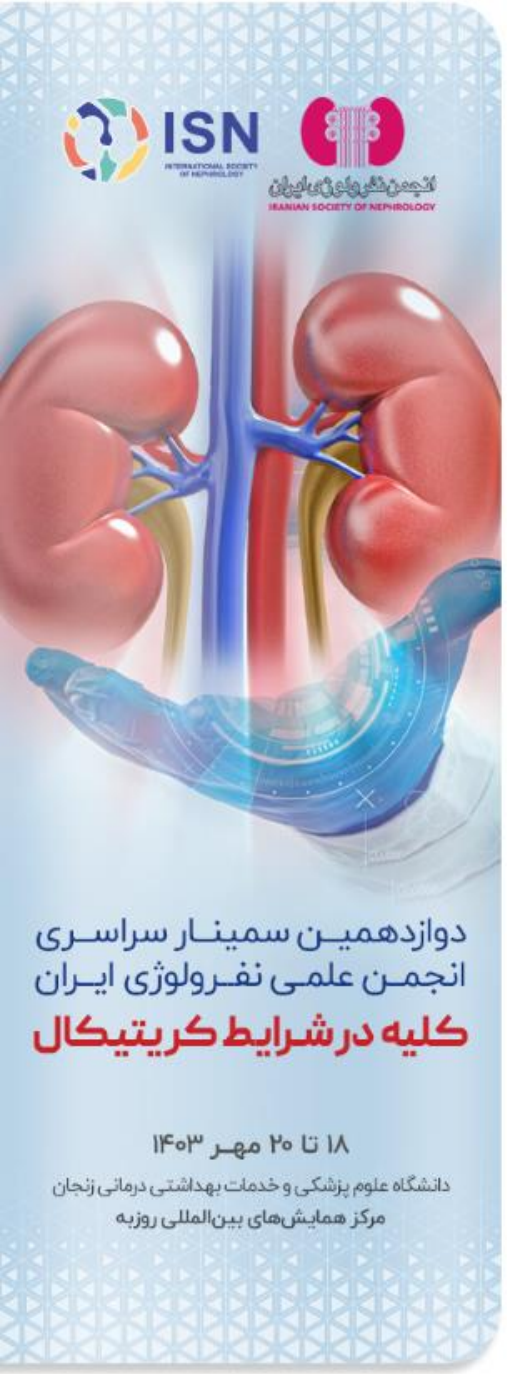
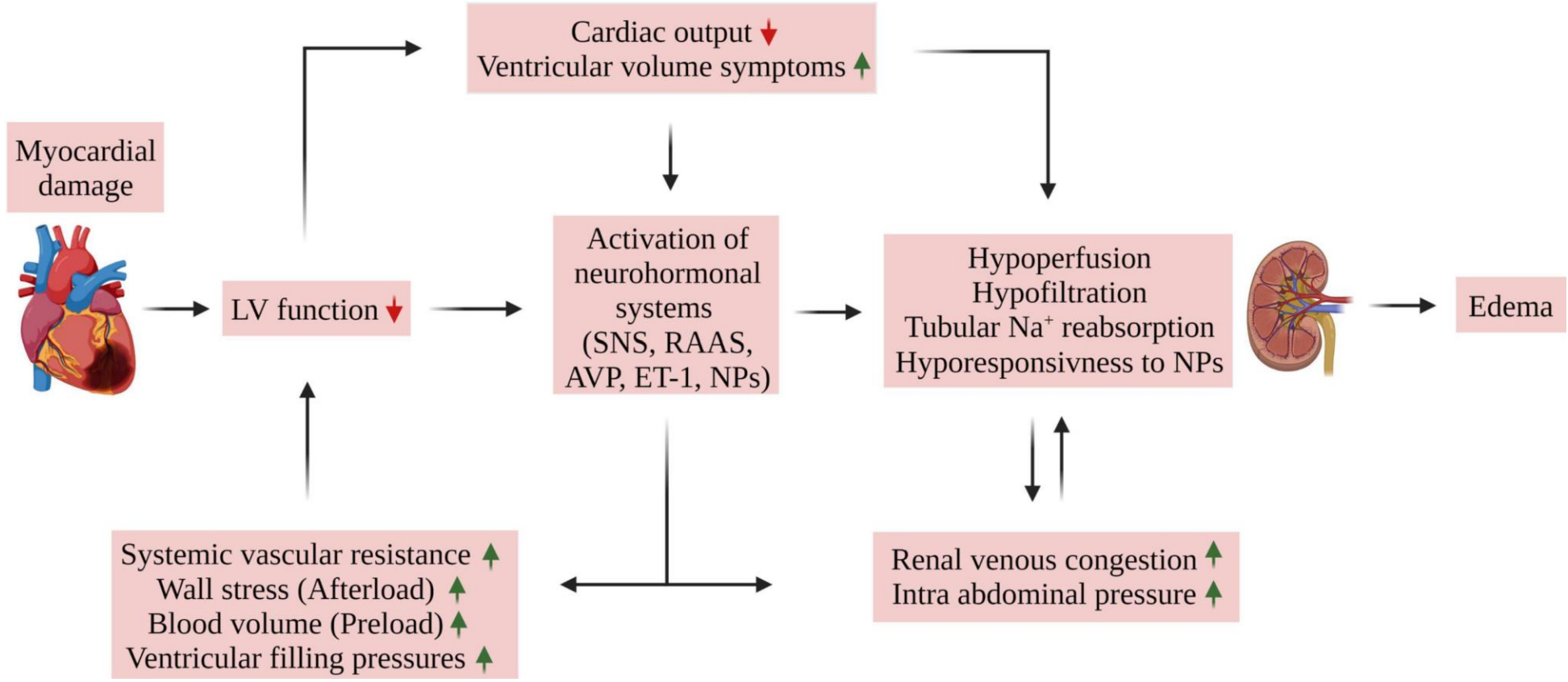
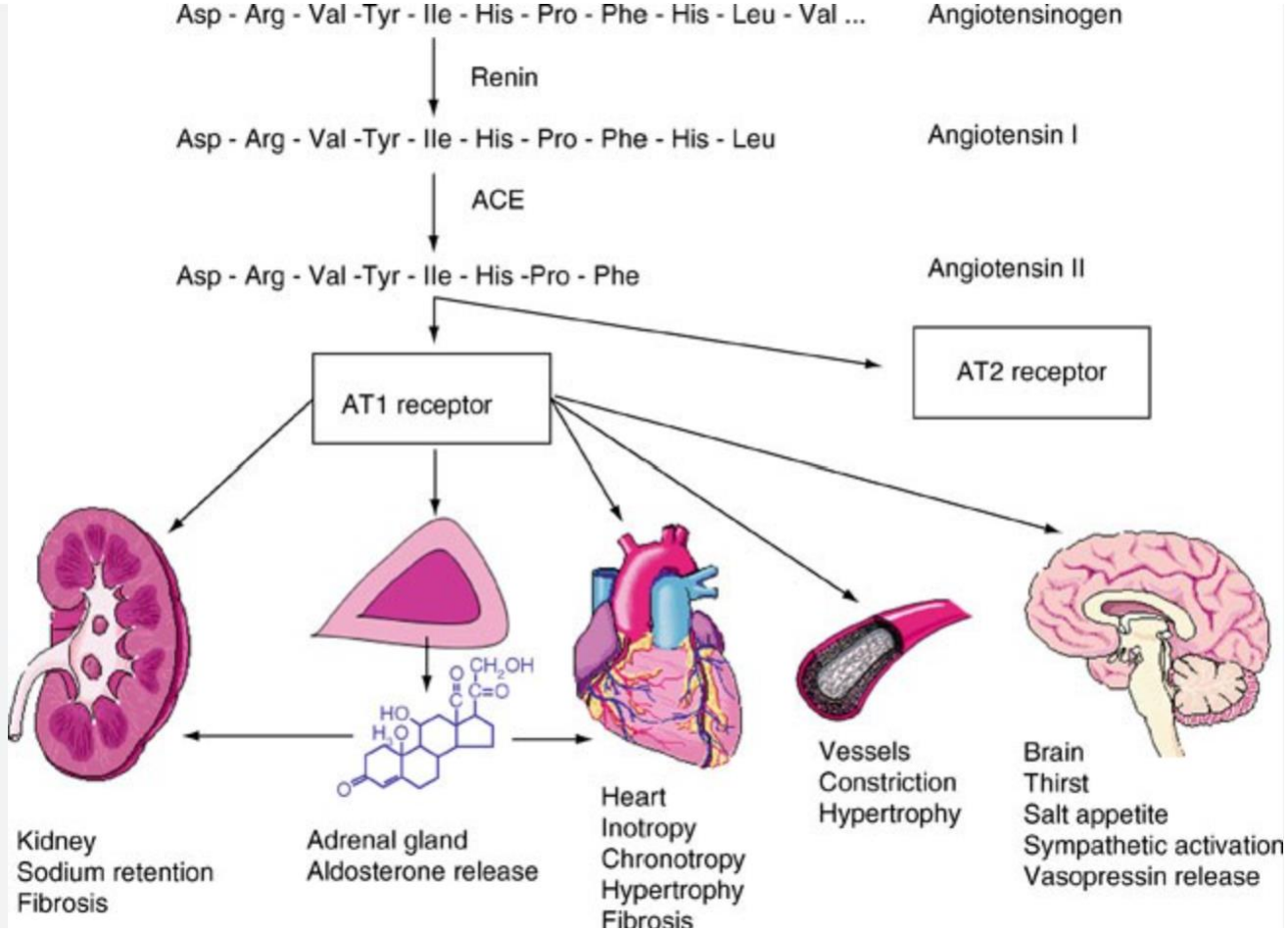


