Resistant congestion syndrome- my patient also has hyponatremia, what should I do?

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10.06.2023


WHAT SHOULD I DO?

Diuretics

NYHA class II-IV heart failure with reduced ejection fraction (LVEF ≤40%) (1)

Recommendations	Class	Level
Loop diuretics		
Diuretics are recommended in patients with HFrEF with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce HF hospitalizations.	I	C

Pharmacological treatments to be considered in patients with (NYHA class II-IV) heart failure with mildly reduced ejection fraction

ESC

Recommendations	Class	Level
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs.	I	C

Recommendations for the initial treatment of acute heart failure (2)

ESC

Recommendations	Class	Level
Diuretics		
Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms.	I	C

ESC European Society of Cardiology

European Journal of Heart Failure (2019) 21, 137–155
doi:10.1002/ejhf.1369

POSITION PAPER

The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1,2]*, Kevin Damman[3], Veli-Pekka Harjola[4], Alexandre Mebazaa[5], Hans-Peter Brunner-La Rocca[6], Pieter Martens[1,2], Jeffrey M. Testani[7], W.H. Wilson Tang[8], Francesco Orso[9], Patrick Rossignol[10], Marco Metra[11], Gerasimos Filippatos[12,13], Petar M. S… and Andrew J. Coats[16]

Parameter	Sensitivity	Specificity	Comparator	Comment
Clinical evaluation				
Right-sided				
JVP > 8 cm	48%	78%	RAP > 7 mmHg	Difficult in obese patient
Jugular venous reflux	50%	75%	RAP > 7 mmHg	Difficult in obese patient
Hepatomegaly	51%	62%	RAP > 7 mmHg	Difficult in obese patient, non-HF causes
Bilateral leg oedema	94%	10%	RAP > 7 mmHg	Non-HF oedema gives false positive
Left-sided				
Dyspnoea	50%	73%	PCWP > 18 mmHg	Multiple reasons for dyspnoea
Dyspnoea on exertion	66%	52%	PCWP > 18 mmHg	Multiple reasons for dyspnoea on exertion
Orthopnoea	66%	47%	PCWP > 18 mmHg	May be non-cardiac in origin or absent
S3	73%	42%	PCWP > 18 mmHg	Intra-observer variability
Rales	13%	90%	PCWP > 18 mmHg	May be non-cardiac in origin or absent
Echocardiographic evaluation				
Right-sided				
Collapse (< 50%) IVC	12%	27%	RAP > 7 mmHg	Difficult to use in positive pressure ventilated patients
Inspiratory diameter IVC < 12 mm	67%	91%	RAP > 7 mmHg	Cannot be used in positive pressure ventilated patients
Left-sided				
Mitral inflow E-wave velocity > 50 (cm/s)	92%	28%	PCWP > 18 mmHg	Difficult when fusion of E and A wave
Lateral E/e' > 12	66%	55%	PCWP > 18 mmHg	Less accurate in advanced heart failure and CRT
Deceleration time < 130 ms	81%	80%	PCWP > 18 mmHg	Difficult when fusion of E and A wave
Pulmonary vein S/D < 1	83%	72%	PCWP > 18 mmHg	Intra-observer variability in Doppler measurements of the vein
Diffuse B-lines on lung ultrasound[a]	85.7%	40%	PCWP > 18 mmHg	B-lines might be present in non-cardiac conditions

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	Variable	EUVOLEMIA → CONGESTED				
Clinical congestion	Orthopnea	None		Mild	Moderate	Severe/worst
	JVP (cm)	<8 and no HJR	<8	8-10 or HJR+	11-15	>16
	Hepatomegaly		Absent	Liver edge	Moderate pulsatile enlargement	Massive enlargement and tender
	Edema		None	+1	+2	+3/+4
	6MWT	>400m	300-400m	200-300m	100-200m	<100m
Technical evaluation	NP (one of both): -BNP -NT-proBNP		<100 <400°	100-299 400-1500	300-500 1500-3000	>500 >3000
	Chest X-ray	clear	clear	cardiomegaly	- pulmonary venous congestion* - small pleural effusions*	- Interstitial or alveolar edema
	Vena Cava imaging [45]	**none of two:** - Max diameter >2.2 cm - collapsibility <50%		**One of two:** - Max diameter >2.2 cm - collapsibility <50%		**Both:** - Max diameter >2.2 cm - collapsibility <50%
	Lung Ultrasound [44]	<15 B-lines when scanning 28-sites		15-30 B-lines when scanning 28-sites		>30 B-lines when scanning 28-sites

