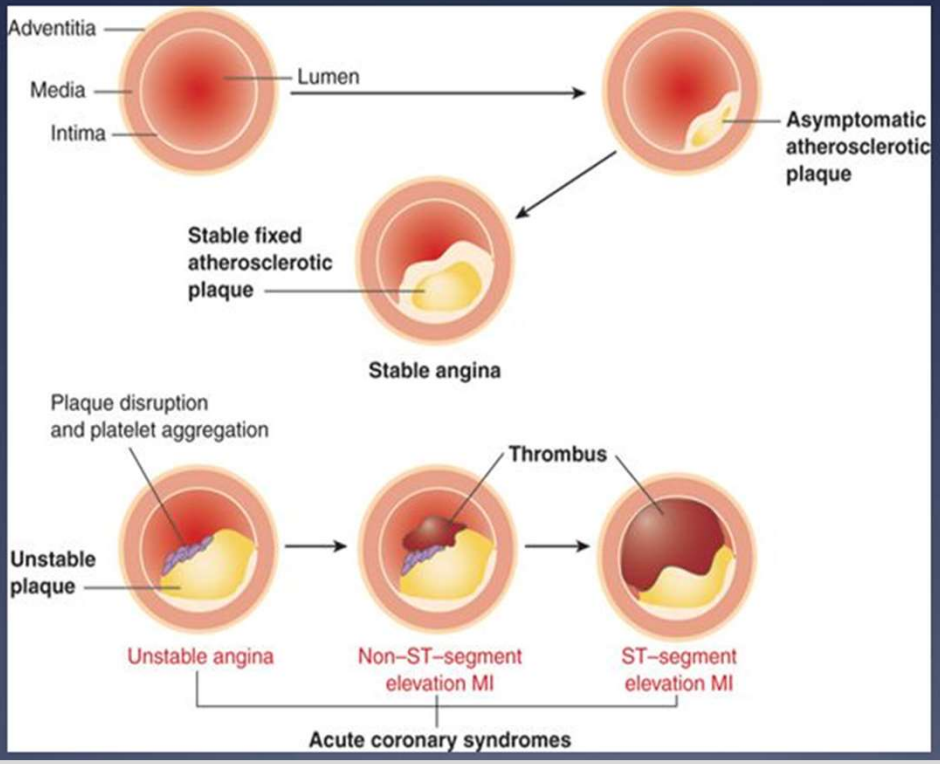
THE PLATELET



ADHESION,

What is Acute Coronary Syndrome?

~~Stable Angina~~ | Unstable Angina | NSTEMI | STEMI



UNSTABLE ANGIA
NO NECROSIS

NSTEMI
NECROSIS

STEMI
TRANSMURAL NECROSIS

STEMI

- PCI CAPABLE FACILITY

  SYSTEM BENCHMARK: 90 min DTB

  - Continuous association between shortening D2B time and reduced risk of 1-year mortality.

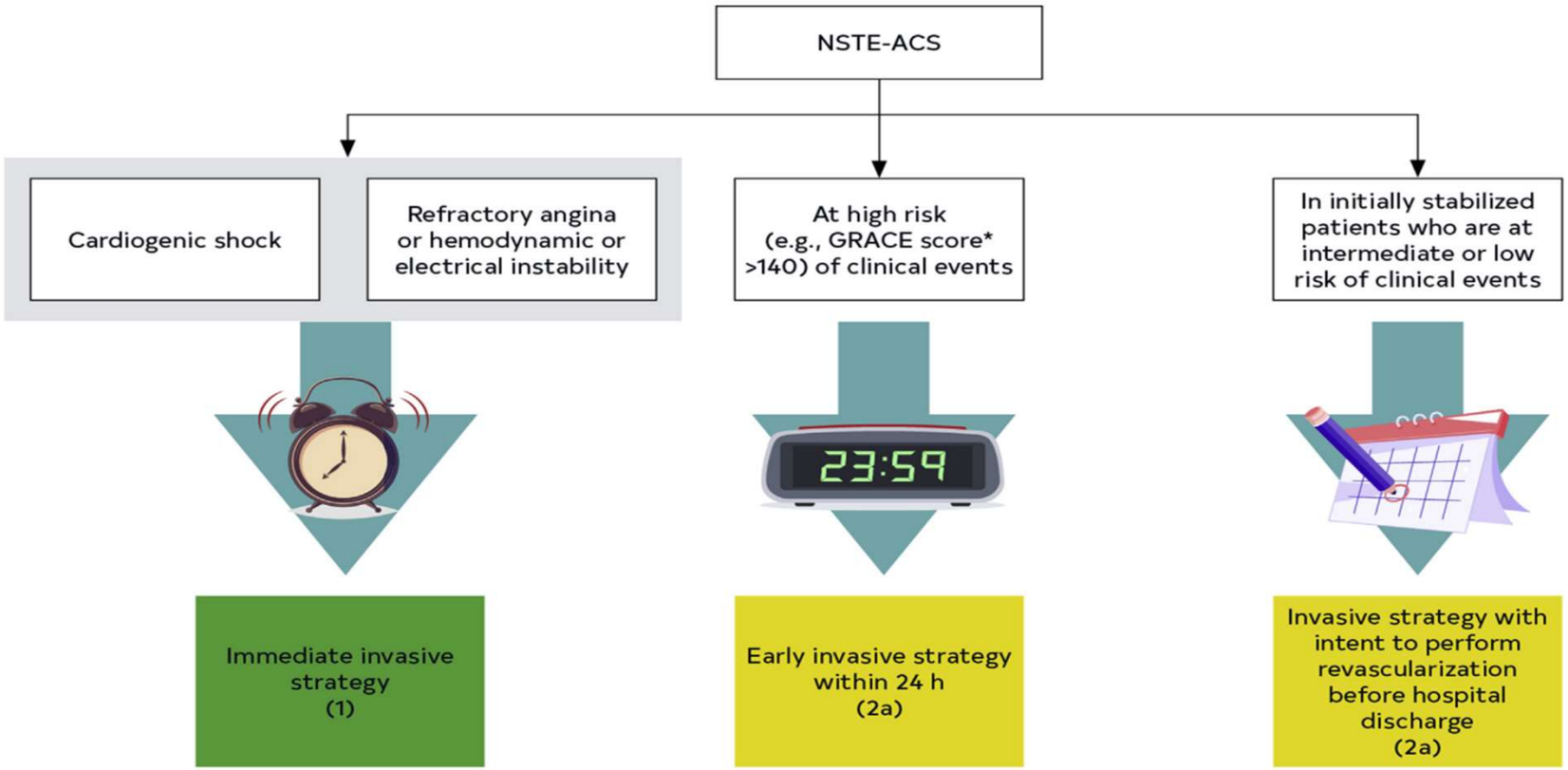
- NON PCI CAPABLE FACILITY

  Transfer to PCI capable facility if
  STEMI DX to PCI TIME <120 minutes

Thrombolysis

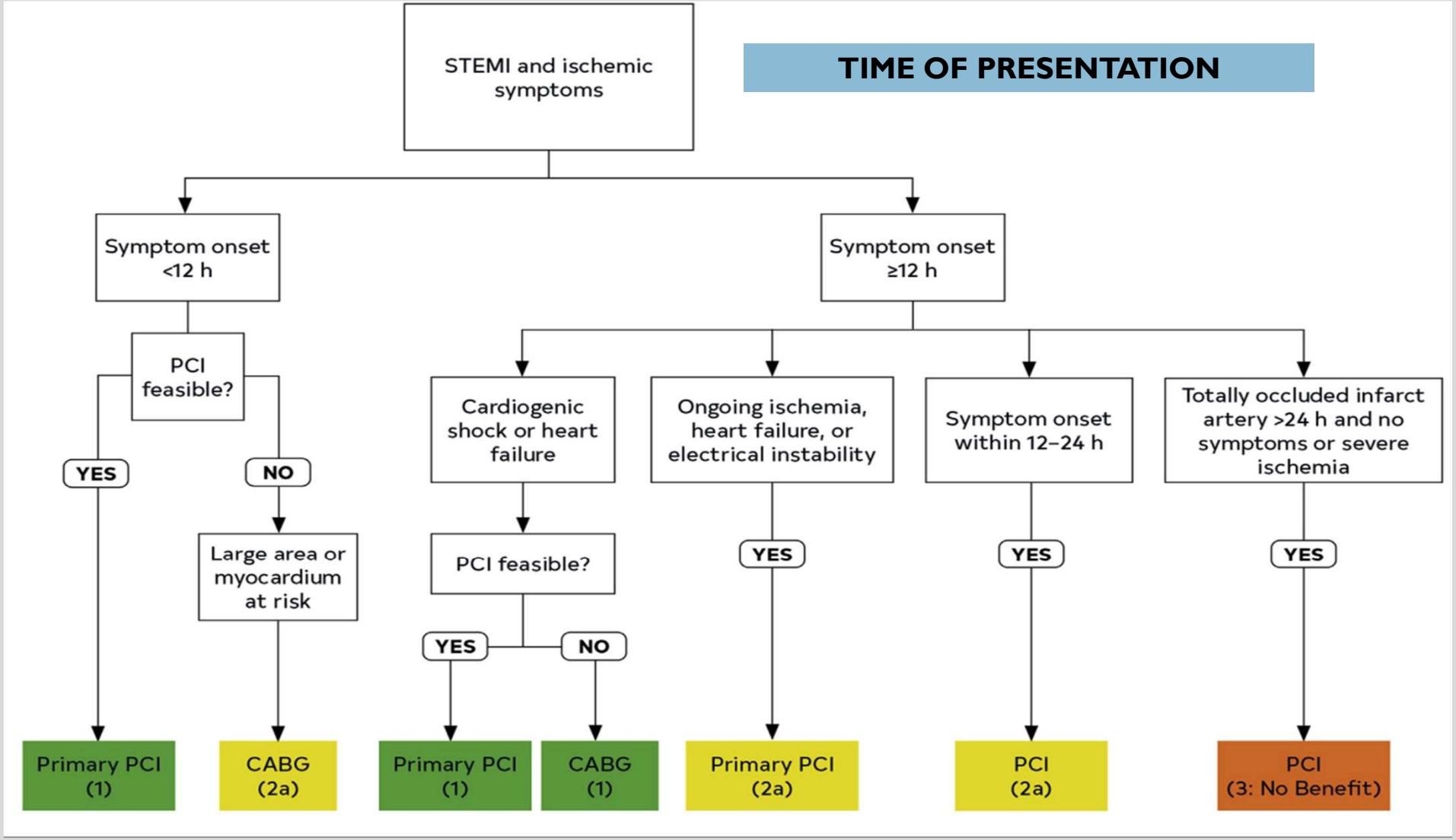
IF >120 minutes (from DX to PCI, PCI facility)=> can consider Fibrinolysis (DOOR TO NEEDLE w/in 30 minutes)

FIGURE 5 Recommendations for the Timing of Invasive Strategy in Patients With NSTE-ACS

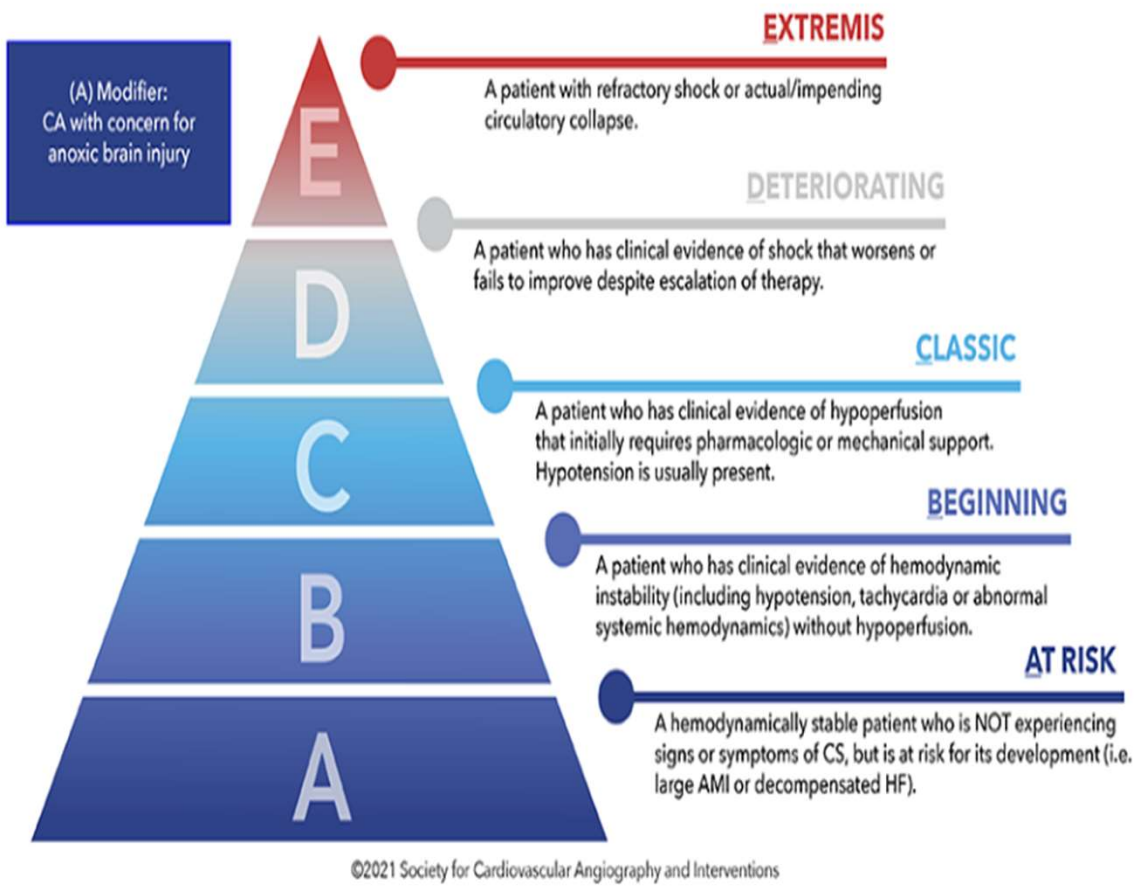


Colors correspond to **Table 2**. GRACE indicates Global Registry of Acute Coronary Events; and NSTE-ACS, non-ST-segment–elevation acute coronary syndrome. *https://www.mdcalc.com/grace-acs-risk-mortality-calculator (31). This algorithm summarizes the recommendations in this guideline for coronary artery angiography with the intent to perform revascularization in NSTE-ACS. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

TIME OF PRESENTATION



SCAI STAGES OF CARDIOGENIC SHOCK



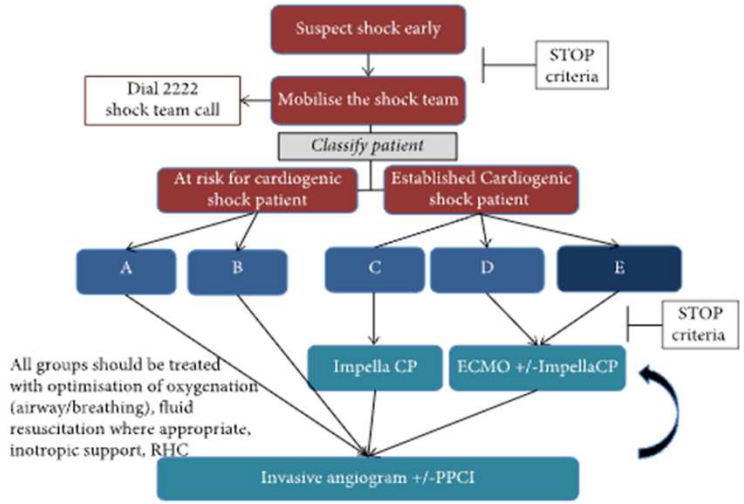
SCAI SHOCK Stages Classification Expert Consensus Update: A Review and Incorporation of Validation Studies (January 2022)

Research Article

Rapid Classification and Treatment Algorithm of Cardiogenic Shock Complicating Acute Coronary Syndromes: The SAVE ACS Classification

Figure 4

Proposed treatment algorithm for patients presenting with acute coronary syndromes and shock. Early use of mechanical circulatory support is advocated for patients in the C-E groups.



ROLE FOR MCS

MEDICAL THERAPY

DAPT

COR	LOE	RECOMMENDATIONS
1	B-R	1. In patients undergoing PCI, a loading dose of aspirin, followed by daily dosing, is recommended to reduce ischemic events (1-4).*
1	B-R	2. In patients with ACS undergoing PCI, a loading dose of P2Y12 inhibitor, followed by daily dosing, is recommended to reduce ischemic events (5-15).
1	C-LD	3. In patients with SIHD undergoing PCI, a loading dose of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events (8,12,15-19).
1	C-LD	4. In patients undergoing PCI within 24 hours after fibrinolytic therapy, a loading dose of 300 mg of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events (5).