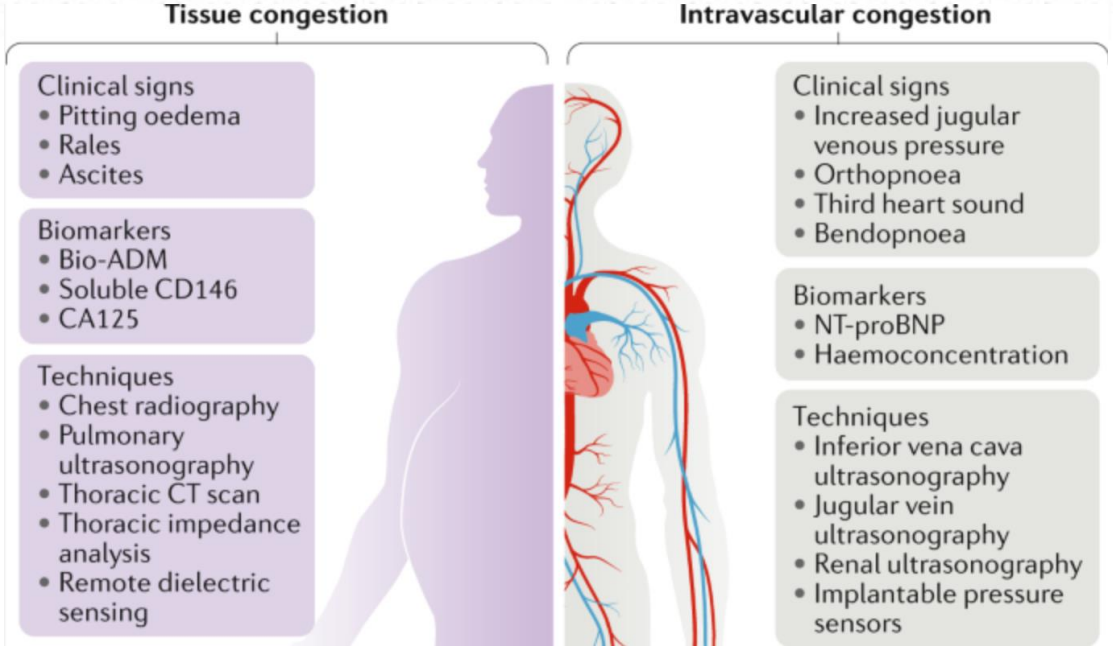
Fluid management in patients with CHF

Elham Ramezanzadeh

Associate professor of nephrology
GUMS


Cardiac output ↓
Ventricular volume symptoms ↑
Myocardial damage
LV function ↓
Activation of neurohormonal systems (SNS, RAAS, AVP, ET-1, NPs)
Hypoperfusion
Hypofiltration
Tubular Na^+ reabsorption
Hyporesponsivness to NPs
Edema
Systemic vascular resistance ↑
Wall stress (Afterload) ↑
Blood volume (Preload) ↑
Ventricular filling pressures ↑
Renal venous congestion ↑
Intra abdominal pressure ↑


Asp - Arg - Val -Tyr - Ile - His - Pro - Phe - His - Leu - Val ...
Angiotensinogen
Renin
Asp - Arg - Val -Tyr - Ile - His - Pro - Phe - His - Leu
Angiotensin I
ACE
Asp - Arg - Val -Tyr - Ile - His -Pro - Phe
Angiotensin II
AT1 receptor
AT2 receptor
Kidney
Sodium retention
Fibrosis
Adrenal gland
Aldosterone release
Heart
Inotropy
Chronotropy
Hypertrophy
Fibrosis
Vessels
Constriction
Hypertrophy
Brain
Thirst
Salt appetite
Sympathetic activation
Vasopressin release


Tissue congestion
Intravascular congestion
Clinical signs
• Pitting oedema
• Rales
• Ascites
Biomarkers
• Bio-ADM
• Soluble CD146
• CA125
Techniques
• Chest radiography
• Pulmonary ultrasonography
• Thoracic CT scan
• Thoracic impedance analysis
• Remote dielectric sensing
Clinical signs
• Increased jugular venous pressure
• Orthopnoea
• Third heart sound
• Bendopnoea
Biomarkers
• NT-proBNP
• Haemoconcentration
Techniques
• Inferior vena cava ultrasonography
• Jugular vein ultrasonography
• Renal ultrasonography
• Implantable pressure sensors