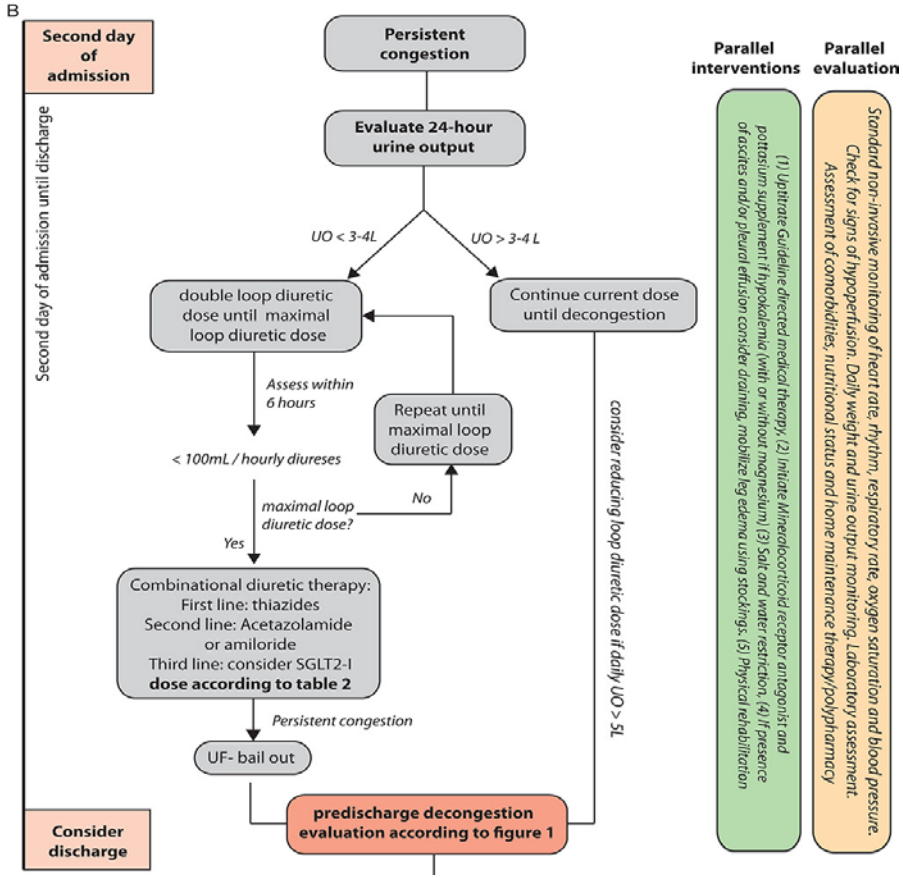
Diuretics: first 24 hours

Diuretics: first 24 hours

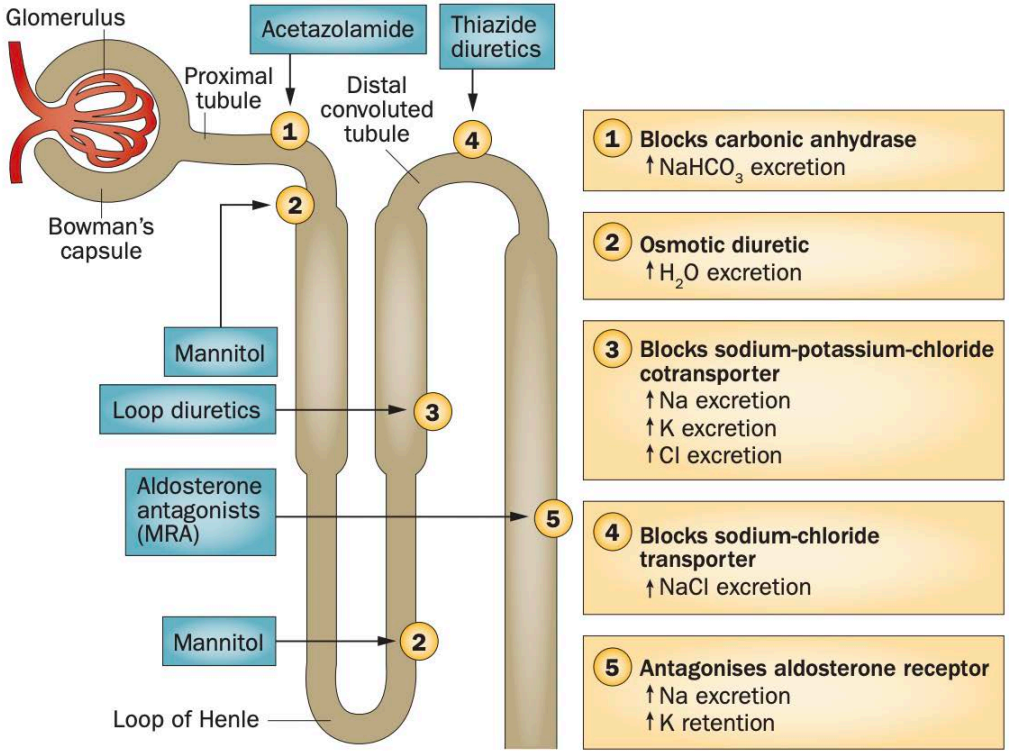
Diuretics: first 24 hours

Diuretics: first 24 hours