TABLE 9 Oral and Parenteral Antiplatelet Agents for Patients Undergoing PCI

Drug	Loading Dose	Maintenance Dose
	Oral antiplatelet agents	
Aspirin	Loading dose of 162-325 mg orally (11) Aspirin may be chewed to achieve faster action	Maintenance dose of 75-100 mg orally daily (24,25)
Clopidogrel	Loading dose of 600 mg orally (19) A lower loading dose of 300 mg should be considered in patients after fibrinolytic therapy (5)	Maintenance dose of 75 mg orally daily (34)
Prasugrel	Loading dose of 60 mg orally (20)	Maintenance dose of 10 mg orally daily (20) In patients with body weight <60 kg, a maintenance dose of 5 mg orally daily is recommended (35) In patients ≥75 years of age, a dose of 5 mg orally daily can be used if deemed necessary (35)
Ticagrelor	Loading dose of 180 mg orally (14) Ticagrelor may be chewed to achieve faster action	Maintenance dose of 90 mg orally twice a day (14)
	Intravenous antiplatelet agents	
Abciximab (GPI)*	Bolus of 0.25 mg/kg (36)	Maintenance of 0.125 μg/kg/min infusion (maximum 10 g/min) for 12 h. (36)
Eptifibatide (GPI)	Double bolus of 180 μg/kg (given at a 10-min interval) (37)	Maintenance infusion of 2.0 μg/kg/min for up to 18 h (37)
Tirofiban (GPI)	Bolus of 25 μg/kg over 3 min (38)	Maintenance infusion of 0.15 μg/kg/min for up to 18 h (38)
Cangrelor	Bolus of 30 μg/kg (39)	Maintenance infusion 4 μg/kg/min for at least 2 h or duration of the procedure, whichever is longer (39)

*Abciximab may not be readily available to clinicians in the United States.

GPI indicates glycoprotein IIb/IIIa inhibitor; and PCI, percutaneous coronary intervention.

Clopidogrel, prasugrel and ticagrelor

Characteristics of various ADP P2Y12 inhibitors

TRITON-TIMI 38

PLATO

	Clopidogrel	Prasugrel	Ticagrelor
Prodrug	Yes	Yes	No
CYP450 activation	Yes	Yes	No
Interaction with PPI	Yes	No	No
Time to peak IPA	6–12 h	2 h	2 h
Reversibility	No	No	Yes, in 3–5 days
Plasma half-life	7–8 h	7–8 h	7–12 h
Preparation	Oral	Oral	Oral
Administration	Once daily	Once daily	Twice daily

CYP450, cytochrome p450; IPA, inhibition of platelet activity; IV, intravenous.

PRASUGREL: CLASS 3 HARM IF H/O CVA/TIA
INCREASED RISK FOR BLEEDING WITH LOW BODY WEIGHT, >75 y/o

SAPIENZA UNIVERSITÀ DI ROMA

Tan et al, Cardiovasc Ther 2012

2a	B-R	5. In patients with ACS undergoing PCI, it is reasonable to use ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events, including stent thrombosis (6,14,20).
2b	B-R	6. In patients <75 years of age undergoing PCI within 24 hours after fibrinolytic therapy, ticagrelor may be a reasonable alternative to clopidogrel to reduce ischemic events (21).
3: Harm	B-R	7. In patients undergoing PCI who have a history of stroke or transient ischemic attack, prasugrel should not be administered (6).

*Contraindications to ticagrelor: previous intracranial hemorrhage or ongoing bleeding. Contraindications to prasugrel: previous intracranial hemorrhage, previous ischemic stroke or transient ischemic attack, or ongoing bleeding. Prasugrel should be used with caution at a lower dose in patients ≥75 years of age or with a body weight <60 kg.

ISAR 5	Randomized, open label Composite end point	Secondary:(safety outcome): bleeding	Prasugrel reduced events no difference bleeding
Analysis ISAR5			SEVERAL FLAWS TO STUDY
Circulation, Volume 124, No 24	Head to head STEMI Subgroup analysis of ISAR React -5		Suggested Ticagrelor associated with significant increase in risk for recurrent MI, no safely difference.
Registry SWEDE Heart BNJ journal, Heart, Volume 107			no difference between Ticagrelor and Prasugrel
JAMA Cardiol. 2021;6(10):1121-1129. doi:10.1001/jamacardio.2021.2228	Prasugrel versus ticagrelor in patients with myocardial infarction undergoing percutaneous coronary intervention		Prespecified subgroup analysis suggested prasugrel superior to Ticagrelor
Prasugrel vs. Ticagrelor for Acute Coronary Syndrome Patients Undergoing Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis Am J Cardiovascular Drugs 2019 Oct;19(5):465-476.			The present analysis suggests that prasugrel might have a better efficacy profile than ticagrelor in patients with ACS undergoing PCI. However, this advantage was only seen in pooled observational studies and is likely to be affected by selection bias.

CANGRELOR

COR	LOE	RECOMMENDATION
2b	B-R	1. In patients undergoing PCI who are P2Y12 inhibitor naïve, intravenous cangrelor may be reasonable to reduce periprocedural ischemic events (1-3).

Potent, direct, reversible, short acting P2Y12 inhibitor
Rapid onset
Restoration platelet activity within 1 hour discontinuation

Patient selection:
-pretreated with P2Y12
-inhibited oral absorption
-unable to take oral med

Bridging from oral to intravenous $P2Y_{12}$-inhibiting therapy with cangrelor is associated with sustained $P2Y_{12}$ inhibitory effects and does not lead to a DDI.[28] However, transitioning from cangrelor to a thienopyridine (clopidogrel and prasugrel), but not ticagrelor, can be associated with a DDI.[26–31]

CHAMPION Platform, Champion PCI, Champion Phoenix
CHAMPIION PLATFROM, PCI: no reduction in primary outcome (death, MI or ischemia driven revascularization at 48 hours)
CHAMPION platform: Cangrelor= lower stent thrombosis/death
CHAMPION phoenix significant reduction in composition endpoint-driven by reduction periprocedural MI and intraprocedural stent thrombosis
Pooled meta analysis supported findings associated with 41% reduction stent thrombosis
Major bleeding similar

ANTICOAGULATION

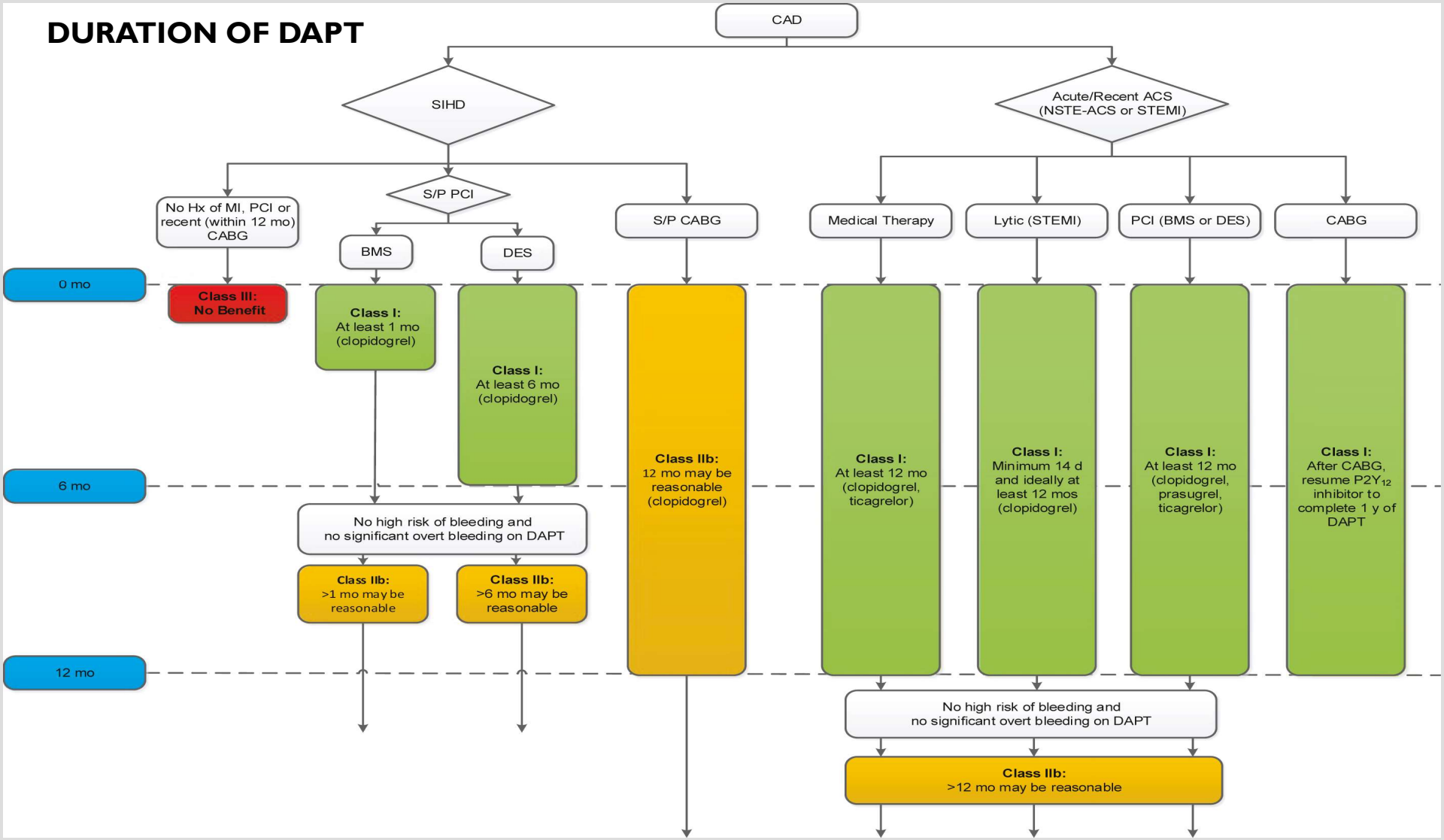
COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients undergoing PCI, administration of intravenous unfractionated heparin (UFH) is useful to reduce ischemic events.
1	C-LD	2. In patients with heparin-induced thrombocytopenia undergoing PCI, bivalirudin or argatroban should be used to replace UFH to avoid thrombotic complications (1,2).
2b	A	3. In patients undergoing PCI, bivalirudin may be a reasonable alternative to UFH to reduce bleeding (3-12).
2b	B-R	4. In patients treated with upstream subcutaneous enoxaparin for unstable angina or NSTE-ACS, the use of intravenous enoxaparin may be considered at the time of PCI to reduce ischemic events (13-17).
3: Harm	B-R	5. In patients on therapeutic subcutaneous enoxaparin, in whom the last dose was administered within 12 hours of PCI, UFH should not be used for PCI and may increase bleeding (14,18,19).

GPIIBIIIA (GP2B3A)

COR	LOE	RECOMMENDATIONS
2a	C-LD	1. In patients with ACS undergoing PCI with large thrombus burden, no-reflow, or slow flow, intravenous glycoprotein IIb/IIIa inhibitor agents are reasonable to improve procedural success (1,2).
3: No Benefit	B-R	2. In patients with SIHD undergoing PCI, the routine use of an intravenous glycoprotein IIb/IIIa inhibitor agent is not recommended (3-5).

ROLE FOR GP2B3A INHIBITORS

- In ACS Trials GP2B3A inhibitors did not show improved outcomes-may increase bleeding complications
- In era of more potent oral anti platelet agents, GP2B3A inhibitors are reserved for patients with a large thrombus burden or no reflow or slow flow that is believed to be d/t distal embolization of thrombus


DURATION OF DAPT
CAD
SIHD
Acute/Recent ACS (NSTE-ACS or STEMI)
No Hx of MI, PCI or recent (within 12 mo) CABG
S/P PCI
S/P CABG
Medical Therapy
Lytic (STEMI)
PCI (BMS or DES)
CABG
BMS
DES
0 mo
6 mo
12 mo
Class III: No Benefit
Class I: At least 1 mo (clopidogrel)
Class I: At least 6 mo (clopidogrel)
Class IIb: 12 mo may be reasonable (clopidogrel)
Class I: At least 12 mo (clopidogrel, ticagrelor)
Class I: Minimum 14 d and ideally at least 12 mos (clopidogrel)
Class I: At least 12 mo (clopidogrel, prasugrel, ticagrelor)
Class I: After CABG, resume P2Y12 inhibitor to complete 1 y of DAPT
No high risk of bleeding and no significant overt bleeding on DAPT
Class IIb: >1 mo may be reasonable
Class IIb: >6 mo may be reasonable
No high risk of bleeding and no significant overt bleeding on DAPT
Class IIb: >12 mo may be reasonable

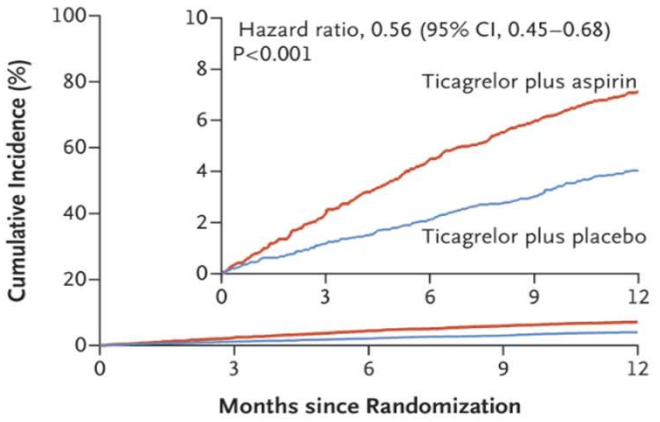
TWILIGHT

NOVEMBER 21, 2019 N ENGL J MED 2019; 381:2032-2042

- Double blind, 9006 patients, intention to treat, 64.8% PCI for ACS/NSTEMI
- Ticagrelor plus placebo (after 3 months DAPT) vs DAPT (x 12 months)
- Adherence similar in both arms
- Composite end point (all cause mortality, non fatal MI or non fatal CV)
- Non inferiority
- No higher risk of composite end point with lower bleeding in SAPT arm (BARC type 2,.3, 5)

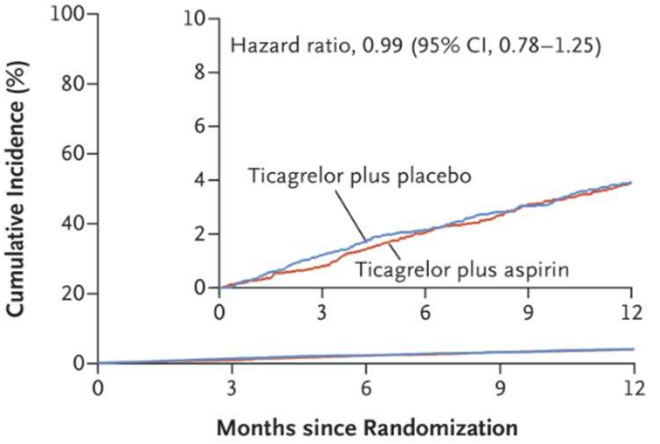
Table 2. Bleeding and Ischemic Events 1 Year after Randomization.*

Variable	Ticagrelor plus Placebo (N=3555)	Ticagrelor plus Aspirin (N=3564)	Hazard Ratio (95% CI)†	P Value
	no. of patients (%)‡			
Bleeding end points				
Primary end point: BARC type 2, 3, or 5§	141 (4.0)	250 (7.1)	0.56 (0.45–0.68)	<0.001¶
BARC type 3 or 5§	34 (1.0)	69 (2.0)	0.49 (0.33–0.74)	
TIMI minor or major	141 (4.0)	250 (7.1)	0.56 (0.45–0.68)	
GUSTO moderate or severe	26 (0.7)	49 (1.4)	0.53 (0.33–0.85)	
ISTH major	39 (1.1)	72 (2.1)	0.54 (0.37–0.80)	
Ischemic end points				
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	135 (3.9)	137 (3.9)	0.99 (0.78–1.25)	<0.001‖
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal ischemic stroke	126 (3.6)	130 (3.7)	0.97 (0.76–1.24)	
Death from any cause	34 (1.0)	45 (1.3)	0.75 (0.48–1.18)	
Death from cardiovascular causes	26 (0.8)	37 (1.1)	0.70 (0.43–1.16)	
Myocardial infarction	95 (2.7)	95 (2.7)	1.00 (0.75–1.33)	
Ischemic stroke	16 (0.5)	8 (0.2)	2.00 (0.86–4.67)	
Stent thrombosis, definite or probable	14 (0.4)	19 (0.6)	0.74 (0.37–1.47)	



No. at Risk

Ticagrelor plus aspirin	3564	3454	3357	3277	3213
Ticagrelor plus placebo	3555	3474	3424	3366	3321



No. at Risk

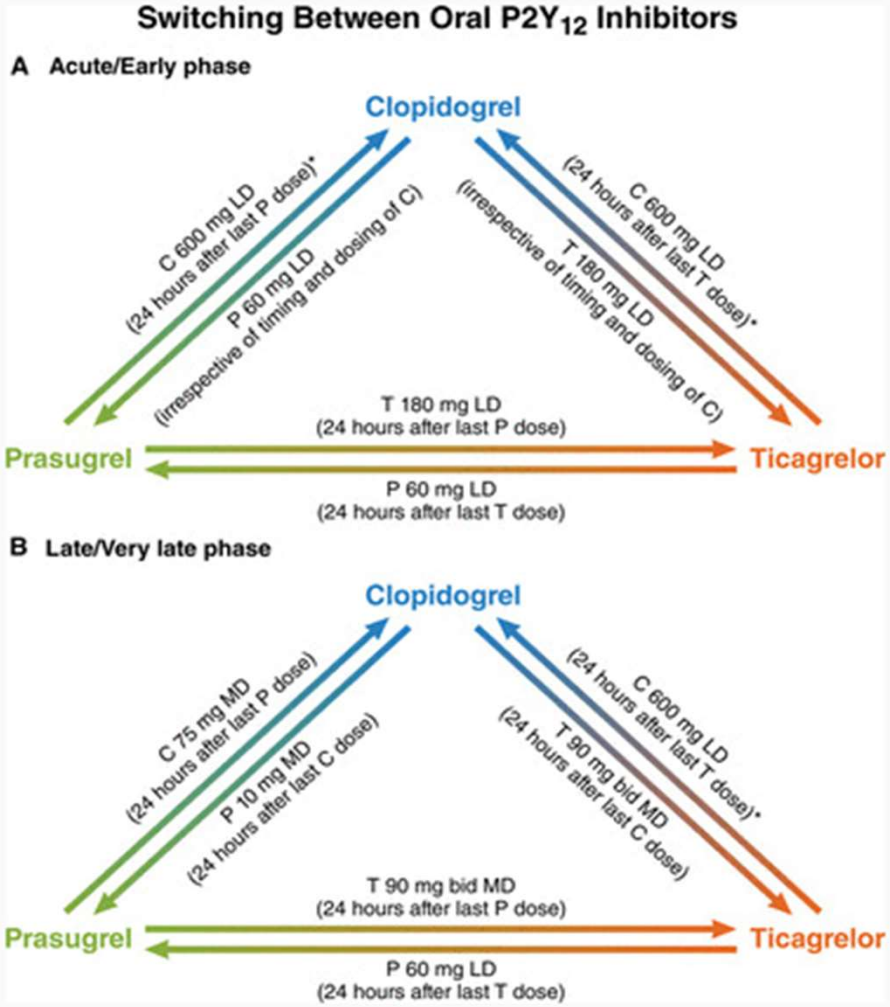
Ticagrelor plus aspirin	3515	3466	3415	3361	3320
Ticagrelor plus placebo	3524	3457	3412	3365	3330

IS THERE A ROLE FOR PATELET FUNCTION TESTING?