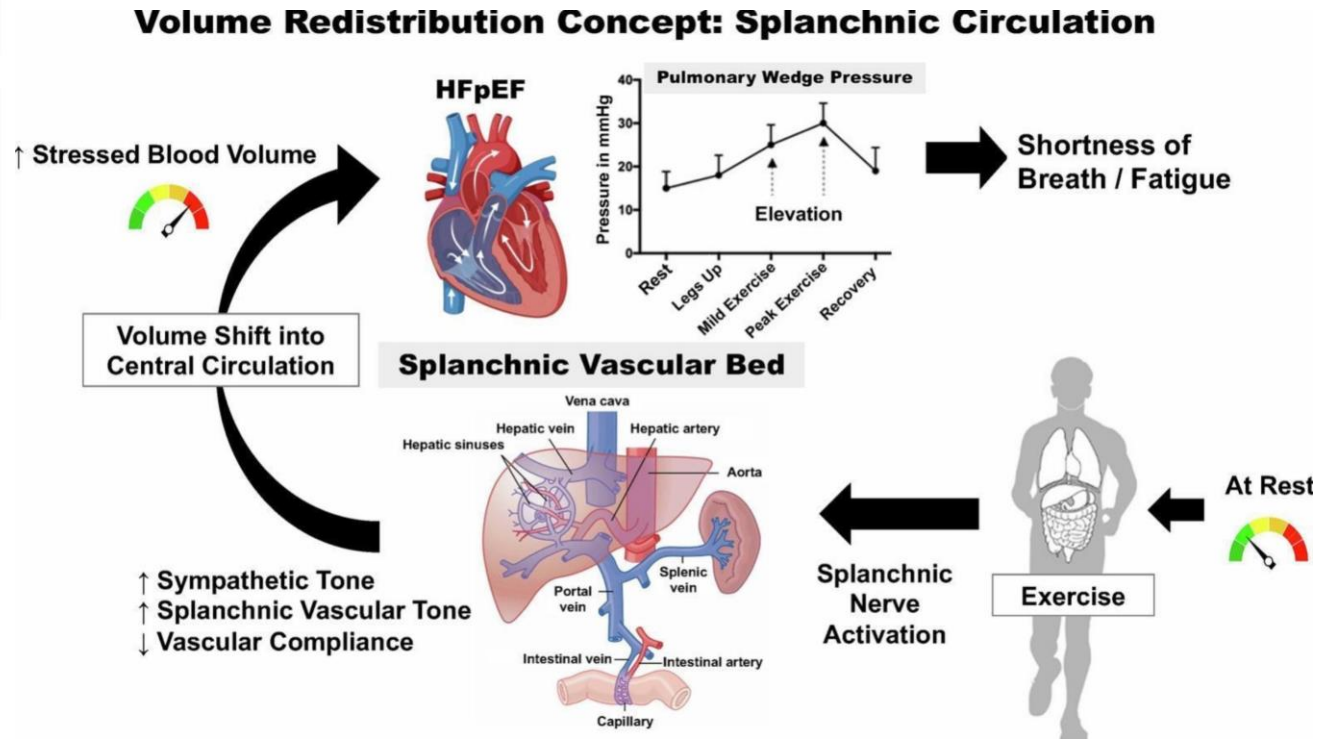

Volume Redistribution Concept: Splanchnic Circulation
↑ Stressed Blood Volume
HFpEF
Pulmonary Wedge Pressure
Pressure in mmHg
40
30
20
10
0
Elevation
Rest
Legs Up
Mild Exercise
Peak Exercise
Recovery
Shortness of Breath / Fatigue
Volume Shift into Central Circulation
Splanchnic Vascular Bed
Vena cava
Hepatic vein
Hepatic artery
Hepatic sinuses
Aorta
Splenic vein
Portal vein
Intestinal vein
Intestinal artery
Capillary
↑ Sympathetic Tone
↑ Splanchnic Vascular Tone
↓ Vascular Compliance
Splanchnic Nerve Activation
Exercise
At Rest

Table 1. Main clinical findings of dehydration and overhydration (congestion).

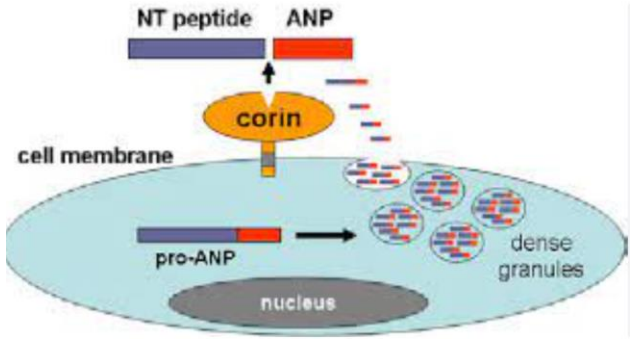
Clinical Finding	Overhydration (Congestion)	Dehydration
Symptoms	Dyspnea (also paroxysmal nocturnal dyspnea), orthopnea, bendopnea, peripheral edema (ankle swelling)	Confusion, fatigue
Signs	Jugular venous distention, the third heart sound, pitting edema	Tongue dryness and furrows, dry mucous membranes, low urine output, speech difficulty, sunken eyes, low blood pressure, increased pulse rate
Laboratory findings	Elevated circulating levels of natriuretic peptides	Elevated plasma osmolality (direct laboratory measurement or calculated); creatinine, urinary sodium, BUN (blood urea nitrogen)/urea
Non-invasive methods	Bioelectrical impedance analysis (BIA) and bioelectrical impedance vector analysis (BIVA); lung ultrasound (LUS); chest X-ray; chest computed tomography (CT)	Tracer dilution techniques for total body water (TBW) measurement (gold standard); bioelectrical impedance analysis (BIA), especially resistance at 50 kHz
Invasive methods	Cardiac catheterization—measurement of the right atrial pressure and pulmonary capillary wedge pressure (PCWP)	-

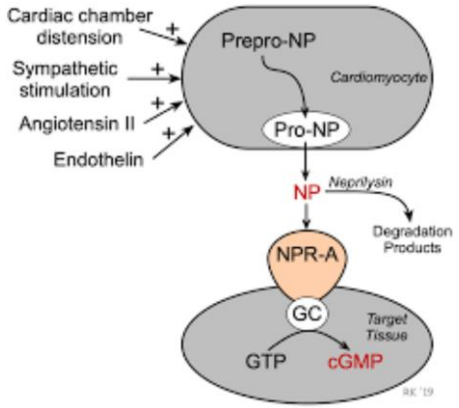
- **Laboratory Tests:**

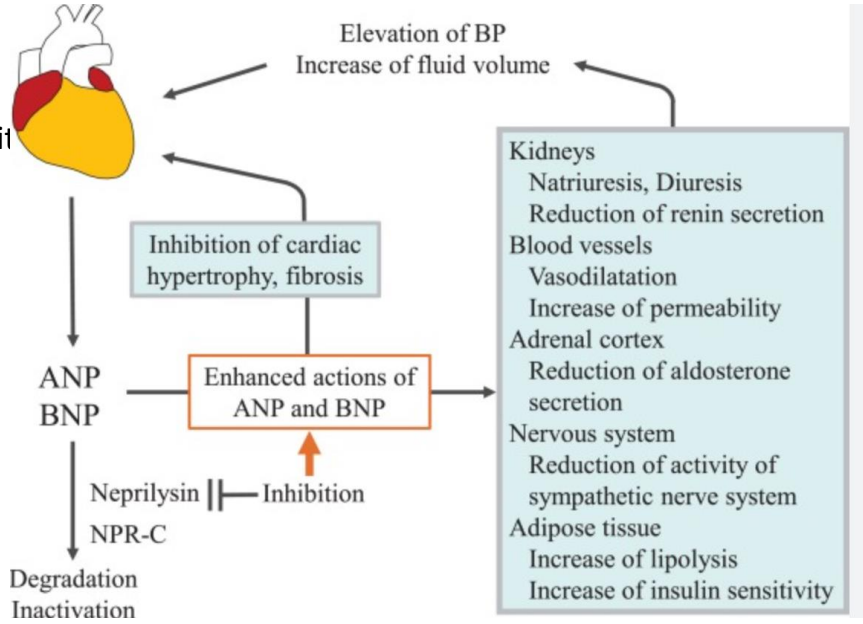
- ANP and B-type NP ..volume/pressure overload .
- BNP and N-terminal-pro BNP diagnostic tools … present acutely with dyspnea .

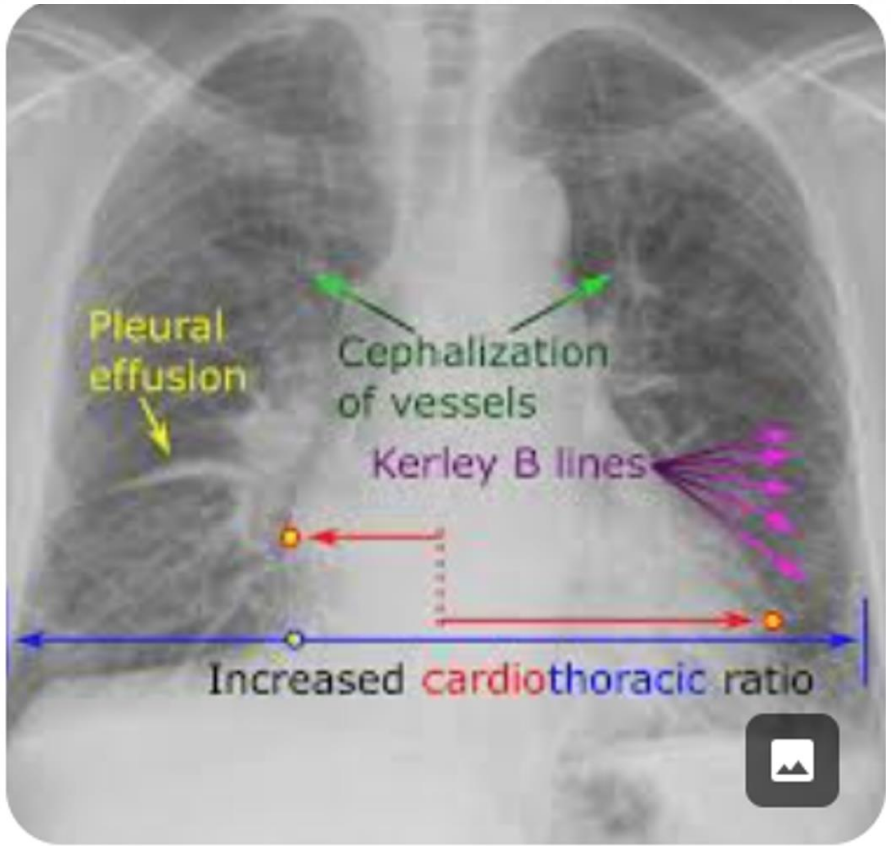
- intravascular and /intracardiac congestion rather than of tissue congestion . However, despit
  their exceptionally elevated circulating levels in plasma, their effects are attenuated [22].