Diuretics: second day

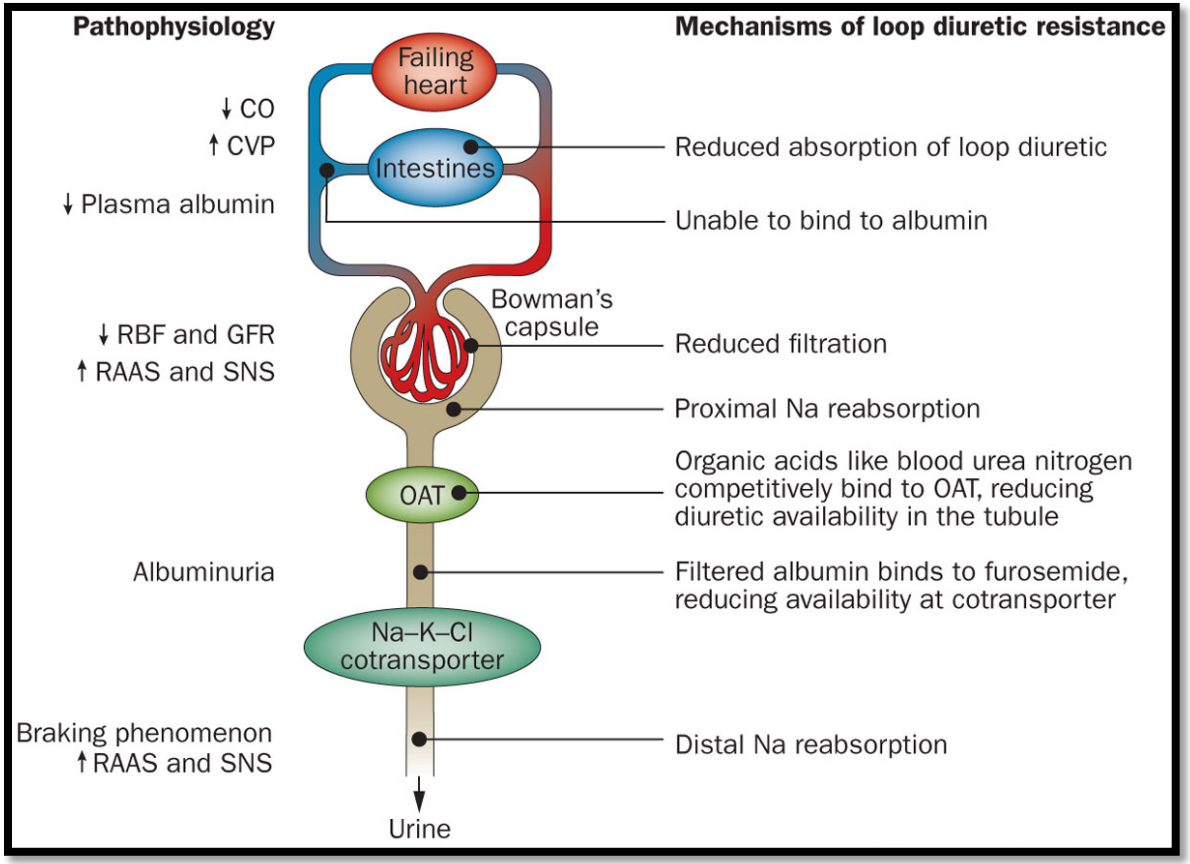


Diuretic therapy



ter Maaten, J. M. *et al.* (2014) *Nat. Rev. Cardiol.* doi:10.1038/nrcardio.2014.215