3.4 Platelet Function Testing, Genetic Testing, and Switching of $P2Y_{12}$ Inhibitors

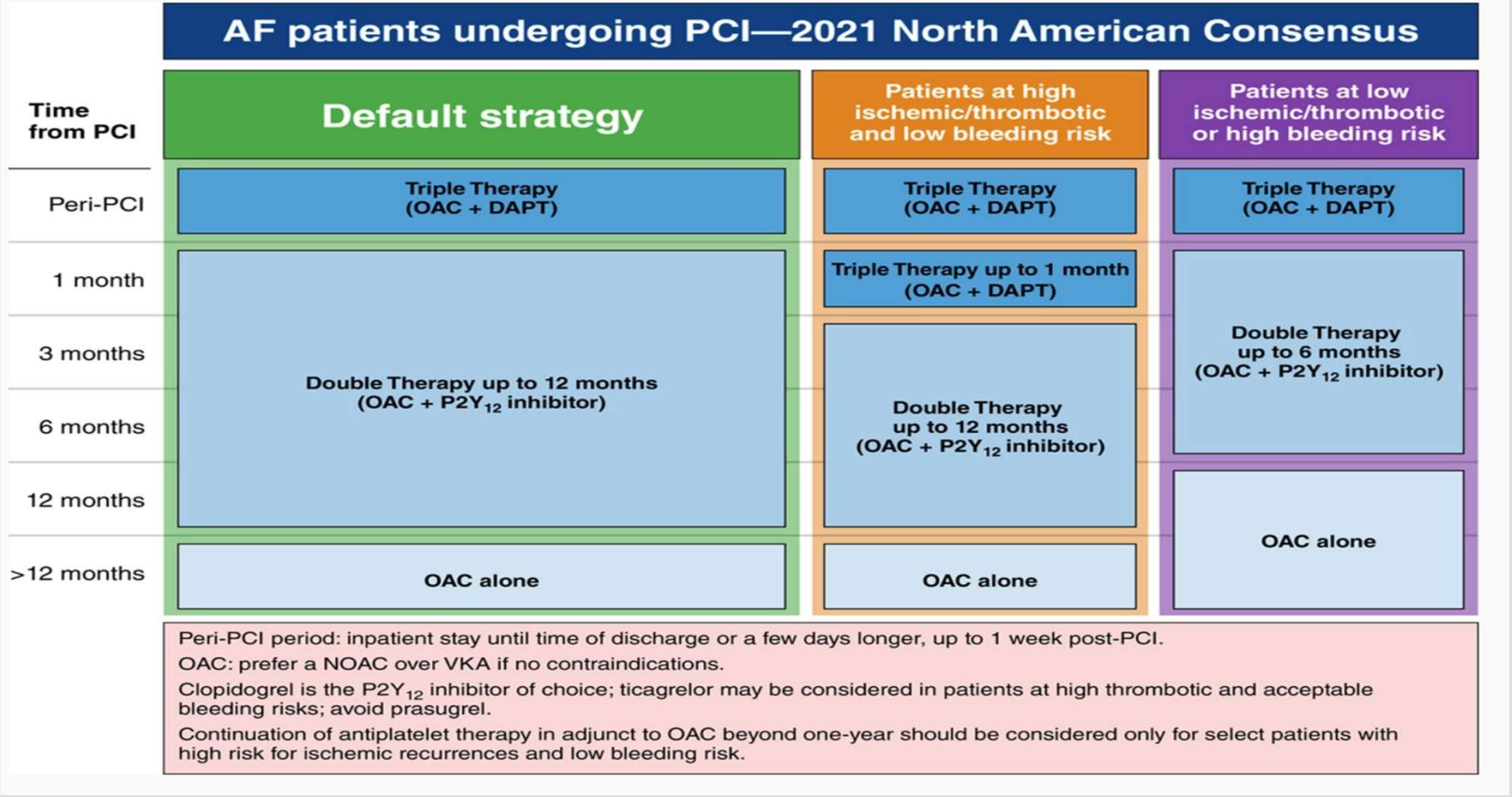
The role of platelet function testing and genetic testing in patients treated with DAPT is addressed in the 2011 ACCF/AHA/SCAI PCI guideline and the 2014 ACC/AHA NSTE-ACS guideline **(9,14)**. To date, no RCT has demonstrated that routine platelet function testing or genetic testing to guide $P2Y_{12}$ inhibitor therapy improves outcome; thus, the routine use of platelet function and genetic testing is not recommended (Class III: No Benefit).

No randomized data are available on the long-term safety or efficacy of "switching" patients treated for weeks or months with a $P2Y_{12}$ inhibitor to a different $P2Y_{12}$ inhibitor.



What do you do if someone is diagnosed with AF or VTE after you have already loaded the patient with Ticagrelor or Prasugrel in setting of ACS?

2020 ACC EXPERT CONSENSUS PATHWAY OAC + ANTI PLATELET



MEDICATION	INDICATION	RECOMMENDATION	CLASS 3
BB		Class 1A AT DC Duration 3 years *COPD w/o bronchospasm is not contraindication	DO NOT USE: First 24 hours if s/o HF, low CO, increased risk for cardiogenic shock, other contraindication, reassess prior to DC Class 3: IV BB in PT with risk factors for shock
ACE (OR ARB)	EF <40%, HTN, DM, stable CKD	Class 1A	
MRA	Post STEMI, on TX doses of ACE/ARB, EF <40	Class 1A	SCr>2 female, >2.5 male K>5.0
NSAID			CLASS 3 (HARM)
NITRATE w/in 24 hours sildenafil, vardenafil w/in 48 hours tadalafil			Class 3 (Harm)
Nifedipine-immediate release			Class 3 (Harm)

VT

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with ventricular fibrillation, polymorphic ventricular tachycardia (VT), or cardiac arrest, revascularization of significant CAD is recommended to improve survival (1-4).
3: No Benefit	C-LD	2. In patients with CAD and suspected scar-mediated sustained monomorphic VT, revascularization is not recommended for the sole purpose of preventing recurrent VT (5-9).

NON CARDIAC SURGERY

COR	LOE	RECOMMENDATION
3: No benefit	B-R	1. In patients with non-left main or noncomplex CAD who are undergoing noncardiac surgery, routine coronary revascularization is not recommended solely to reduce perioperative cardiovascular events (1).

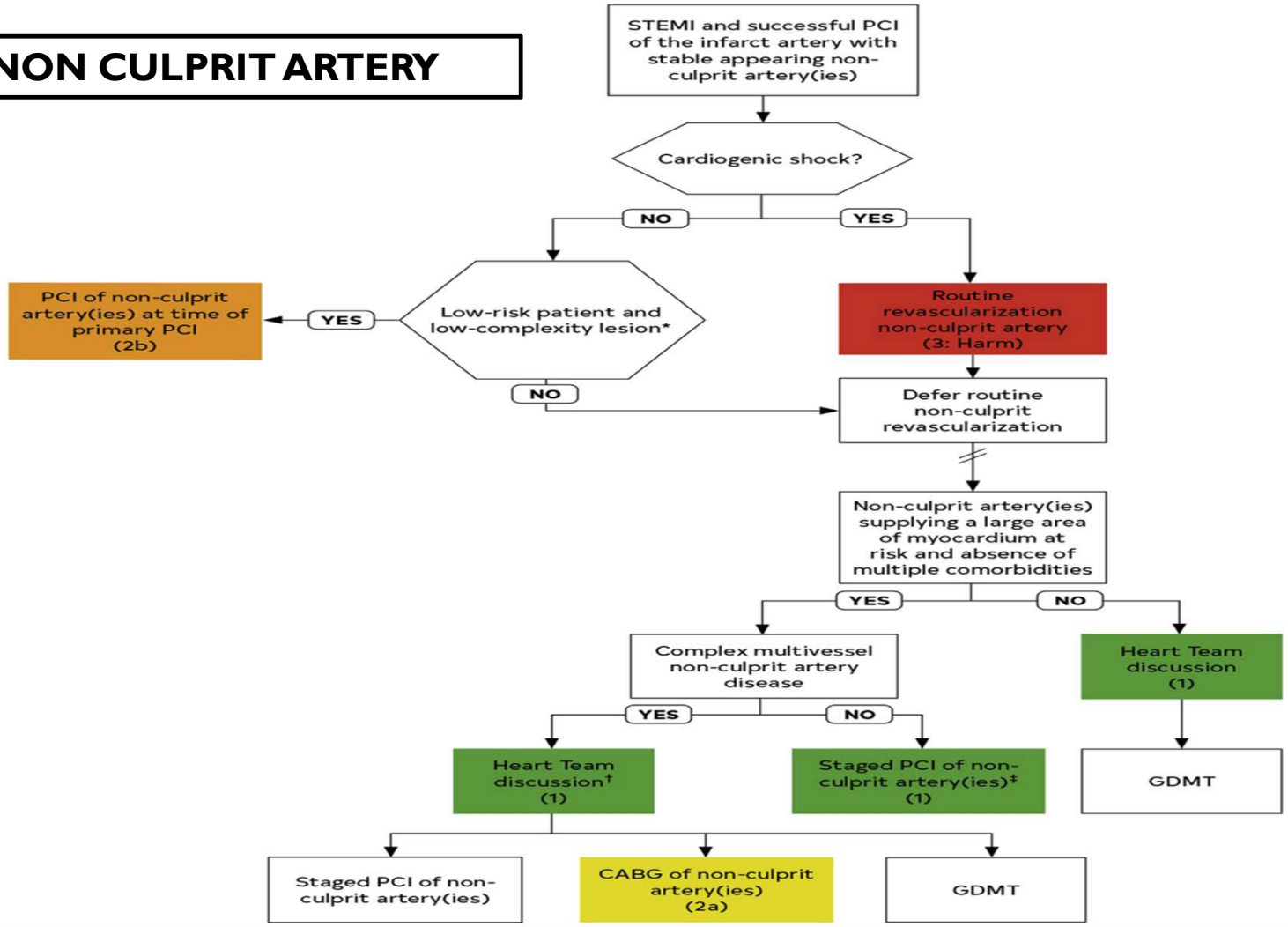
How long do you wait post ACS for:
Elective surgery
What do you do with recent ACS + urgent/time sensitive surgery

ELDERLY

COR	LOE	RECOMMENDATION
1	B-NR	1. In older adults, as in all patients, the treatment strategy for CAD should be based on an individual patient's preferences, cognitive function, and life expectancy (1,2).

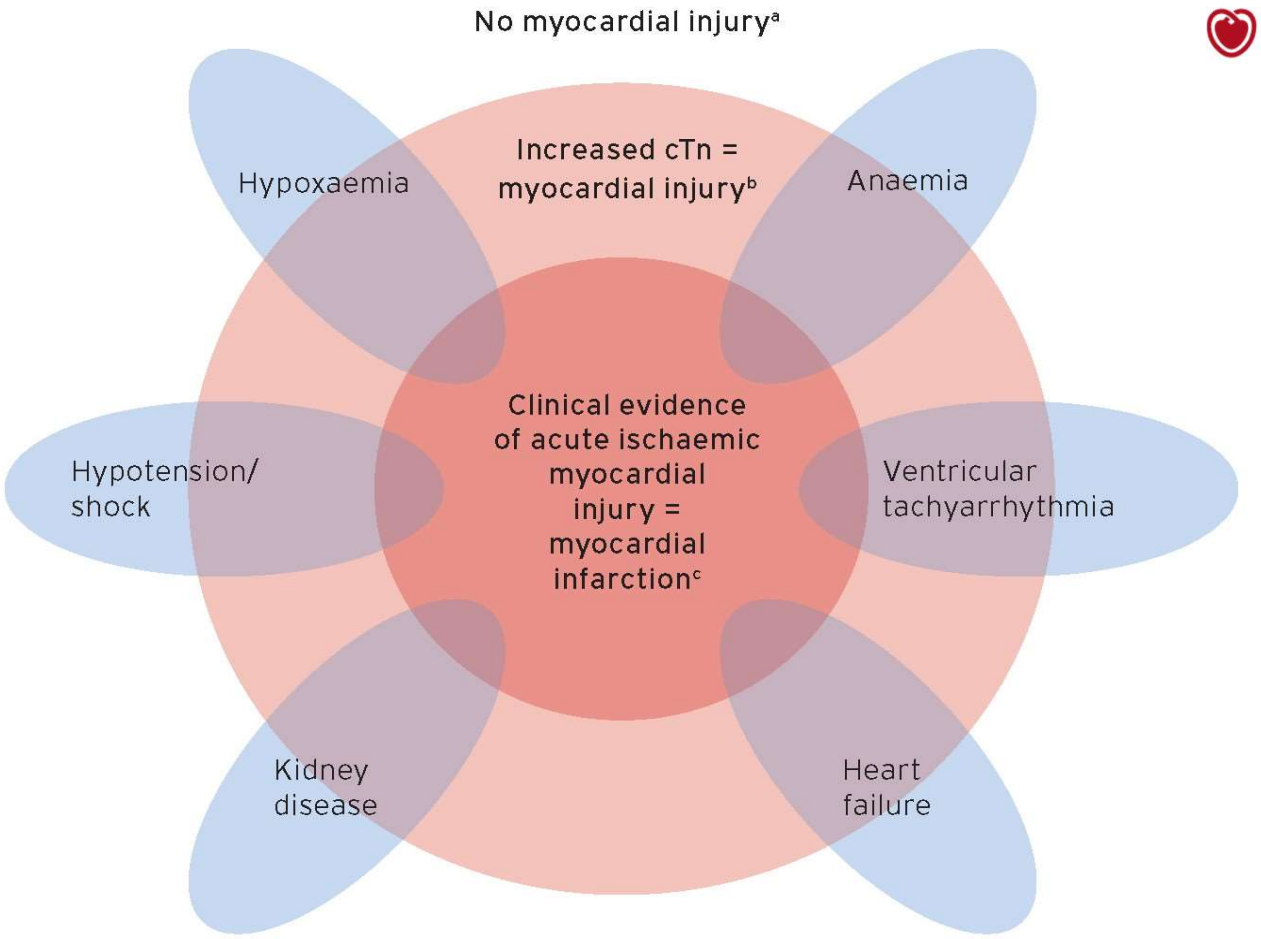
NON CULPRIT ARTERY

FIGURE 4 Revascularization of Noninfarct-Related Coronary Artery Lesions in Patients With STEMI



FOURTH DEFINITION MI (ESC)

- **Type 1 myocardial infarction (STEMI/NSTEMI. ACS)**
  Atherosclerotic plaque rupture, ulceration, fissure, or erosion with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolization and subsequent myocardial necrosis.
- **Type 2 myocardial infarction**
  Myocardial necrosis in which a condition other than coronary plaque instability causes an imbalance between myocardial oxygen supply and demand.[3]
  Mechanisms include hypotension, hypertension, tachyarrhythmias, bradyarrhythmia's, anemia, hypoxemia, but also by definition, coronary artery spasm, spontaneous coronary artery dissection (SCAD), coronary embolism, and coronary microvascular dysfunction.[6–8]
- **Unstable angina (ACS/UA)**
  Unstable angina is defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis.
- **Elevated Troponin that does not meet MI criteria**
  Degree of elevation/ pattern does not meet MI criteria=Myocardial injury (w/o necrosis). Includes: demand: supply mismatch, chronic, non ischemia mediated, alternative DX's to include PE, CVA



ESC European Society of Cardiology

Eur Heart J, Volume 40, Issue 3, 14 January 2019, Pages 237–269, https://doi.org/10.1093/eurheartj/ehy462

OXFORD UNIVERSITY PRESS

MINOCA

MINOCA

It is increasingly recognized that there is a group of MI patients with no angiographic obstructive coronary artery disease (≥50% diameter stenosis in a major epicardial vessel), and the term "myocardial infarction with non-obstructive coronary arteries (MINOCA)" has been coined for this entity.