- CA125









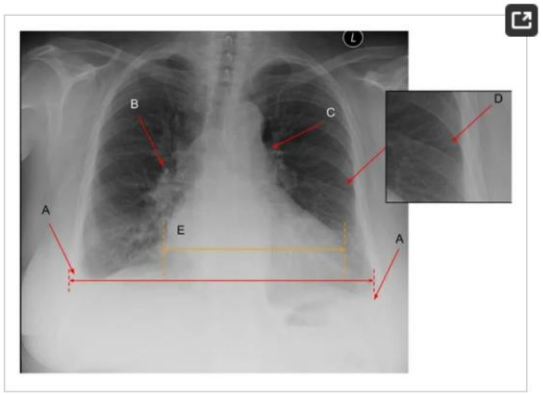
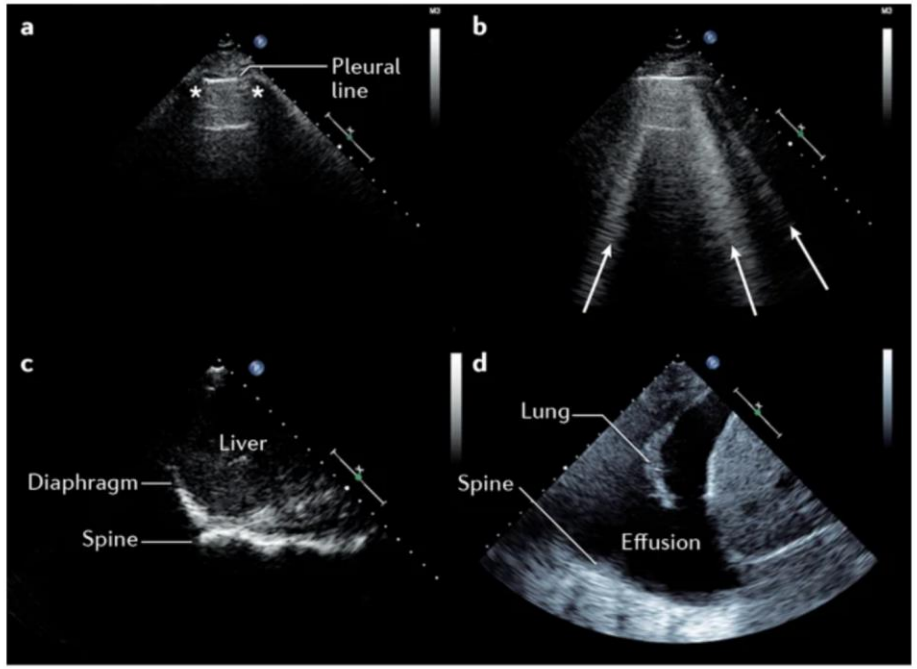


Figure 3. Pulmonary findings in a patient with HF. A: bilateral pleural effusion; B: increased diameter of the pulmonary vessels and the hazy contours, enlarged intermediate artery; C: Prominent pulmonary trunk; D: Interstitial oedema (Kerley B lines); E: Increased CTR > 0.5. B and C may signify the presence of pulmonary hypertension. Figure obtained with permission from the 2nd Department of Radiology, Medical University of Warsaw.

Echocardiography and lung ultrasonography for the assessment and management of acute heart failur

Figure 1: Lung and pleural ultrasonography.



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a | Normal lung with pleural line, and ribs (*) with shadowing. **b** | Pulmonary oedema with multiple vertical B-lines (arrows) arising from the pleural line. **c** | Diaphragmatic view with spine ending at the level of the diaphragm, with no pleural effusion. **d** | Pleural effusion seen as anechoic (echo-free) space above the diaphragm with atelectatic lung. Spine can be visualized beyond the diaphragm owing to the effusion.

biomedicines
MDPI
Review

The Importance of Optimal Hydration in Patients with Heart Failure—Not Always Too Much Fluid

Andrzej Wittczak [1,2,*], Maciej Śliwiński [2,3] and Agata Bielecka-Dabrowa [1,2,*]

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2 Department of Cardiology and Congenital Diseases of Adults, Polish Mother's Memorial Hospital Research Institute, 93-338 Lodz, Poland; maciej.sliw@wcm.umed.lodz.pl
3 Faculty of Physics and Applied Informatics, University of Lodz, 90-236 Lodz, Poland
* Correspondence: andrzejw1020@gmail.com (A.W.); agabiel79@poczta.onet.pl (A.B.-D.)

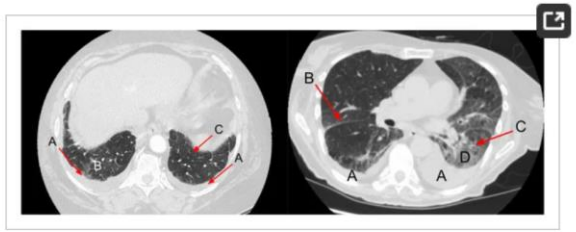

Figure 10. (**left**) Pulmonary findings related to HF in CT. A: Bilateral pleural effusion; B: Ground-glass opacities in gravity-dependent part of the lungs; C: Smooth septal thickening. (**right**) Image of the lungs in HF. A: Bilateral pleural effusion; B: interlobar septal thickening; C: Thickening of interlobular fissures; D: Ground-glass opacities in gravity-dependent part of the lungs. Figure obtained with permission from the 2nd Department of Radiology, Medical University of Warsaw.

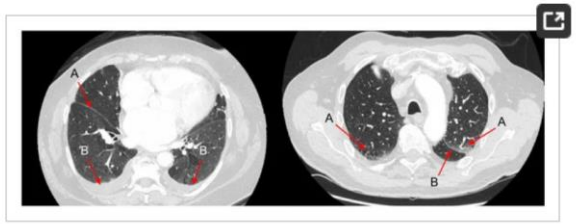

Figure 11. (**left**) Image of the lungs in CT in a patient with HF. Note the non-homogenous increased diffuse parenchymal density of the lungs. A: Thickening of interlobar fissure; B: Bilateral pleural effusion. (**right**) A: Cephalisation—widened upper lobe vasculature. B: Thickening of interlobar fissure and marginally increased density of the interstitium with a patchy appearance in the gravity-dependent part of the lungs within the lobes. Figure obtained with permission from the 2nd Department of Radiology, Medical University of Warsaw.

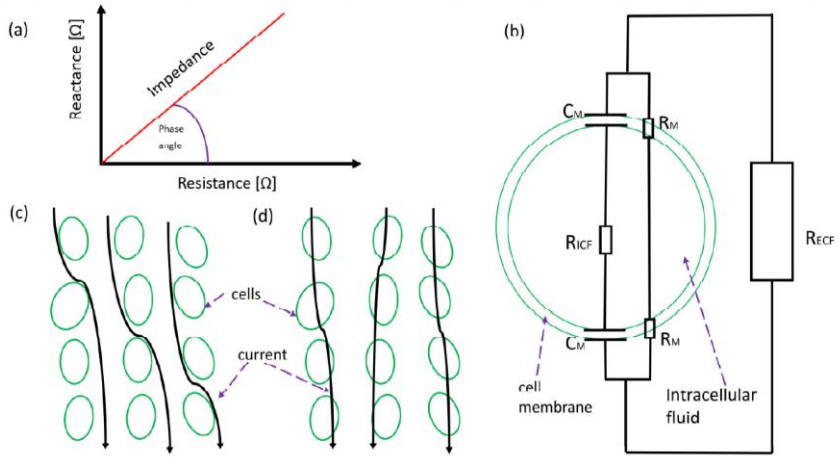

Figure 2. (**a**) Graphical definition of electrical impedance; (**b**) Equivalent circuit of human tissues according to Hayden model: CM—capacitance of cell membrane, RM—resistance of cell membrane, RICF—resistance of intracellular fluid, RECF—resistance of extracellular fluids; (**c**) Schematic of the flow of current through tissues for signal in range of kHz; (**d**) Schematic of the flow of current through tissues for signal in range of MHz, which according to simulations is more "direct" than in kHz frequencies.

- Volume management and diuretics have a narrow therapeutic path in AHF and CRS.

- Diuretics play a key role in treating CRS since they quickly alleviate symptoms caused by fluid expansion in the patient.

- They positively affect hypertension, increased intraabdominal pressure, and renal congestion [30].