Diuretics: mechanism of diuretics resistance



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Hyponatremia

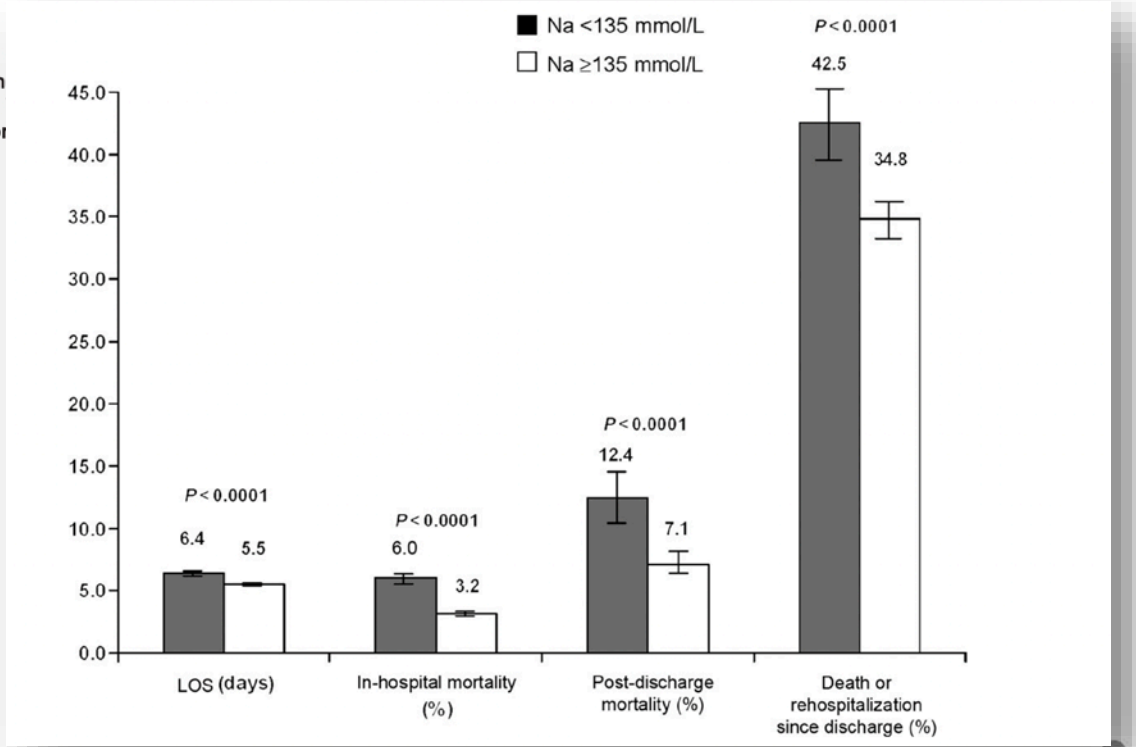
Background

- Approximately 20-30% of HF classes III-IV have hyponatremia
- It is associated with increased risk of death, independent of other comorbidities
- Hyponatraemic patients with HF demonstrate more severe congestive symptoms with worse diuretic response and might present with neurological manifestations, from subtle cognitive impairment to life-threatening symptoms in severe or rapid-onset hyponatraemia
- Even mild hyponatremia among with ADHF, regardless of LVEF, is associated with increased in-hospital and post-discharged mortality, prolonged hospital length of stay and frequent hospitalization

European Heart Journal (2007) 28, 980–988
doi:10.1093/eurheartj/ehl542

Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry

Mihai Gheorghiade[1]*, William T. Abraham[2], Nancy M. Albert[3], Wen
Barry H. Greenberg[6], Christopher M. O'Connor[7], Lilin She[8], Clyde
and Gregg C. Fonarow[11] on behalf of the OPTIMIZE-HF Investigator



Potential causes and factors in heart failure

Dilutional

- ► *Elevated AVP due to reduced cardiac output in advanced heart failure.*
- ► *SIADH, including drug-induced SIADH, most commonly due to antidepressants, antipsychotic agents, anticonvulsants, cytotoxic agents and pain medications (rare reports of SIADH in the course of amiodarone or ACEi therapy).*
- ► *Adrenal insufficiency, hypothyroidism (due to elevated AVP).*
- ► *Advanced kidney disease.*
- ► *Liver cirrhosis.*

Depletional

- ►► *Low sodium intake (salt-restricted diet).*
- ►► *Intensive diuretic treatment (combination therapy, high doses of diuretics).*
- ►► *Acute gastrointestinal losses (diarrhoea, vomiting).*
- ►► *Third-space losses (ascites, intestinal obstruction).*
- ►► *Flecainide—sodium channel blocker (rare reports of hyponatraemia, probably due to inhibition of sodium reabsorption in the distal nephron).*
- ►► *Potassium and/or magnesium deficiency (extracellular sodium depletion due to a shift of sodium into the intracellular compartment).*
- ►► *Severe hyperglycaemia (hypovolaemic hyponatraemia due to glucosuria-induced osmotic diuresis*).*