POTENTIAL CAUSES:
-plaque with spontaneous thrombolysis prior to LHC
-microvascular disease
-Type 2 MI
-spasm

TREAT WITH MEDICAL THERAPY INCLUDING DAPT

TAKOTSUBO:

Diagnosis is made on LV gram/LHC.
Favorable prognosis

DON'T FORGET……

CARDIAC REHAB

PENNY NICKEL

EMERGENTLY TAKEN TO CATH LAB:

CULPRIT 100% PROXIMAL LAD, ALSO HAD SEVERE DISEASE LCX (90% OSTIAL)/RCA (95% OSTIAL, DISTAL CTO, left to right collaterals)

EF: 30% ON LV GRAM (ECHO NOT DONE YET)

VF ON TABLE

CARDIOGENIC SHOCK

What is your strategy?

- PCI culprit ? How do you manage non culprit?
- CABG if not at AWC, if AWC Transfer for emergent CABG?

MCS?

What if Echo shows LV thrombus and you decided to proceed with PCI and loaded with Effient or Ticagrelor in cath lab?

Disclosures:

Sharon Dickinson PAC FACC:
None

Raj Sugumaran MD FACC:

Speaker and Advisor for:
Novartis
Boehringer Ingelheim
Novo Nordisk

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Objectives

- Definitions
- Physiology Overview
- Pillars (medical therapy)
- Clinical management ADHF

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HF is NOT equivalent to cardiomyopathy or to LV dysfunction; these latter terms describe possible structural or functional reasons for the development of HF.

HF is defined as a CLINICAL SYNDROME

- symptoms (dyspnea, orthopnea and fatigue)
- signs (edema, rales, elevated JVP)
- Objective findings (Pulmonary edema, BNP)

THERE IS NO SINGLE DIAGNOSTIC TEST

HF is largely a clinical diagnosis that is based on a careful history and physical examination.

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STAGES OF HEART FAILURE

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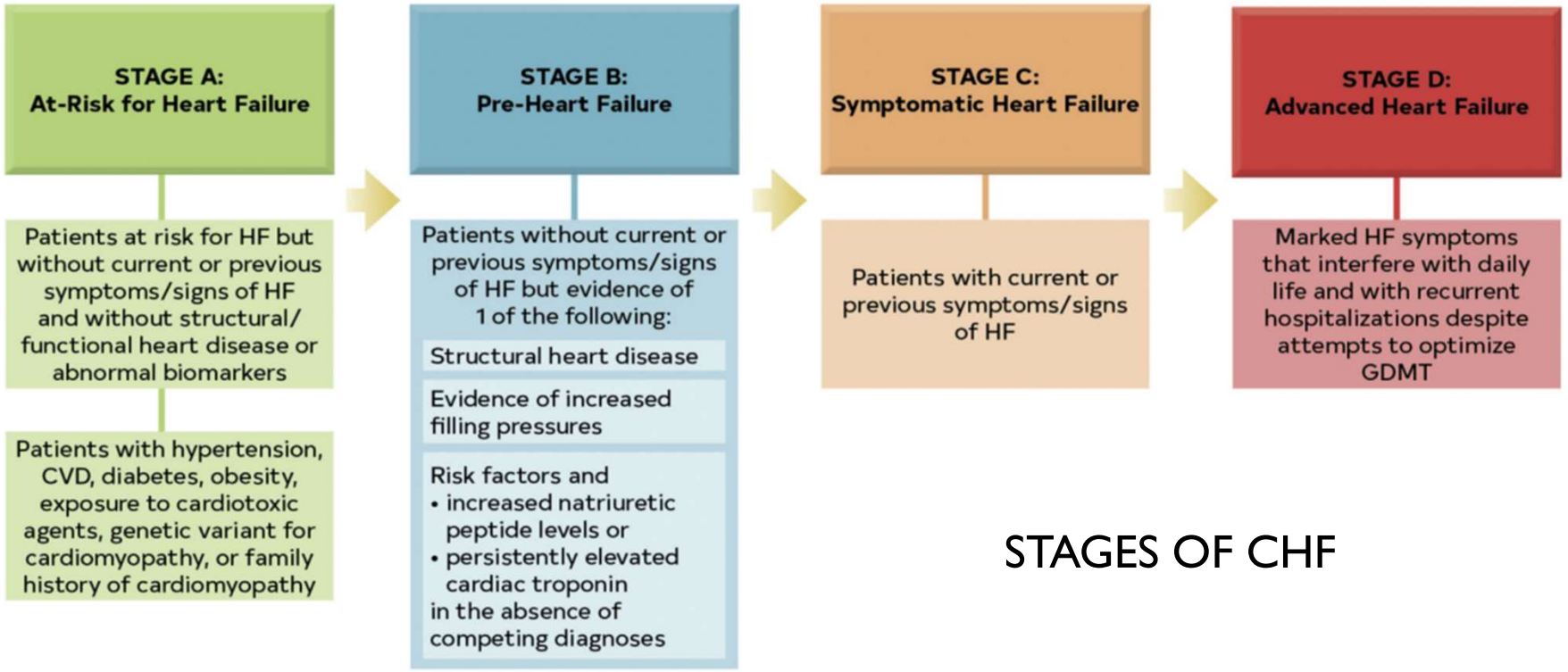
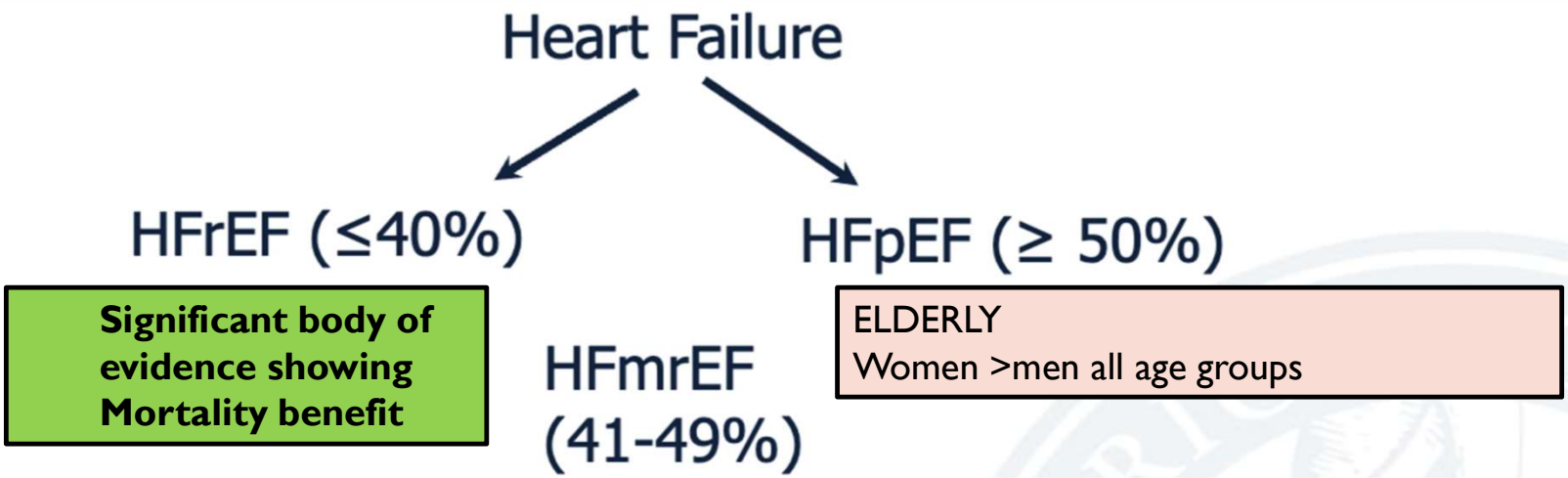
FIGURE 1 ACC/AHA Stages of HF



STAGES OF CHF

The ACC/AHA stages of HF are shown. ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.



HFmrEF = mildly reduced EF

Adapted: Bozkurt, Universal Definition of HF, JCF, 2021

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HF IMPROVED EF

- Prior EF <=40%
- >=10% increase from baseline + second measurement >40%

- Current data suggest better prognosis than other HF phenotypes
- Current guidelines and trial data emphasize the importance of continued GDMT use in these patients.

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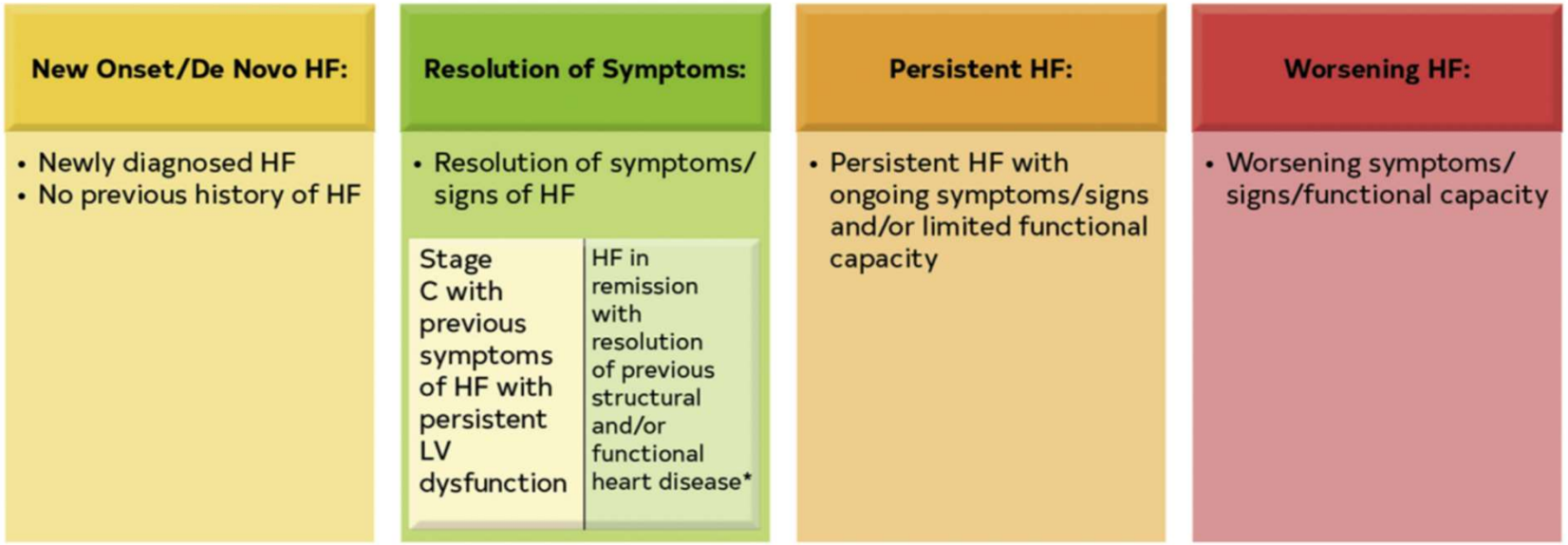
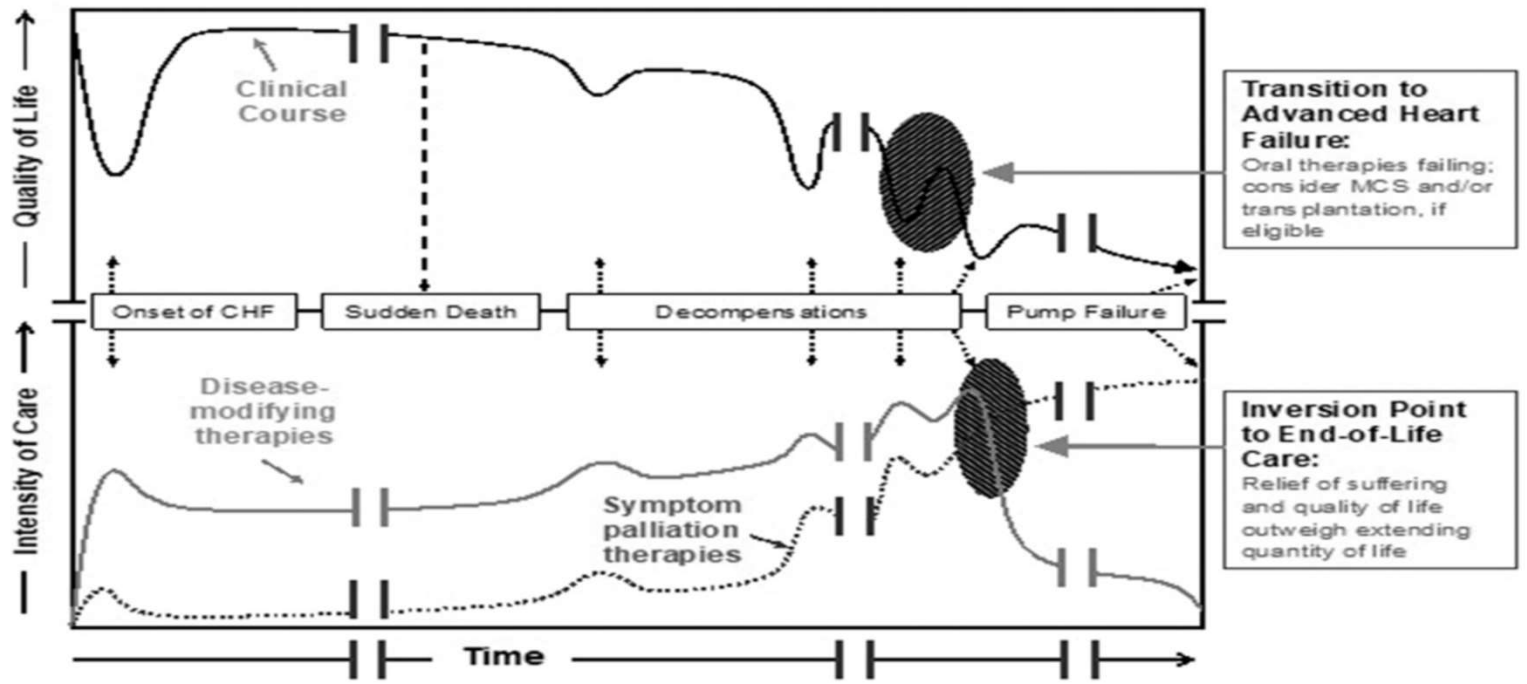
TRAJECTORY

FIGURE 2 Trajectory of Stage C HF



The trajectory of stage C HF is displayed. Patients whose symptoms and signs of HF are resolved are still stage C and should be treated accordingly. If all HF symptoms, signs, and structural abnormalities resolve, the patient is considered to have HF in remission. HF indicates heart failure; and LV, left ventricular. *Full resolution of structural and functional cardiac abnormalities is uncommon.

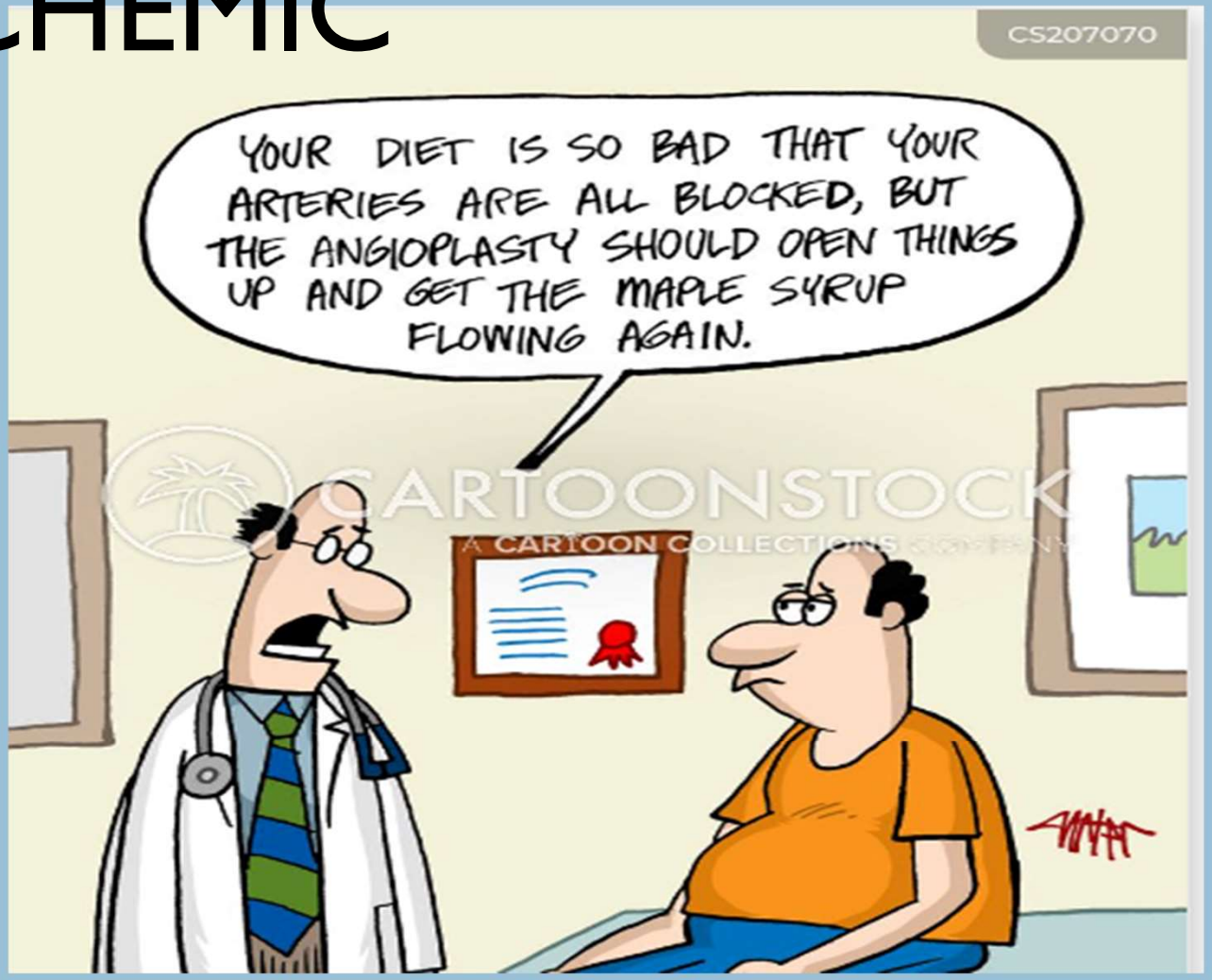
FIGURE 15 **A Depiction of the Clinical Course of HF With Associated Types and Intensities of Available Therapies Over Time (12)**



CHF indicates congestive heart failure; HF, heart failure; and MCS, mechanical circulatory support. Adapted with permission of the American Thoracic Society. Copyright © 2021 American Thoracic Society. All rights reserved. The American Journal of Respiratory and Critical Care Medicine is an official journal of the American Thoracic Society (13). Readers are encouraged to read the entire article for the correct context at https://www.atsjournals.org/doi/abs/10.1164/rccm.200605-587ST. The authors, editors, and The American Thoracic Society are not responsible for errors or omissions in adaptations. Adapted with permission from the World Health Organization (14). Copyright © 1990 World Health Organization.