- Maintaining hemodynamic stability and guaranteeing tissue perfusion are the key points to prevent type 5 CRS in the hyperacute phase of sepsis, together with fluid control and correct antibiotic treatment.

DIURETIC RESISTANCE

Inadequate response to diuretic therapy (e.g. failure to lose 0.5-1 kg of weight per day) when the following measures are ensured:

- Absence of third-space overload with intravascular volume depletion
- Dietary salt restriction (fractional excretion of sodium <2%)
- Discontinuation of nonsteroidal anti-inflammatory drugs

PATHOPHYSIOLOGY	TREATMENT OPTIONS
Reduced glomerular filtration rate	Higher single dose of loop diuretics
Braking phenomenon	Multiple daily doses of loop diuretics
Post-diuretic sodium retention	Continuous infusion of loop diuretics
Tubular compensatory readaptation	Sequential nephron blockade

Diuretic Resistance in Heart Failure

Pre-renal	Intra-renal		
	Pre-Loop of Henle	Loop of Henle	Post-Loop of Henle
Venous congestion Increased intra-abdominal pressure	Increased proximal tubule sodium reabsorption	Loop diuretic dose	Compensatory distal tubular sodium reabsorption
Reduced cardiac output Hypoalbuminemia High sodium intake	Reduced GFR Increased organic anions Albuminuria	Naturetric response at Loop of Henle's level Hypochloremic alkalosis	Proteolytic activation of ENaC by filtered proteases Upregulation of NCC, Pendrin, NDCBE, ENaC

Mechanism Significance

- Significant
- Unknown but hypothesized to be significant
- Not significant with the mild/moderate derangement found in the average patient with heart failure

Cox, Zachary L., and Jeffrey M. Testani. "Loop diuretic resistance in a patient with acute heart failure." *Cardiorenal Syndrome in Heart Failure*. Springer, Cham, 2020. 153-173

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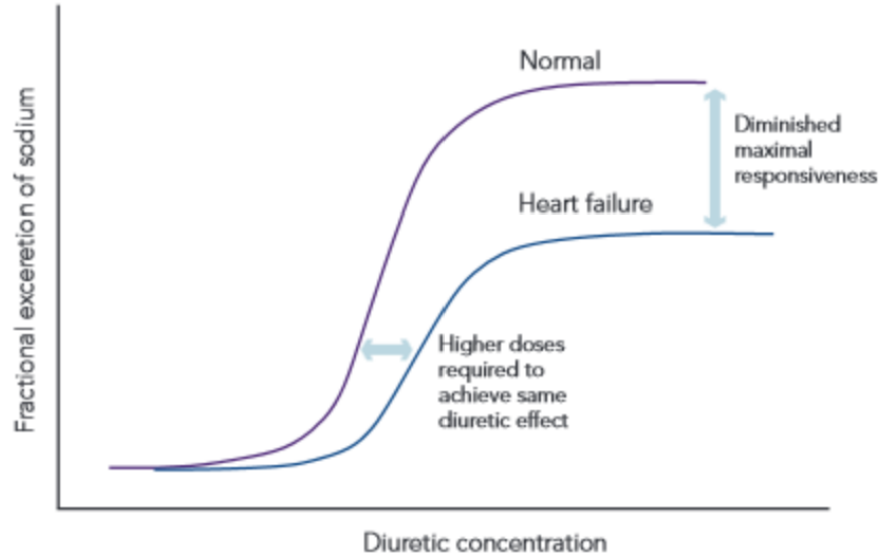
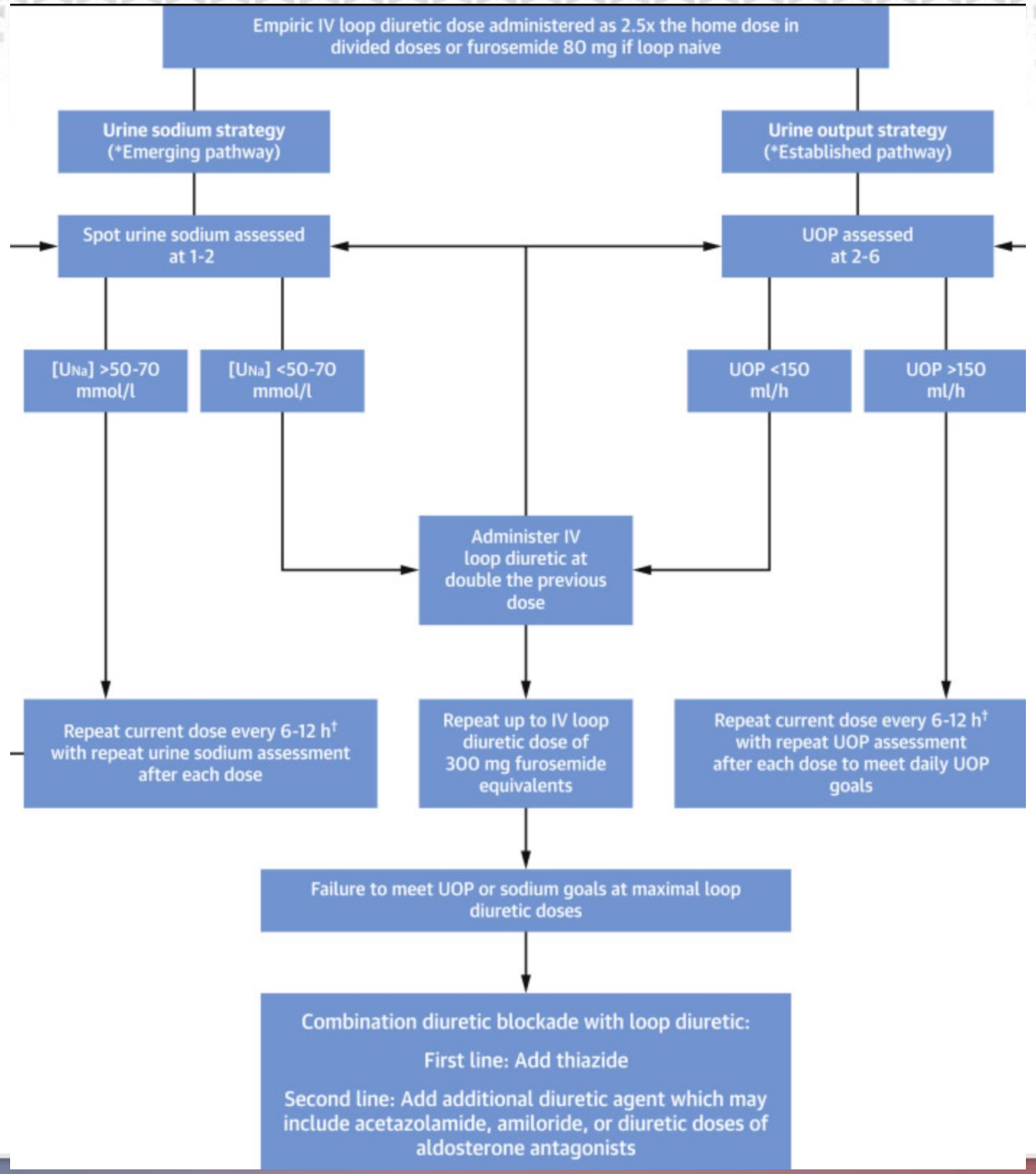
Schematic of a Dose-response Curve of Loop Diuretics in Heart Failure Patients Compared with Controls

Figure 1: Schematic of a Dose-response Curve of Loop Diuretics in Heart Failure Patients Compared with Controls