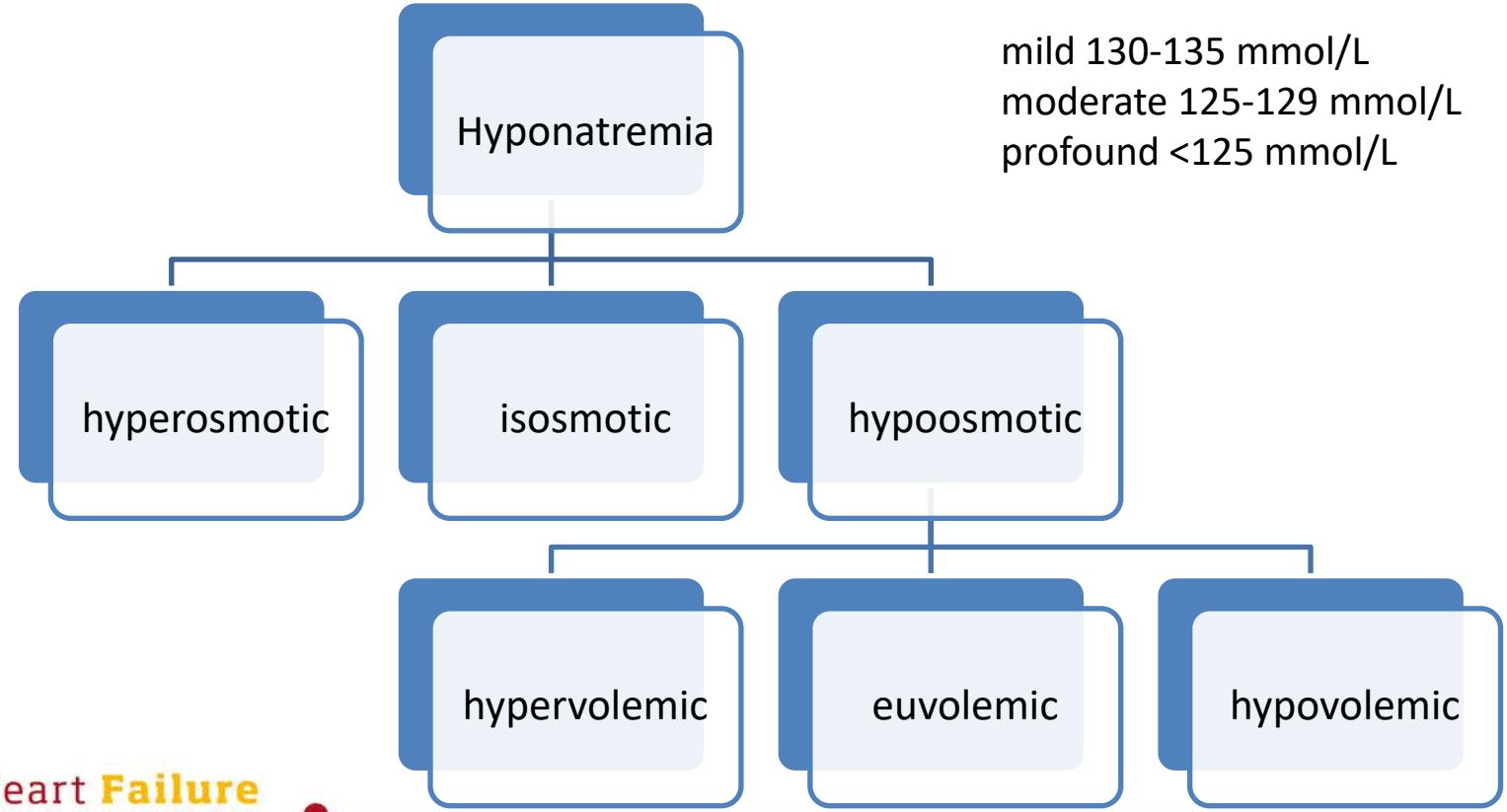
Pseudohyponatremia

(increased plasma osmolality leading to a fluid shift to intravascular compartment and dilution)

(laboratory artefacts, normal plasma osmolality)

- ►► *Severe hyperglycaemia.*
- ►► *Hyperosmolar radiocontrast media.*
- ►► *Hypertriglyceridaemia, hypercholesterolaemia.*