CAUSES OF SYSTOLIC DYSFUNCTION

ISCHEMIC


CS207070
YOUR DIET IS SO BAD THAT YOUR ARTERIES ARE ALL BLOCKED, BUT THE ANGIOPLASTY SHOULD OPEN THINGS UP AND GET THE MAPLE SYRUP FLOWING AGAIN.
CARTOONSTOCK
A CARTOON COLLECTIONS

NON ISCHEMIC CAUSES … INPATIENT SETTING

MOST COMMON

- AF RVR (ARRHYTHMIA)
- VIRAL
- TAKOTSUBO/ STRESS INDUCED*
- TOXINS

CAN BE ACUTE ON CHRONIC OR ACUTE*

* Stress induced CMP can recur, usually is acute

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- It’s all about. physiology

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GRADES OF DIASTOLIC DYSFUNCTION

- Diastolic Dysfunction=Impaired Relaxation
  DIASTOLIC DYSFUNCTION DOES NOT =HEART FAILURE

- Grade I: normal filling pressures
  Impaired relaxation with

- Grade II:
  Impaired relaxation with elevated LA (filling) pressures.
  PSEUDONORMALIZATION

- Grade III and IV:
  Restrictive pattern-small chamber size, non compliant ventricle with elevated filling pressures

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MY TRAIN ANALOGY

GRADE 1

GRADE 3

GRADE 2

GRADE 4

WHAT CONDITIONS IMPACT MYOCARDIAL COMPLIANCE?

- AGE
- HTN
- Infiltrative process/disease (i.e. Amyloid)
- Rheumatoid/autoimmune disease
- Comorbid conditions: DM, COPD, OSA, Renal disease

Does this remind you of any of our patients?

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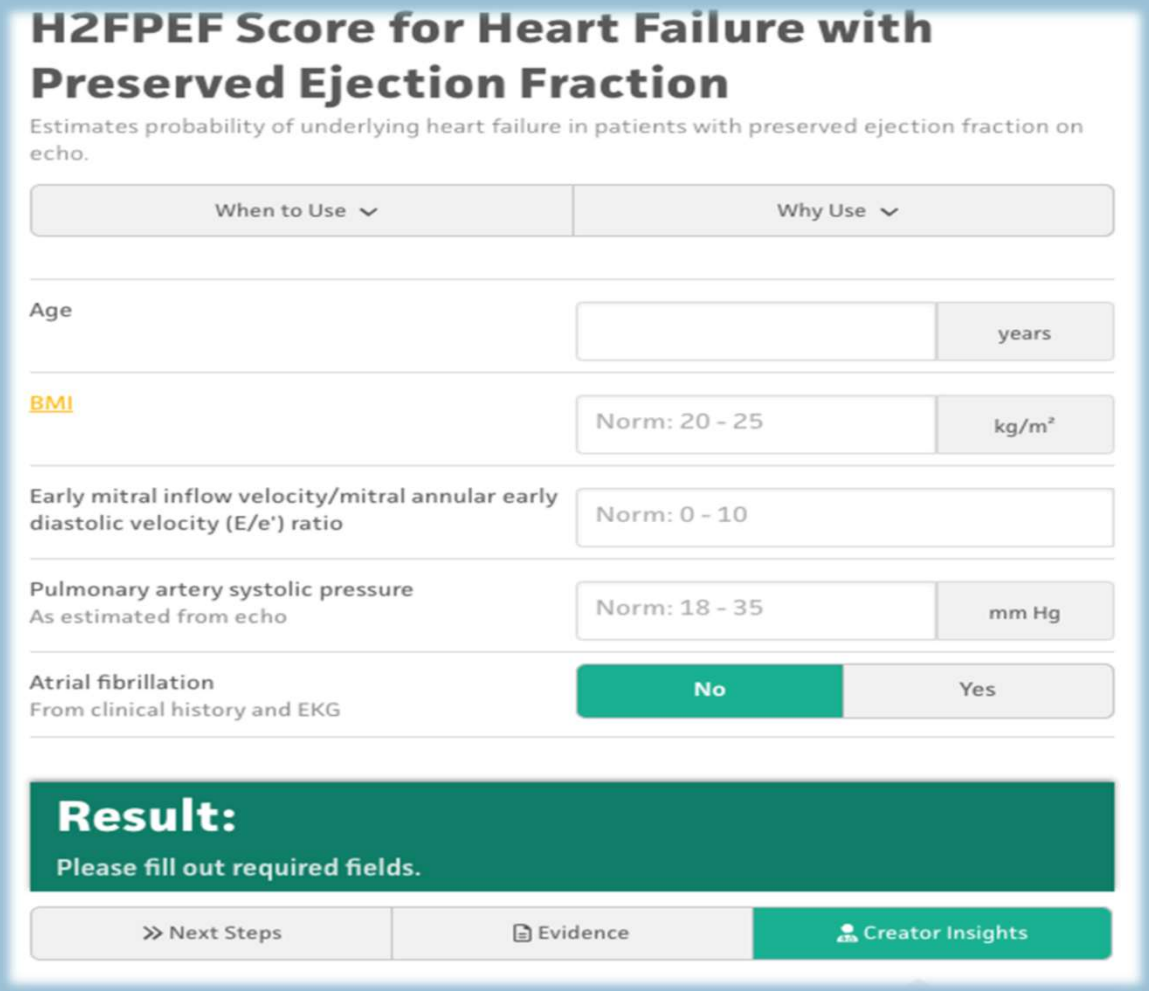

- https://www.mdcalc.com/calc/10105/h2fpef-score-for-heart-failure-with-preserved-ejection-fraction

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HF REDUCED EF

MICROSCOPIC CHANGES THAT INFLUENCE REMODELING

- Increased Cardiac fibrosis/collagen
- Alterations in calcium fluxes
- Alterations in metabolism/energetics (Energy starved", reduced ATP)
- Dependence on glycolysis rather than oxidation FFA

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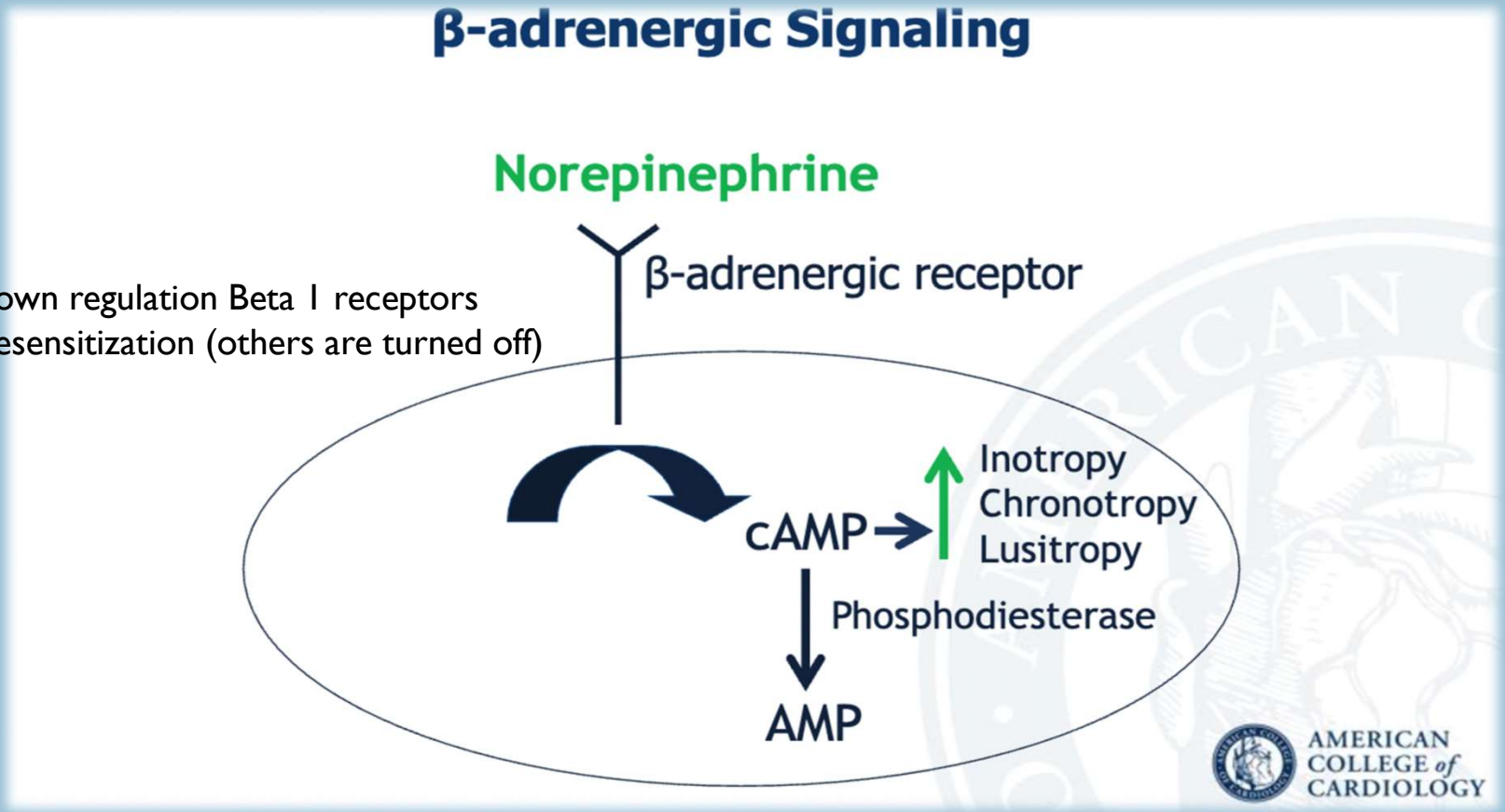
BETA RECEPTOR

Down regulation Beta 1 receptors
Desensitization (others are turned off)



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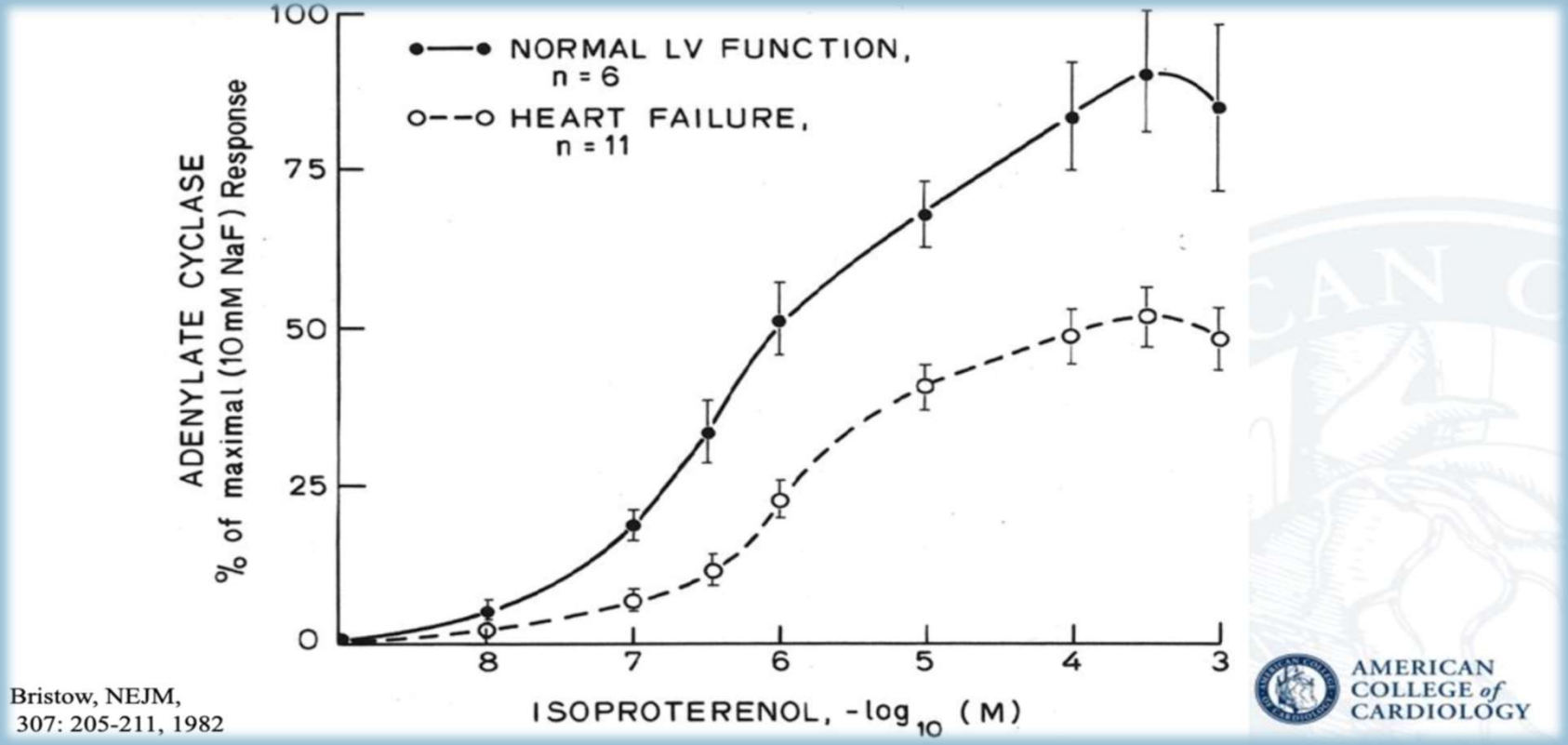
DIFFERENCES BETWEEN BETA RECEPTOR RESPONSE



Bristow, NEJM,
307: 205-211, 1982

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Normal Cardiac Physiology

- MAP = CO X SVR [Ohm's law: V = IR]
- CO = HR X SV
- HR is controlled by autonomic nervous system
  - Increased HR leads to increased contractility (Treppe effect: force-frequency relationship)
- Stroke volume controlled by variations in:
  - Preload
  - Afterload
  - Contractility

> LVEF is **load-dependent**

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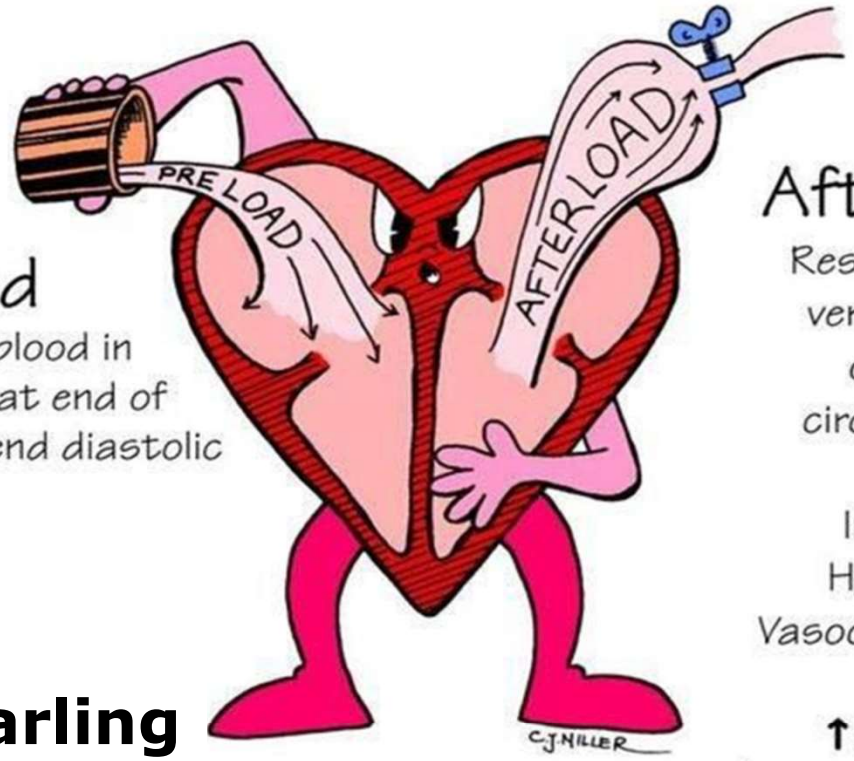
PRELOAD AND AFTERLOAD



Preload

Volume of blood in ventricles at end of diastole (end diastolic pressure)