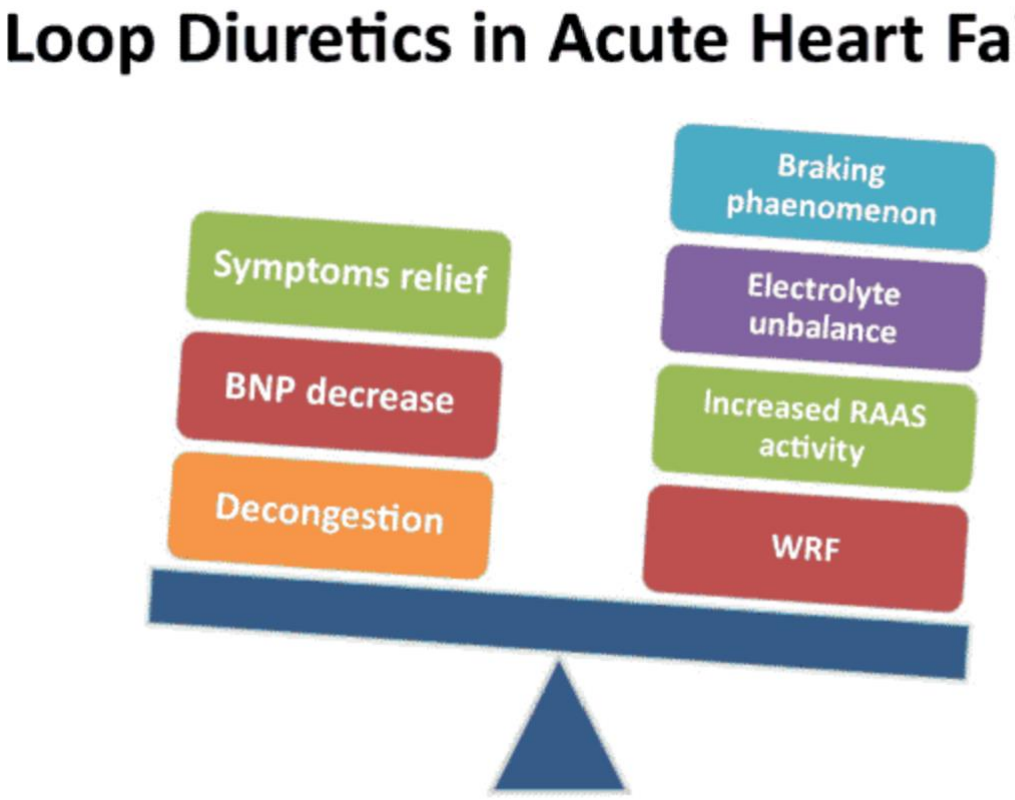
In heart failure patients, higher doses are required to achieve a given diuretic effect and the maximal effect is blunted. Adapted, with permission, from Ellison[21] and reprinted, with permission, from Felker Reproduced with permission from Felker.[22]

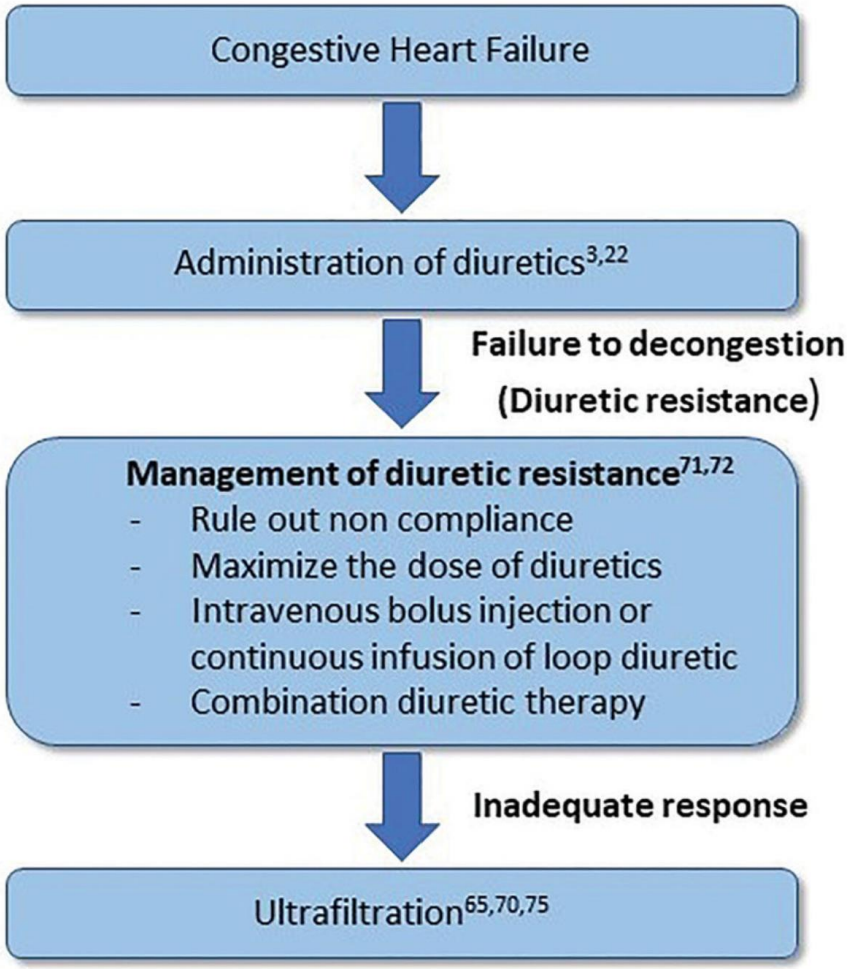
- INFUSION OR DIVIDED ?
- ALLOPURINOL?
- VAPTAN?



Electrolytes (particularly sodium and potassium) should be closely monitored during sequential nephron blockade. This is especially true when triple diuretic therapy is used, such as with a loop diuretic, thiazide diuretic, MRA, or diuretics in combination with SGLT2i. Carbonic anhydrase inhibitors should be avoided because of the risk of severe metabolic acidosis.

Early ultrafiltration seems to improve renal outcomes in septic shock patients, but these data have to be confirmed in further clinical trials [95].





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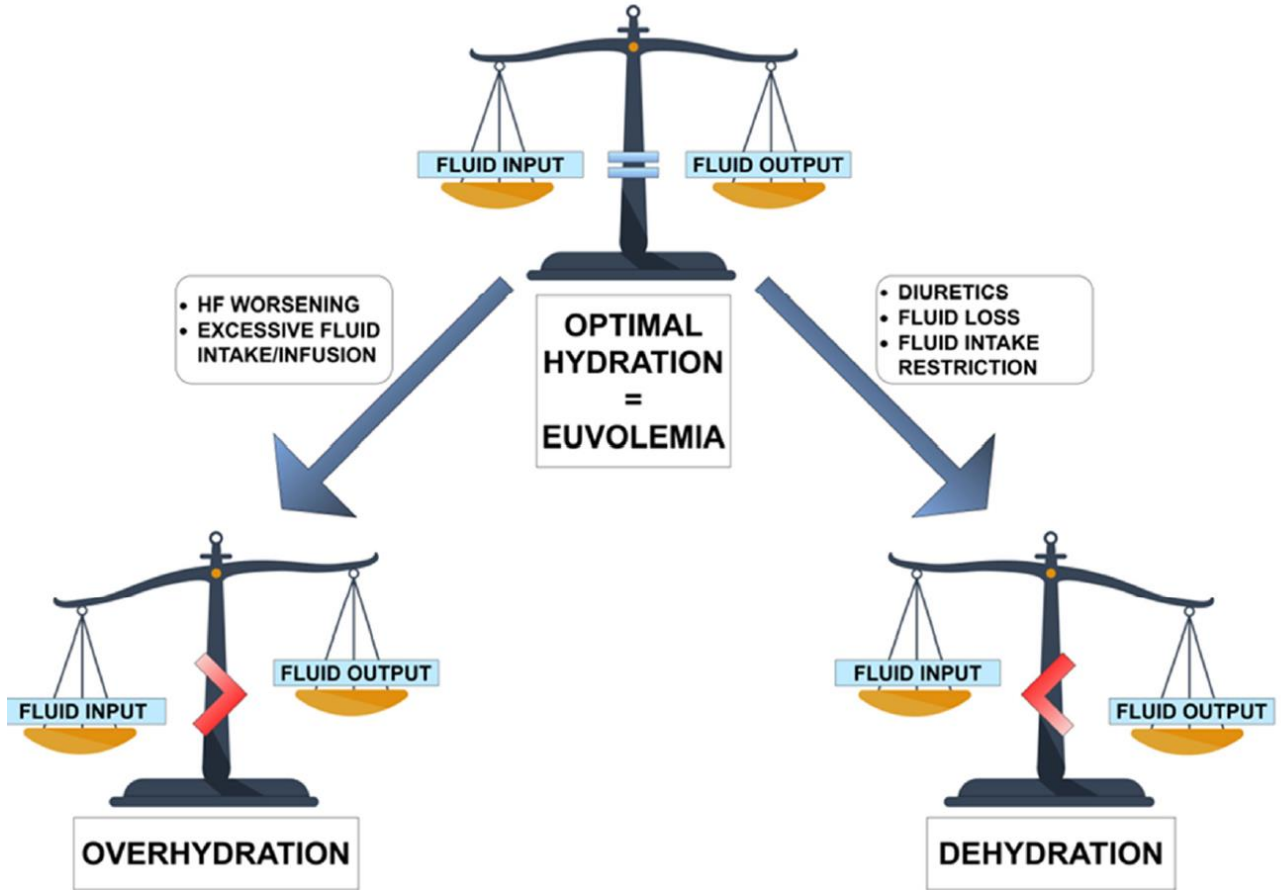