- ►► *Monoclonal gammopathies.*

Classification



mild 130-135 mmol/L
moderate 125-129 mmol/L
profound <125 mmol/L

Plasma osmolality

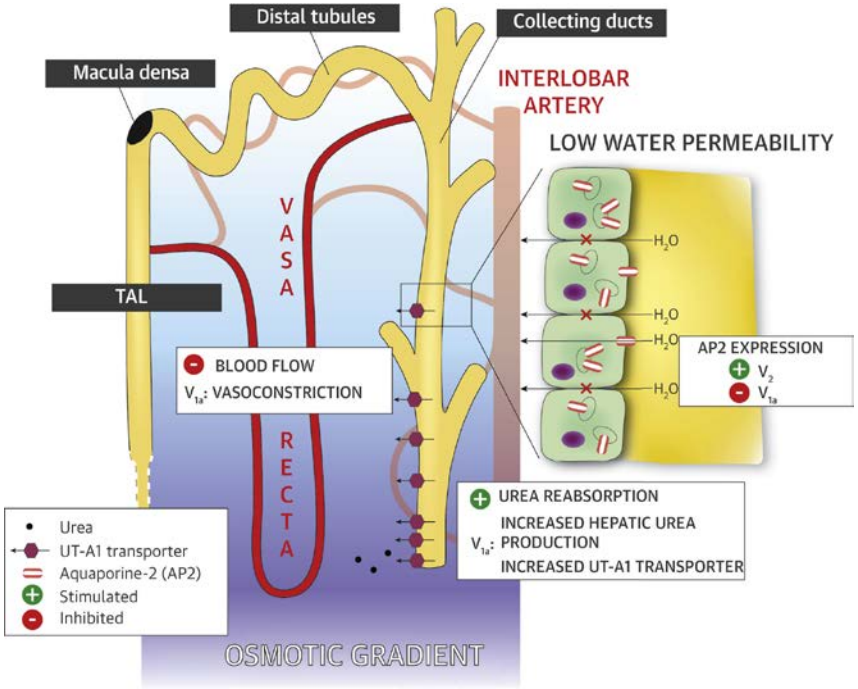
- are primarily determine by changes in serum concentration of sodium in its associated anions
- normal value 285-295 mOsm/L