Afterload

Resistance left ventricle must overcome to circulate blood

Increased in:
Hypertension
Vasoconstriction

↑ Afterload =
↑ Cardiac workload

Dr. Starling

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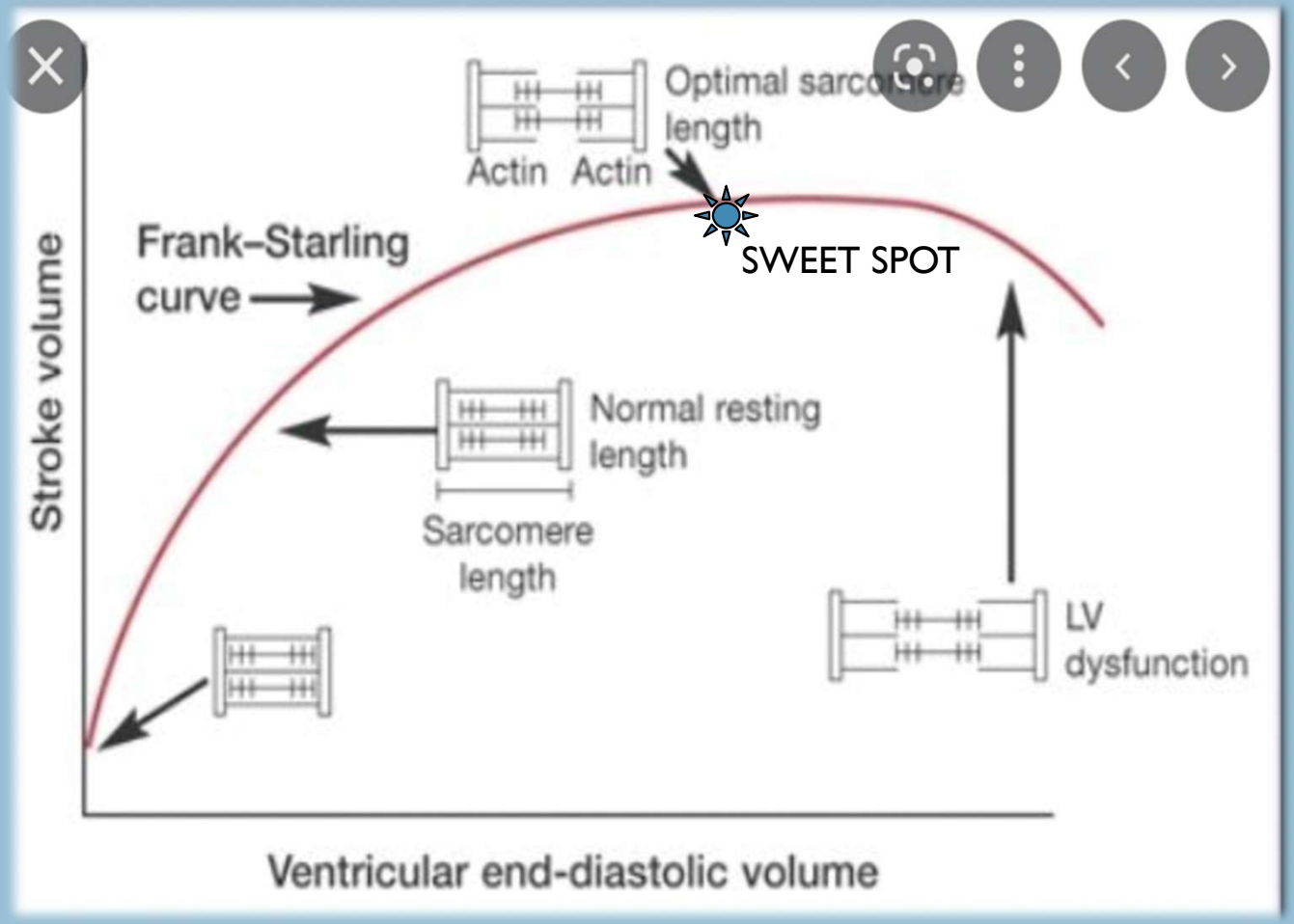

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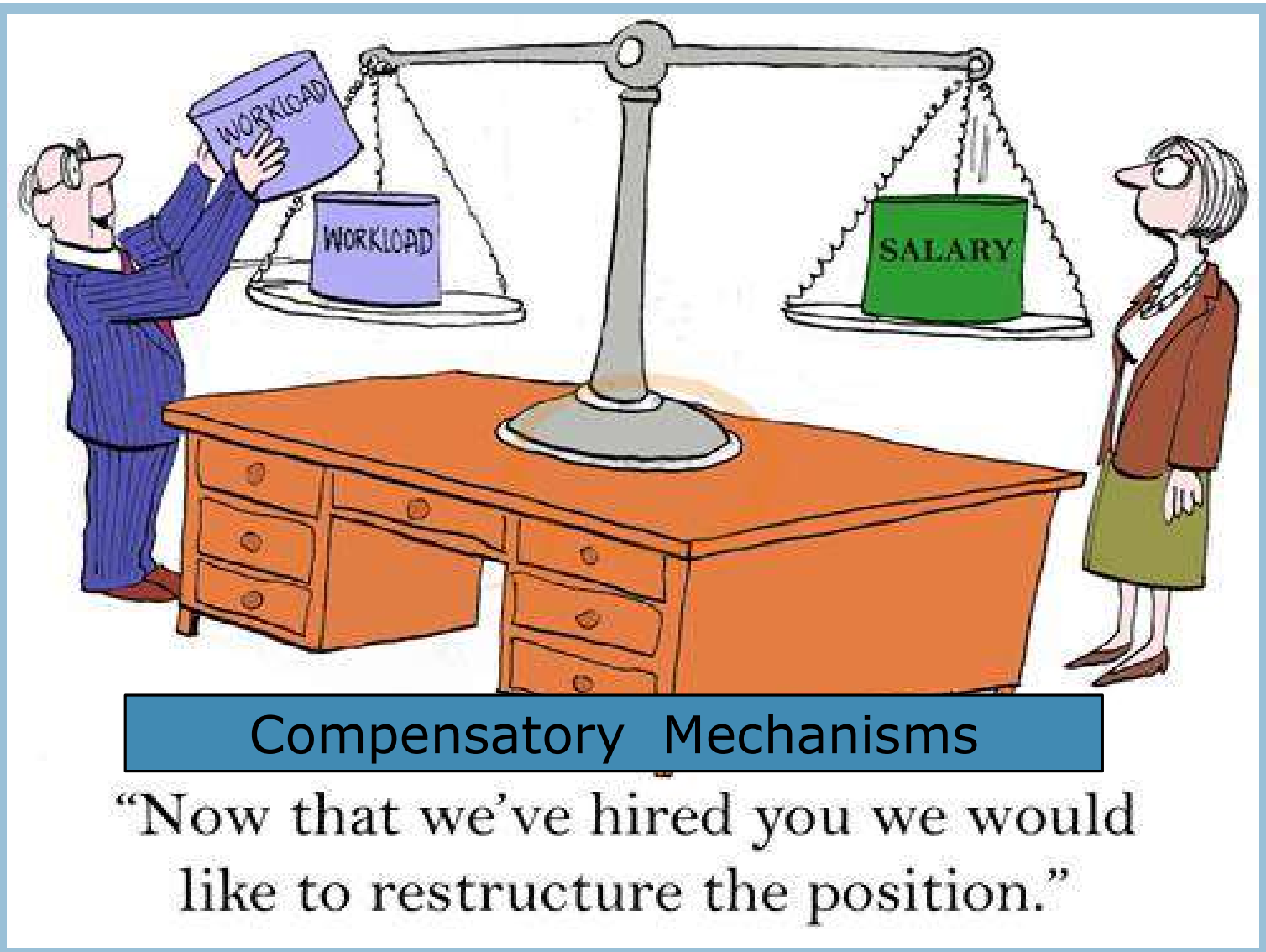
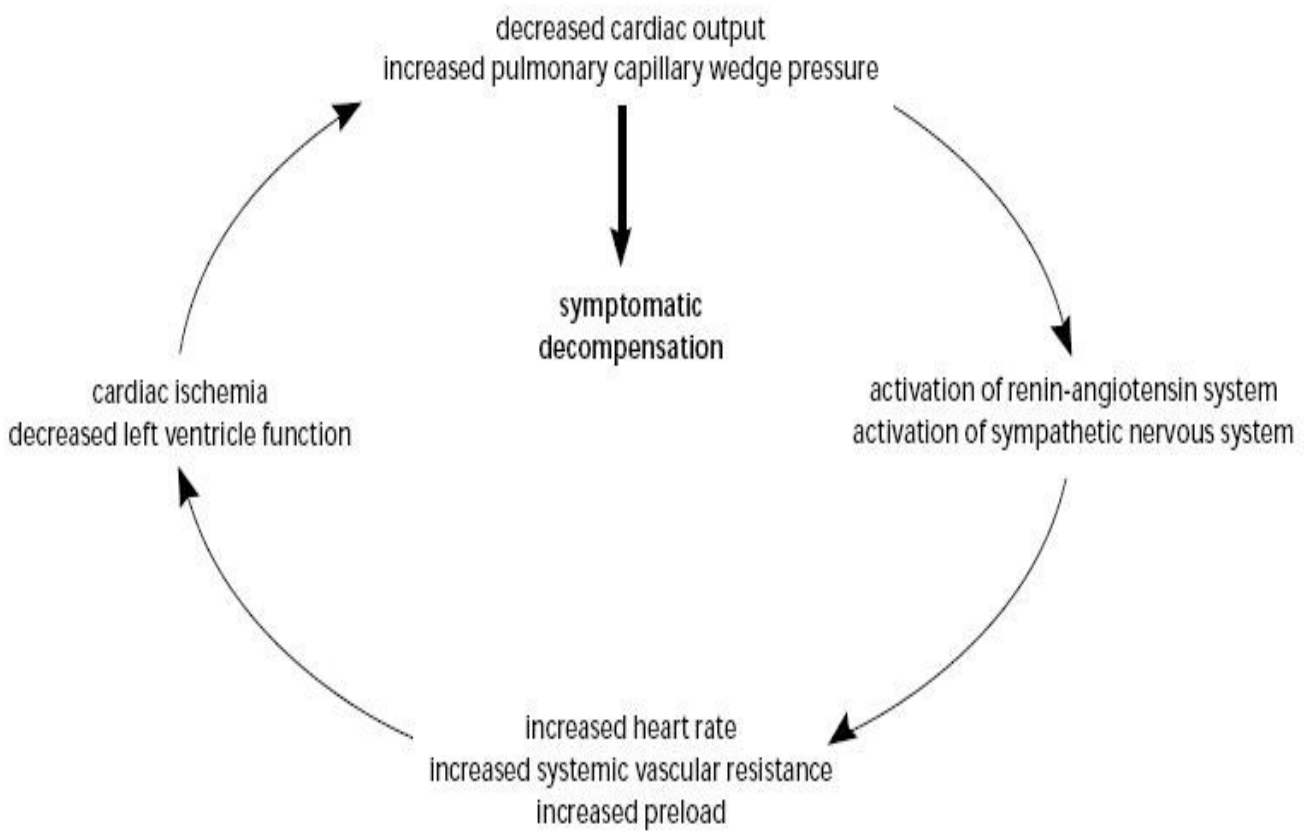
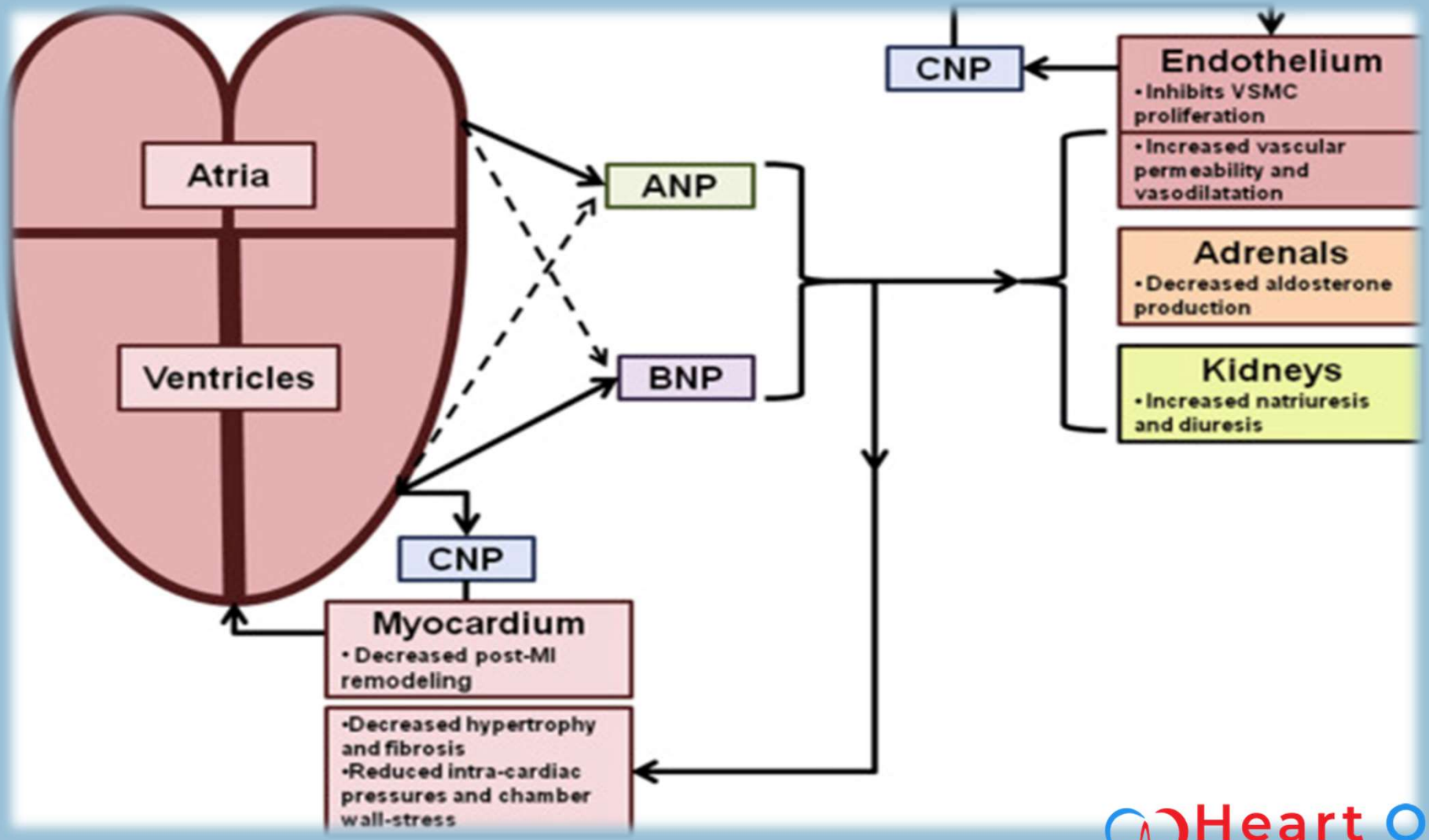

WORKLOAD
WORKLOAD
SALARY
Compensatory Mechanisms
"Now that we've hired you we would like to restructure the position."

Figure 1. Heart Failure Pathophysiology Diagram.