Clinical Diagnosis of Dehydration:

- Classical physical signs are too insensitive and nonspecific to draw conclusions about dehydration .
- They **should not be used in isolation for detecting abnor**malities in hydration (to approximate volume or osmolality) .
- According to the NICE guidelines , indicators that a patient **may need urgent fluid** resuscitation are as follows: systolic blood pressure less than 100 mmHg; heart rate more than 90 beats per minute; capillary refill time longer than 2 s or cold to touch peripheries; respiratory rate more than 20 breaths per minute;

Objective Methods for Diagnosing Dehydration:

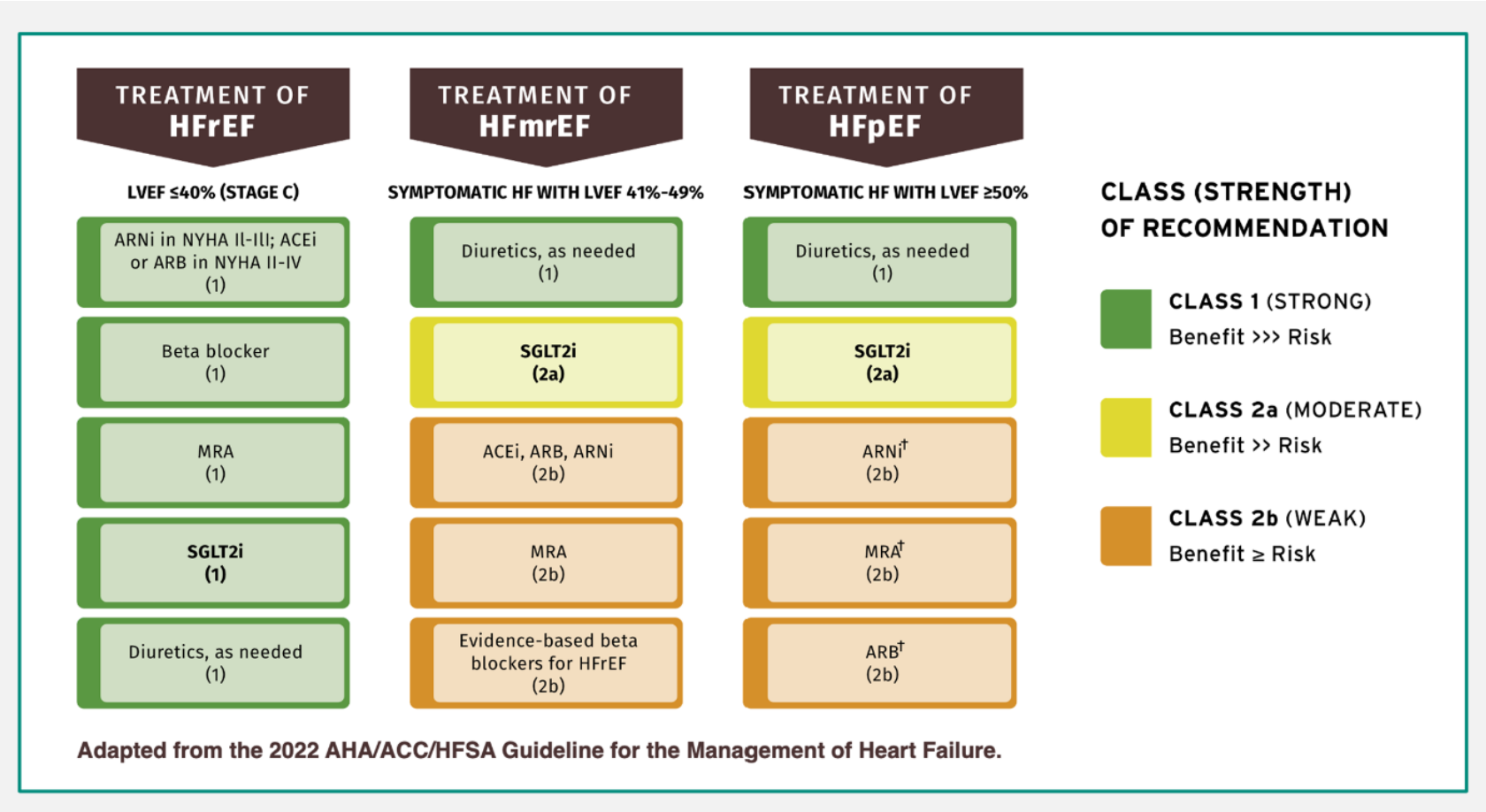
- According to the 2019 multidisciplinary consensus on dehydration, the **gold standard for determining** dehydration is a direct measurement of serum/plasma osmolality .
- According to the 2019 multidisciplinary consensus on dehydration, measured plasma **osmolality > 300 mOsm**/kg classifies a person as hyperosmolar and plasma osmolality 280 mOsm/kg classifies a person as **hypo-osmola**r [92].**advanced equipment** and competent technicians.

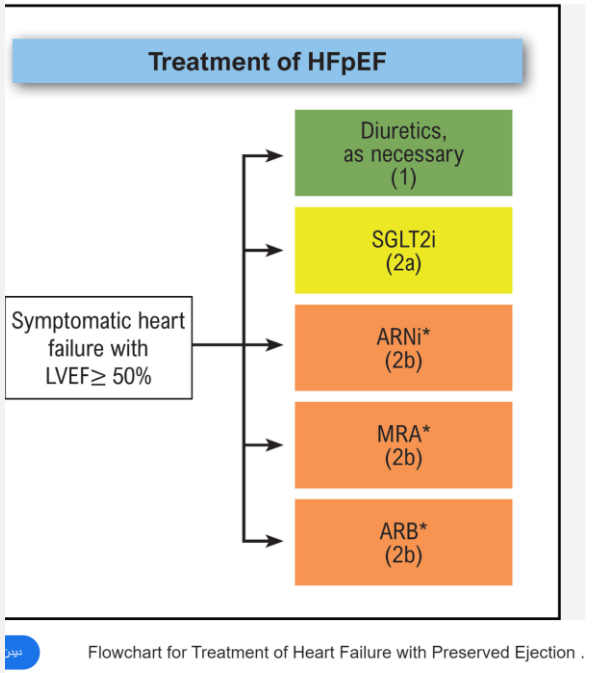
- Dehydration in Heart Failure—Possible Causes
- 1. Diuretics
- 2. Fluid Loss
- 3. Fluid Intake Restriction

- **Scant and low-quality evidence** indicates that restricting fluid intake could potentially lower the risk of HF hospitalization.

- However, contrasting reports suggest that such restrictions do not yield favorable outcomes and may negatively impact patients' quality of life .

- Nevertheless, in the "Patient education and self-care" table of 2023 ESC HF guidelines, the following recommendation is included: "A fluid restriction of 1.5–2 L/day may be considered in patients with severe HF/hyponatremia to relieve symptoms and congestion" (although it is a general recommendation.