	COMPENSATORY ROLE	MALADAPTIVE EFFECT
NOREPINEPHRINE	• Increased HR • Increased Contractility	• Cardiac Hypertrophy • Apoptosis • Arrhythmia
ANGIOTENSIN 2	• Vasoconstriction • Sodium Reabsorption	• Cardiac Fibrosis/Hypertrophy
ALDOSTERONE	• Sodium Reabsorption	• Myocardial Fibrosis



FOUR PILLARS OF THERAPY

BETA BLOCKERS

NNT (36 mo.) =9
NNT (12 mo.) =28

Upregulates Beta 1 Receptors

Block Overstimulation SNS

BISOPROLOL
CARVEDILOL(Copernicus)
TOPROL XL (Merit HF)

ACE/ARB/ARNI

NNT (36 mo.)= 26
NNT (12 mo.) = 77
ARNI NNT (36 mo.)=2

ACE/ARB
Reduces Negative remodeling, Fibrosis and Apoptosis

ARNI
Above and Increases Circulating BNP

Paradigm Trial

MRA

NNT (36 mo.) =6
NNT (12 mo.) =18

Reduces Inflammation, profibrotic mediators induced by excess a Aldosterone

Trials:
Rales
Ephesus
Emphasis HF

SGL2 I

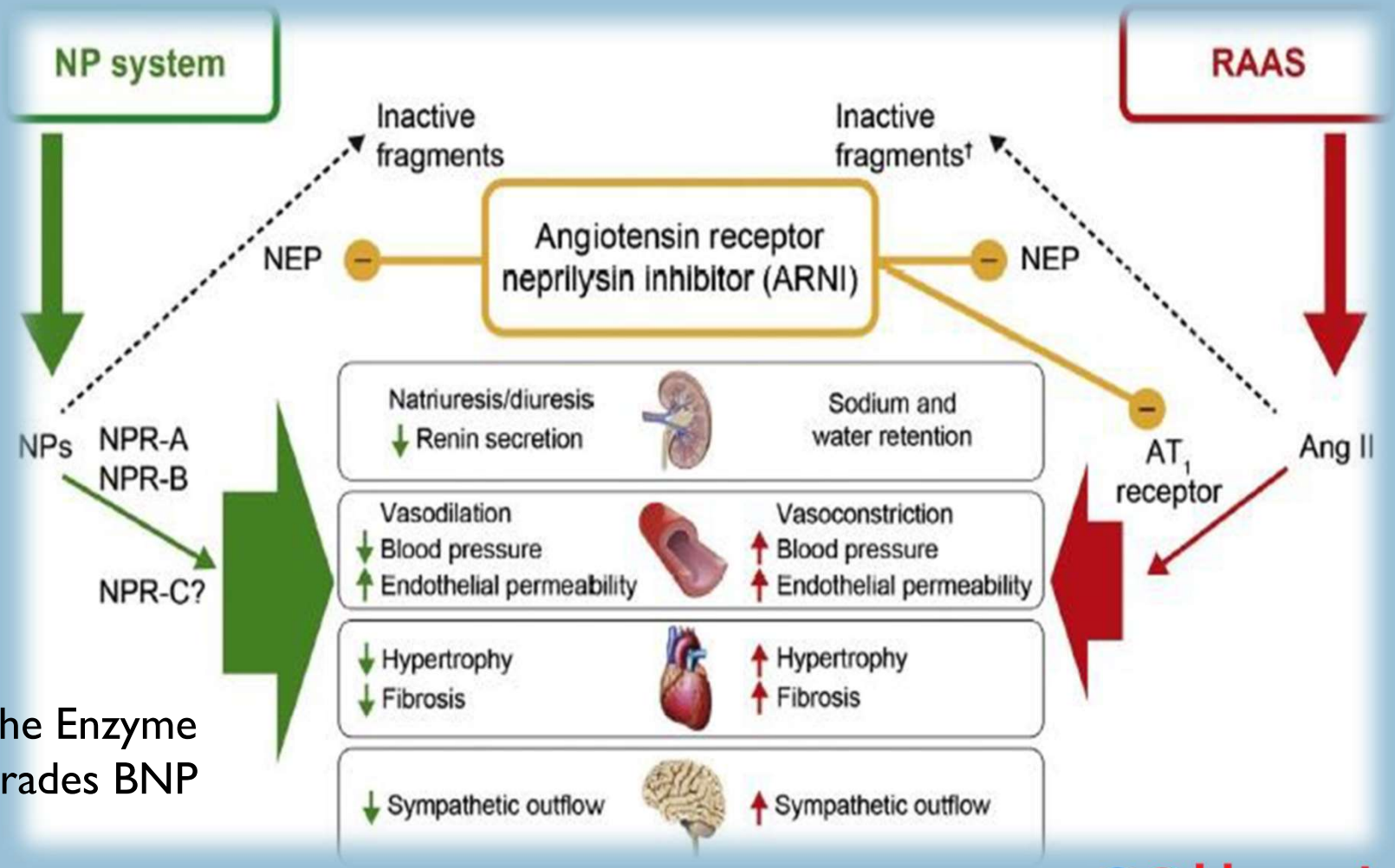
NNT (36 mo.) =22
NNT (12 mo.)= 63

Reduce Hospitalization HFpEF (2A)

Direct Effects on Myocardium
Renal Protective
Diuresis

EMPEROR-Reduced and DAPA-HF trials

ALL OF THE FOUR PILLARS REDUCE MORTALITY/IMPROVE SURVIVAL
ACE/ARB/ARNI AND SGL2 inhibitors improve symptoms



Inhibits the Enzyme
That degrades BNP

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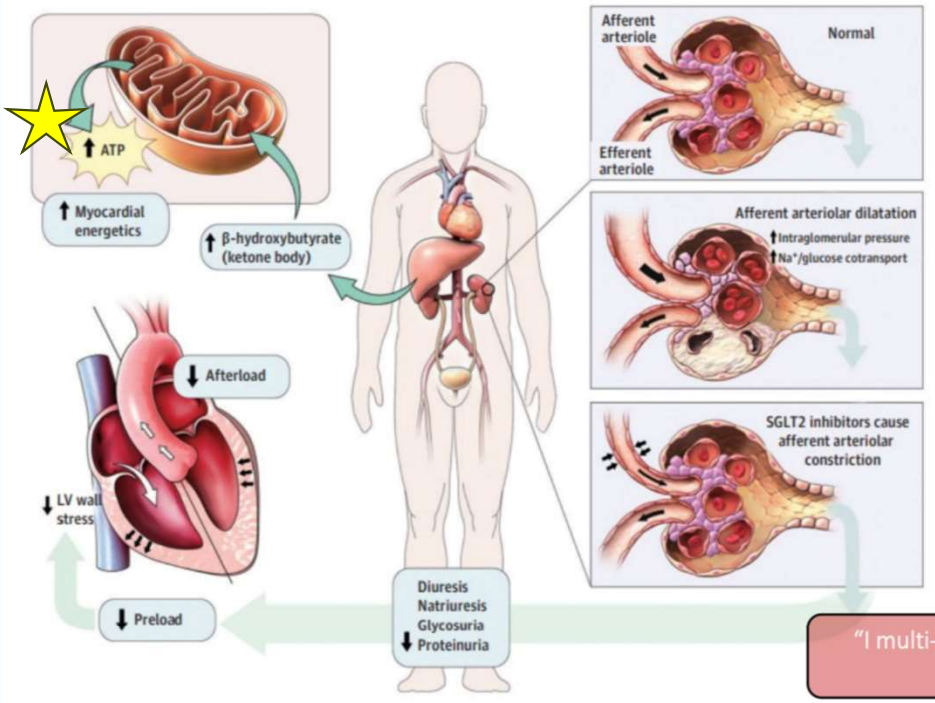
SGLT2i

Multifaceted and Synergistic MOA



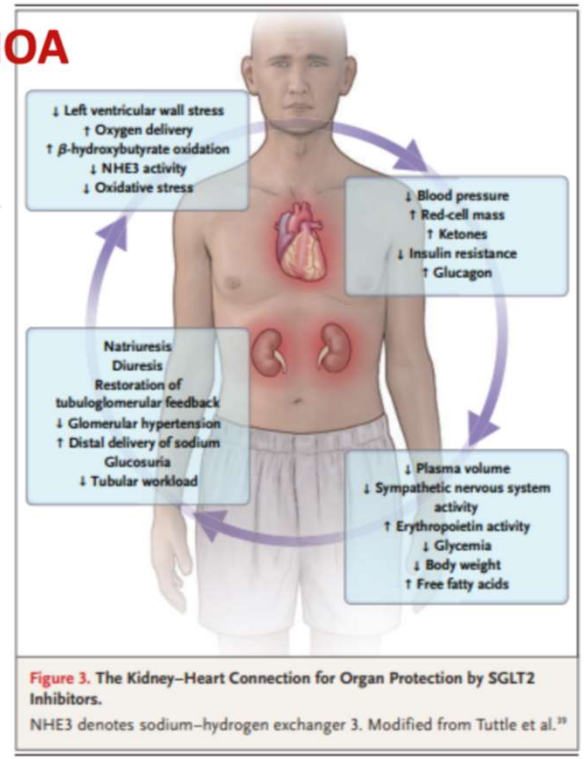


Figure 3. The Kidney–Heart Connection for Organ Protection by SGLT2 Inhibitors.

NHE3 denotes sodium–hydrogen exchanger 3. Modified from Tuttle et al.[39]

"I multi-task well."
- SGLT2i

ne Metabolodiuretic Promise of Sodium-Dependent Glucose Cotransporter 2 Inhibition: The Search for the Sweet Spot in Heart Failure - PubMed (ni
liflozins in the Management of Cardiovascular Disease - PubMed (nih.gov)

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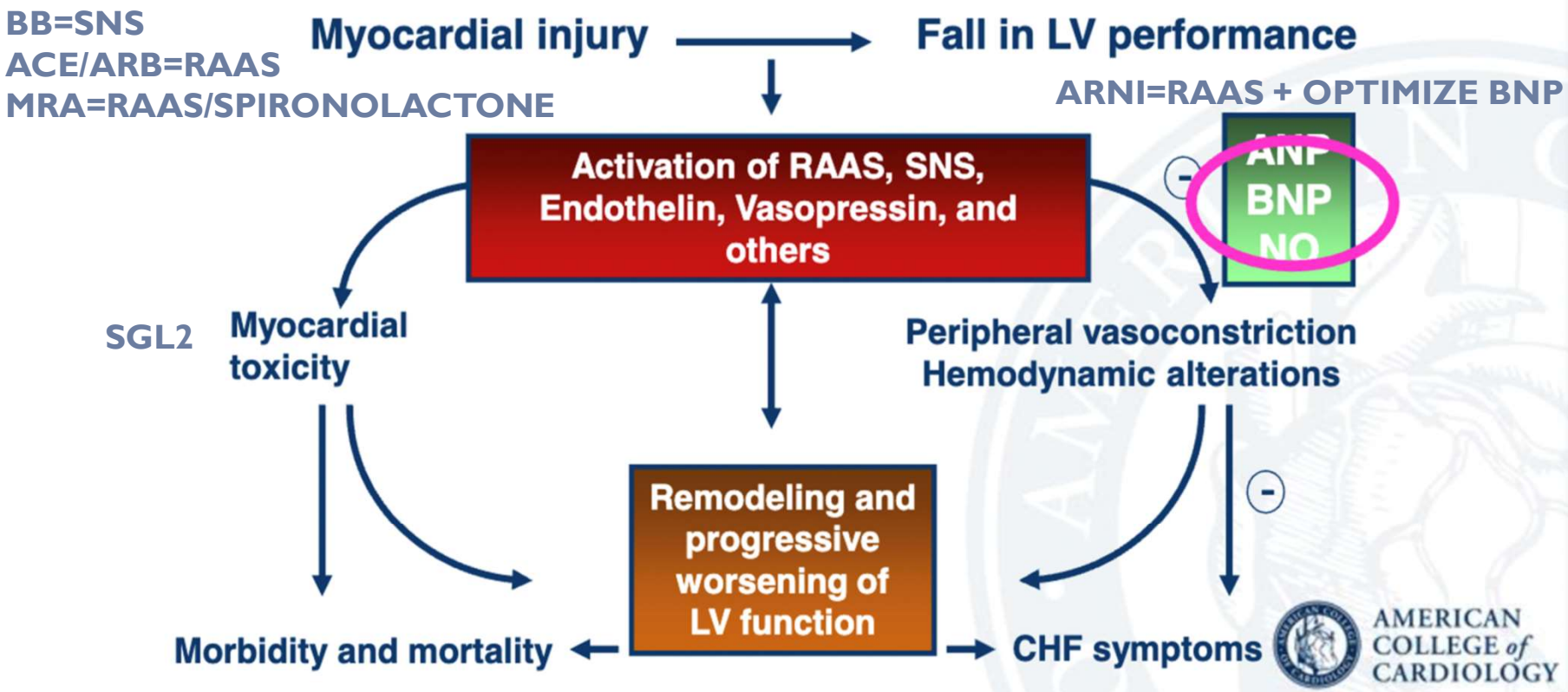
Neurohormonal Activation in Heart Failure



CLASS 3

Amlodipine Felodipine	NO BENEFIT for TX HF	No Harm if used for BP
Vitamins, supplements Hormonal Therapy	NO BENEFIT	Except to treat specific deficits
Non dihydropyridine CCB	HARM (LOE A)	AVOID
CLASS IC anti arrhythmic Dronedarone	HARM (LOE A)	AVOID
Thiazolidines	HARM (LOE A)	Risk for worsening HF sx and hospitalization
DDP-4 Saxagliptin, Alogliptin	HARM	DM2, High CV risk Increased risk HF hospitalization AVOID
NSAIDS	HARM	HFrEF Worsening HF symptoms AVOID OR w/d when possible

WHEN TO USE BNP

DIAGNOSIS

COR	LOE	RECOMMENDATIONS
1	A	1. In patients presenting with dyspnea, measurement of B-type natriuretic peptide (BNP) or N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) is useful to support a diagnosis or exclusion of HF (1-12).
1	A	2. In patients with chronic HF, measurements of BNP or NT-proBNP levels are recommended for risk stratification (11,13-29).
1	A	3. In patients hospitalized for HF, measurement of BNP or NT-proBNP levels at admission is recommended to establish prognosis (11,13-19).

PROGNOSIS

NO BENEFIT HAS BEEN DEMONSTRATED WITH MEASURING SERIAL LEVELS TO GUIDE MANAGEMENT OR DIURESIS

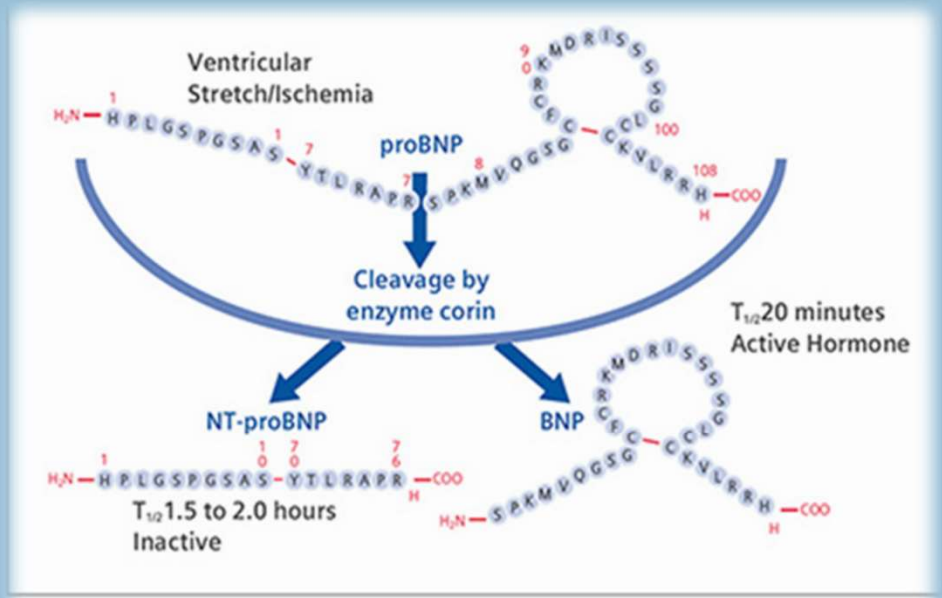
BNP

"False" positives:

- Renal insufficiency (LEVELS WILL BY SKY HIGH WITH ESRD)
- SNS, cytokines, hypothyroidism, ischemia, RV strain (PE)

"False" negatives:

- Obesity



ProBNP molecule cleaved to BNP and NT-proBNP.

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Potential Precipitants of Hospitalization for Worsening Chronic Heart Failure

Patient-level & Clinical Precipitants

- Ischemia or ACS
- Arrhythmia
- Worsening kidney function
- Uncontrolled hypertension
- Infection

Clinician & System-level Precipitants

EF ≤ 40%

Lack of initiation, titration, or persistence of:

- **Beta-blocker**
  (↑ 32-35% relative risk of HF hospitalization)
- **ARNI**
  (↑ ~30% relative risk of HF hospitalization vs. putative placebo)
- **MRA**
  (↑ 35-42% relative risk of HF hospitalization)
- **SGLT2i**
  (↑ 31% relative risk of HF hospitalization)

EF > 40%

Lack of initiation or persistence of:

- **SGLT2i**
  (↑ 29% relative risk of HF hospitalization)

Figure 1 Potential precipitants of hospitalization for worsening chronic heart failure. It should be recognized that eligible patients failing to receive maximally tolerated or target doses of evidence-based therapies during the outpatient phase leads to preventable hospitalizations for heart failure and deaths. Figure is not meant to be all-inclusive of all potential precipitants. ACS, acute coronary syndrome; ARNI, angiotensin receptor–neprilysin inhibitor; EF, ejection fraction; HF, heart failure; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

Reframe thinking:
"Secondary prevention" of HFrEF leads to substantial numbers of preventable hospitalizations.