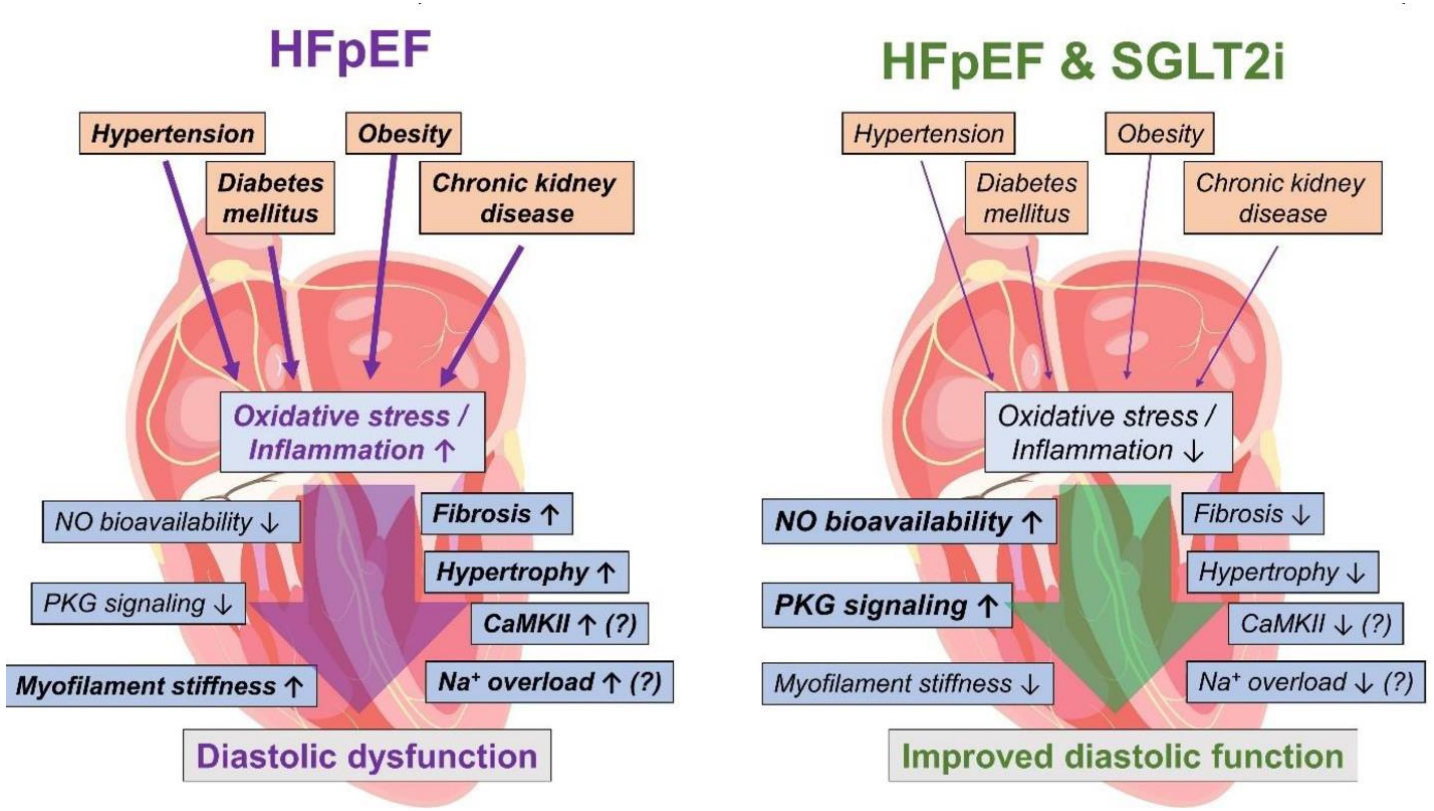


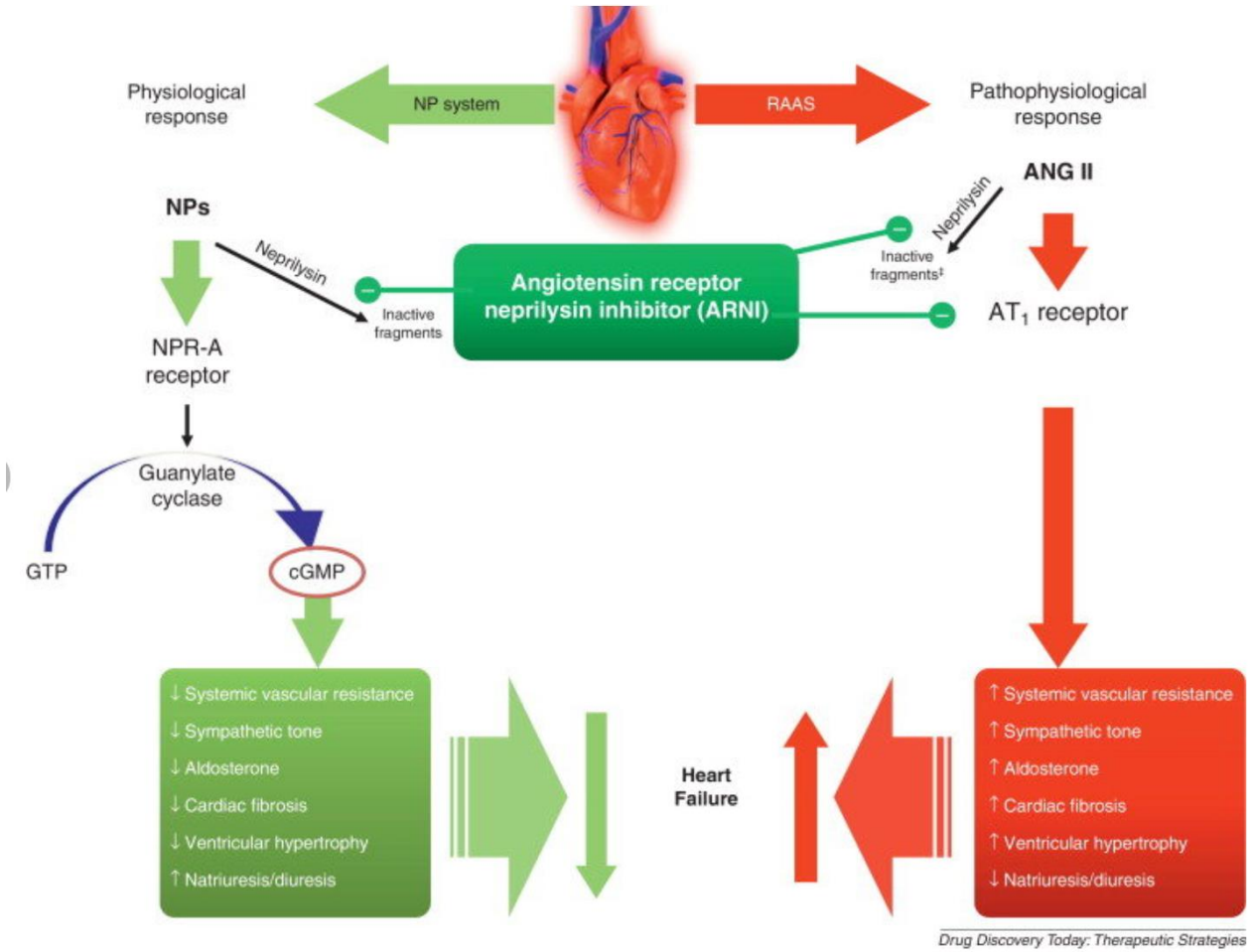


Flowchart for Treatment of Heart Failure with Preserved Ejection .

- RENAL SODUME AVIDIYU
- The Safety, Tolerability and Efficacy of Up-titration of Guideline-directed Medical Therapies for Acute Heart Failure (STRONG-HF) trial has shown the **importance of early initiation and rapid up-titration of GDMT** after an episode of ADHF .
-

SGLT2i


HFpEF
Hypertension
Obesity
Diabetes mellitus
Chronic kidney disease
Oxidative stress / Inflammation ↑
NO bioavailability ↓
Fibrosis ↑
Hypertrophy ↑
PKG signaling ↓
CaMKII ↑ (?)
Myofilament stiffness ↑
Na⁺ overload ↑ (?)
Diastolic dysfunction
HFpEF & SGLT2i
Hypertension
Obesity
Diabetes mellitus
Chronic kidney disease
Oxidative stress / Inflammation ↓
NO bioavailability ↑
Fibrosis ↓
Hypertrophy ↓
PKG signaling ↑
CaMKII ↓ (?)
Myofilament stiffness ↓
Na⁺ overload ↓ (?)
Improved diastolic function



Angiotensin receptor neprilysin inhibitors have the potential to modulate two counter-regulatory neurohormonal systems in HF: the renin–angiotensin–aldosterone system and natriuretic peptide system [6,8,12,27]. ANG: angiotensin; ARNI: angiotensin receptor neprilysin inhibitors; AT1: angiotensin type 1; cGMP: cyclic guanosine monophosphate; GTP: guanosine-5'-triphosphate; HF: heart failure; NP: natriuretic peptide (e.g. atrial natriuretic peptide [ANP], B-type natriuretic peptide [BNP], etc.); NPR-A: NP receptor-A; RAAS: renin–angiotensin–aldosterone system; ‡In vitro evidence.

Thank you