LETS TALK SIGN AND SYMPTOMS

Symptom	Sensitivity	specificity
Exertional SOB	100%	17%
Orthopnea	22%	74%
PND	39%	80%
Edema	49%	47%

SIGN	Sensitivity	specificity
Tachycardia	22%	92%
JVD	17%	98%
Gallop	24%	98%
Rales	29%	77%
Edema	20%	80%
Displaced apical pulse	66%	96%

Davie et al. QJM 1997

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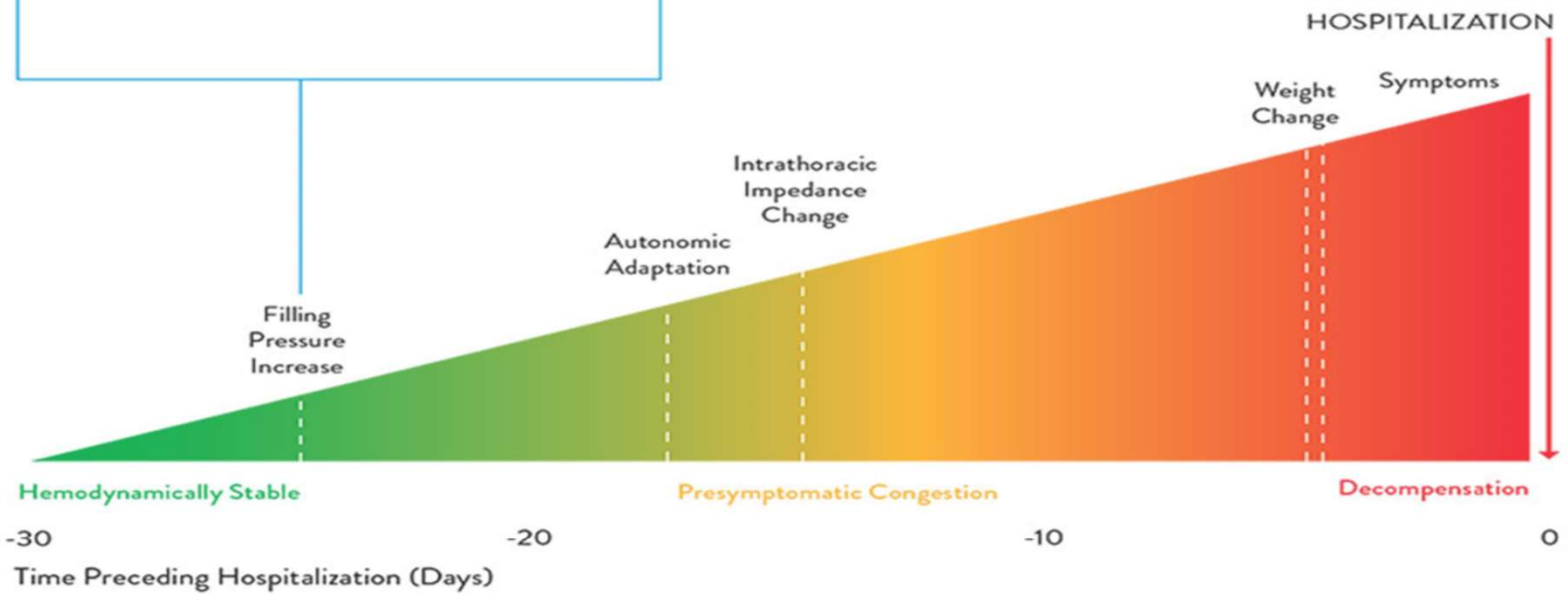
NYHA CLASS

Class	Description	Symptoms
Class I	No limitation of physical activity	Ordinary physical activity does not cause symptoms
Class II	Slight limitation of physical activity	Comfortable at rest, but ordinary physical activity results in HF symptoms as: • Palpitations • Fatigue • Shortness of breath
Class III	Marked limitation of physical activity	Comfortable at rest, but less than ordinary activity results in HF symptoms Common symptoms include: • Shortness of breath • Fatigue • Pain
Class IV	HF symptoms present, even at rest	Discomfort with any physical activity. Unable to carry on any physical activity without symptoms of HF Symptoms increase during any activity including: • Persistent cough • PND • Swelling • Cognitive change

Pathophysiology of Congestion and Decompensation

Asymptomatic

Symptoms…traditional markers
(i.e. weight gain)
Occur late



Graph adapted from Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. *Current Heart Failure Reports*. 2009;6:287-292.

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RALPH LAMBCHOP

- 72 y/o
- No previous cardiac history, no previous cardiac testing
- PMH: DM2, HTN, CKD3, arthritis, BPH, h/o thyroid cancer s/p radiation/surgery
- SURGICAL HISTORY: cholecystectomy, appendectomy, thyroid
- SOCIAL: Retired Electrical engineer, current smoker 1 PPD since 18, NO vaping, occasional ETOH, no drugs
- FH: MOTHER died from CHF 64, father died from MI at 50

Presented to to ED with 6 weeks worsening DOE, orthopnea x 2 weeks, life limiting SOB x 2 weeks, occasional CP with exertion. His family brought him to ED

CLINICAL ASSESSMENT

DIURESIS

DRY	WET
	
WARM	COLD

NAUSEA
ANOREXIA

DECREASED MEMORY/ MENATION

NO WT GAIN DESPITE CONGESTION

WARM THEM UP
+ BP= VASODILATOR
-BP = INOTROPE

RALPH'S EXAM

- VS:100/70, 115 REGULAR, 230 LB., 6 FEET
- GEN: FATIGUED APPEARING
- NECK: JVP NEAR ANGLE OF JAW SITTING UPRIGHT
- LUNGS: CRACKLES BLL
- CARDIAC: NL S1,S2, +S3, 3/6 HSM APEX, PMI SHIFTED TO LET
- GI: MILD DISTENTION, NO HEPATOMEGALY
- EXT: SEVERE EDEMA WITH VENOUS STASIS CHANGES, WARM
- NEURO: NO FOCAL FINDINGS

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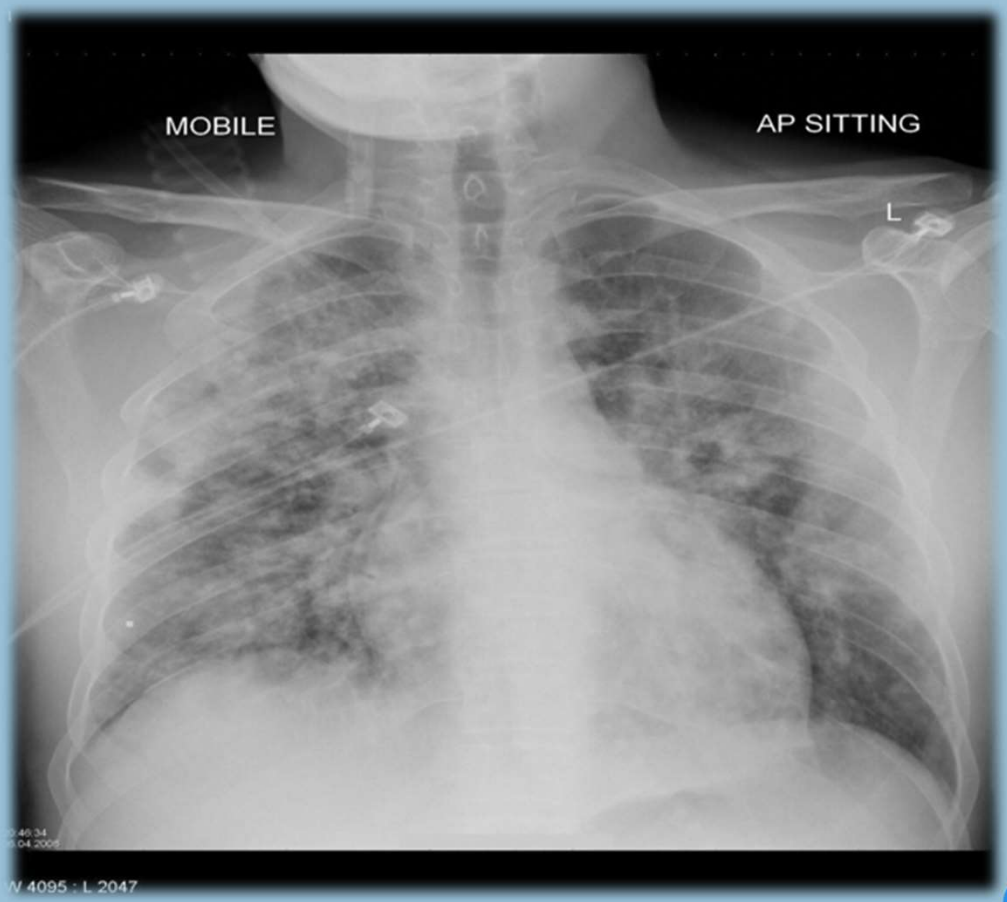

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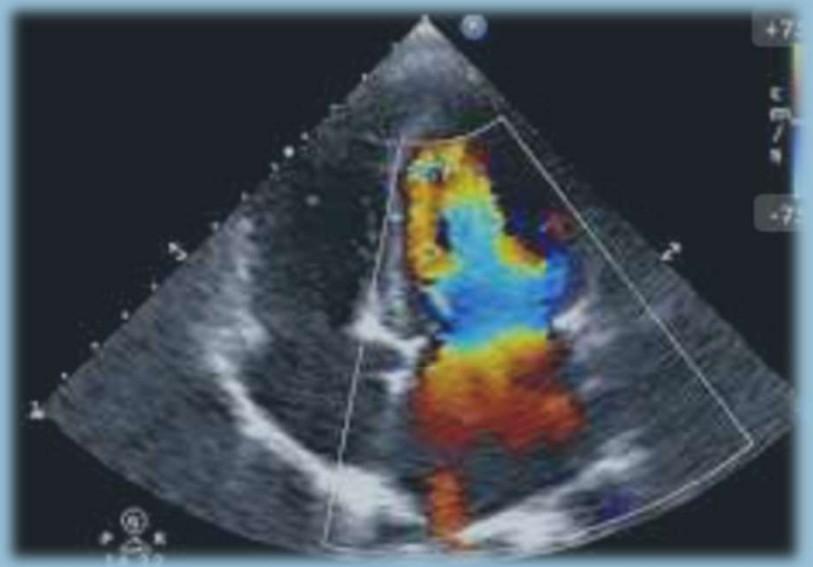
ECHO FINDINGS

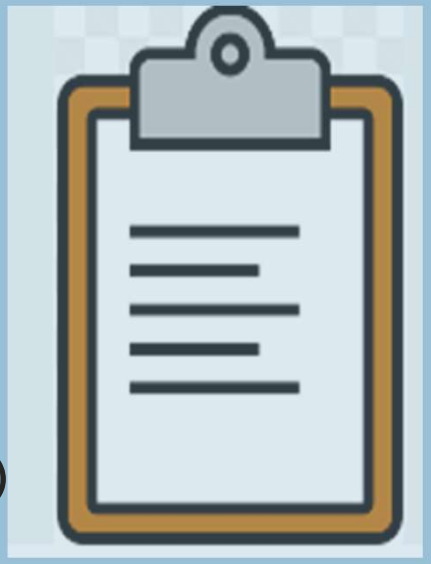
- EF 20%, LVIDD 6.7 cm Grade 3 DD
- Moderate to Severe MR.
- Moderately dilated RV
- DILTATED IVC.



INITIAL WORKUP FOR HFREF

- Assess if ischemic (LHC vs CCTA)

- Assess for non ischemic causes
  - Cardiac MRI
  - Labs: TSH, HIV, Ferritin
  - Arrhythmia? (i.e. AF with RVR, Chronic RV Pacing)
  - Drugs/ETOH? (check UDS even if they deny)
  - Obtain detailed FH
  - Recent viral illness or sick contacts
  - Cancer history- Have they received chemo



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DIURETICS

MAX OUT LOOP BEFORE ADDING THIAZIDE

USE WITH FEAR MONITOR ELECTROLYTE CLOSELY

TABLE 12 Commonly Used Oral Diuretics in Treatment of Congestion for Chronic HF

Drug	Initial Daily Dose	Maximum Total Daily Dose	Duration of Action
Loop diuretics			
Bumetanide	0.5-1.0 mg once or twice	10 mg	4-6 h
Furosemide	20-40 mg once or twice	600 mg	6-8 h
Torsemide	10-20 mg once	200 mg	12-16 h
Thiazide diuretics			
Chlorthiazide	250-500 mg once or twice	1000 mg	6-12 h
Chlorthalidone	12.5-25 mg once	100 mg	24-72 h
Hydrochlorothiazide	25 mg once or twice	200 mg	6-12 h
Indapamide	2.5 mg once	5 mg	36 h
Metolazone	2.5 mg once	20 mg	12-24 h

HF indicates heart failure.

DIURETIC STRATEGIES
ACUTE DECOMPENSATED HF

Initial Dosing

- Start with IV dose at least =current dose of 2 x current dose (never lower)
- Check UOP in one our (Goal is ~ 100 ml in one hour)
- If adequate UOP=> schedule as BID dosing
- If inadequate UOP=> double until reaches target diuresis
- If you do not reach target diuresis with bolus dosing=> start Infusion

IV=> PO

PO dose=current IV Dose (e.g. 40 mg IV BID=40 mg PO BID)

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DIURETIC PEARLS

- THRESHOLD DOSING (Never prescribe dose lower than threshold dose)
- Do not automatically cut back diuretic d/t Creatinine (often if volume long SCR will improve with diuresis or we need renal)
- Remember Dr Starling
- Diuretic dosing is like insulin in DM -it is individual and changes

IV VASODILATORS

- **CLASS 2B : adjunct to diuretic therapy for relief of dyspnea (in absence of hypotension)**

- Clinical benefits have not been shown to be durable for either hospitalization or mortality
- Role for direct vasodilators in acute decompensated CHF remains uncertain
- Patients with HTN, coronary ischemia, significant MR may be suitable for IV NTG
- Tachyphylaxis can develop w/in 24 hours
- Up to 20% develop resistance to high doses

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8.2. Nonpharmacological Management: Advanced HF

Recommendation for Nonpharmacological Management: Advanced HF

COR	LOE	RECOMMENDATION
2b	C-LD	1. For patients with advanced HF and hyponatremia, the benefit of fluid restriction to reduce congestive symptoms is uncertain (1-4).

NO ROLE FOR ROUTINE FLUID RESTRICTION

COR	LOE	RECOMMENDATION
2a	C-LD	1. For patients with stage C HF, avoiding excessive sodium intake is reasonable to reduce congestive symptoms (1-6).

Recommendations for Management of Stage C HF: Activity, Exercise Prescription, and Cardiac Rehabilitation
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	A	1. For patients with HF who are able to participate, exercise training (or regular physical activity) is recommended to improve functional status, exercise performance, and QOL (1-9).
2a	B-NR	2. In patients with HF, a cardiac rehabilitation program can be useful to improve functional capacity, exercise tolerance, and health-related QOL (1,2,5,6,8).

NON-PHARMACOLOGIC INTERVENTIONS

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TABLE 11 Potential Barriers to Effective HF Self-Care and Example Interventions

Potential Barrier	Example Screening Tools	Example Interventions
Medical Barriers		
Cognitive impairment (48-50)	Mini-Cog Mini-Mental State Examination (MMSE) Montreal Cognitive Assessment (MoCA)	Home health aide Home meal deliveries Adult day care Geriatric psychiatry referral Memory care support groups
Depression (51,52)	Hamilton Depression Rating Scale (HAM-D) Beck Depression Inventory-II (BDI-II) Patient Health Questionnaire-9 (PHQ-9)	Psychotherapy Selective serotonin reuptake inhibitors Nurse-led support
Substance use disorders (53)	Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	Referral to social work services and community support partners Referral for addiction psychiatry consultation
Frailty (54)	Fried frailty phenotype	Cardiac rehabilitation Registered dietitian nutritionist evaluation for malnutrition
Social Barriers		
Financial burden of HF treatments (55)	COmprehensive Score for financial Toxicity–Functional Assessment of Chronic Illness Therapy (COST-FACIT)	PharmD referral to review prescription assistance eligibilities
Food insecurity (56,57)	Hunger Vital Sign, 2 items U.S. Household Food Security Survey Module, 6 items	Determine eligibility for the Supplemental Nutrition Assistance Program (SNAP) Connect patients with community partners such as food pantries/food banks Home meal deliveries Registered dietitian nutritionist evaluation for potential malnutrition
Homelessness or housing insecurity (58-60)	Homelessness Screening Clinical Reminder (HSCR)	Referral to local housing services Connect patients with community housing partners
Intimate partner violence or elder abuse (61,62)	Humiliation, Afraid, Rape, Kick (HARK) questionnaire Partner Violence Screen (PVS) Woman Abuse Screening Tool (WAST)	Referral to social work services and community support partners
Limited English proficiency or other language barriers (63)	Routinely inquire in which language the patient is most comfortable conversing	Access to interpreter services covering a wide range of languages, ideally in person or, alternatively, via video platform Printed educational materials in a range of appropriate languages
Low health literacy (64)	Short Assessment of Health Literacy (SAHL) Rapid Estimate of Adult Literacy in Medicine–Short Form (REALM-SF) Brief Health Literacy Screen (BHLS), 3 items	Agency for Healthcare Research and Quality (AHRQ) Health Literacy Universal Precautions Toolkit Written education tools provided at sixth grade reading level or below Graphic educational documents
Social isolation or low social support (65)	Patient-Reported Outcomes Measurement Information System (PROMIS) Social Isolation Short Form	Determine eligibility for home care services Support group referral
Transport limitations	No validated tools currently available.	Referral to social work services Determine eligibility for insurance or state-based transportation, or reduced-cost public transportation Maximize opportunities for telehealth visits and remote monitoring

HF indicates heart failure.


STAGED

I NEED HELP

I	IV Inotrope
N	NYHA class IIIB/IV or persistently elevated BNP
E	End organ dysfunction
E	EF <35%, especially if <=20%
D	Defibrillator shock
H	Hospitalization >1
E	Edema (congestion) despite escalating diuretic
L	Low blood pressure, high heart rate (ST)
P	Prognostic medication-progressive intolerance or down titration of GDMT

REFER TO ADVANCED CHF PROGRAM FOR ADVANCED THERAPIES INCLUDING TRANSPLANT
HOSPICE FOR APPROPRIATE PATIENTS

END OF LIFE

Recommendations for Palliative and Supportive Care, Shared Decision-Making, and End-of-Life
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	C-LD	1. For all patients with HF, palliative and supportive care—including high-quality communication, conveyance of prognosis, clarifying goals of care, shared decision-making, symptom management, and caregiver support—should be provided to improve QOL and relieve suffering (1).

(continued)

1	C-LD	2. For patients with HF being considered for, or treated with, life-extending therapies, the option for discontinuation should be anticipated and discussed through the continuum of care, including at the time of initiation, and reassessed with changing medical conditions and shifting goals of care (2,3).
2a	B-R	3. For patients with HF—particularly stage D HF patients being evaluated for advanced therapies, patients requiring inotropic support or temporary mechanical support, patients experiencing uncontrolled symptoms, major medical decisions, or multimorbidity, frailty, and cognitive impairment—specialist palliative care consultation can be useful to improve QOL and relieve suffering (4-6).
2a	C-LD	4. For patients with HF, execution of advance care directives can be useful to improve documentation of treatment preferences, delivery of patient-centered care, and dying in preferred place (7).
2a	C-LD	5. In patients with advanced HF with expected survival <6 months, timely referral to hospice can be useful to improve QOL (8).

Did we meet our Objectives

- Definitions
- Physiology Overview
- Pillars (medical therapy)
- Clinical management ADHF

- Questions???