- Total osmolality is defined as the concentration of all solutes in a given weight water, regardless of whether or not the osmoles can move across biological membranes

- Effective osmolality (tonicity) refers to the number of osmoles that contribute water movement between the intracellular and extracellular compartment

- Formula: 2 Na (mmol/) + 2 K (mmol/L) + urea (mmol/L) + glucose (mmol/L) + 0.033 protein (g/L)

Effects of AVP in the Nephron



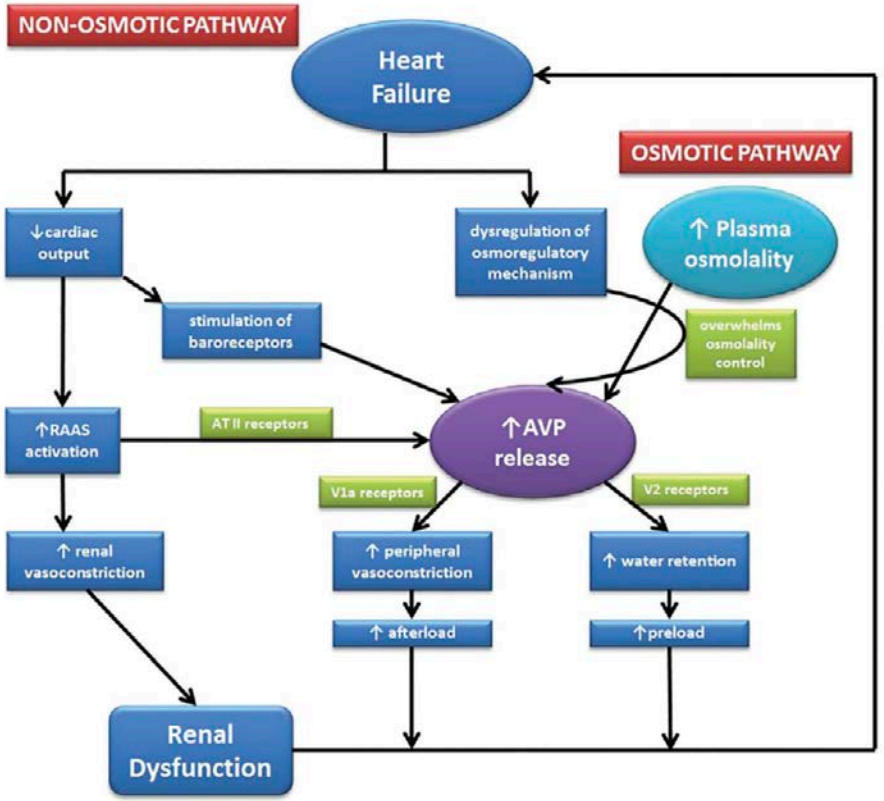
V1aR:	Myocardium Vascular smooth muscle Hepatocytes Myometrium	Myocardial hypertrophy Vasoconstriction Glycogenolysis Uterine contractions
V1bR and V3R	Anterior pituitary gland	Release of ACTH
V2R	Vascular endothelium and smooth muscle Kidneys (collecting tubules)	Vasodilatation Release of von Willebrand Factor Release of Factor VIII Water reabsorption

Ferbrugge et al. https://doi.org/10.1016/j.jacc.2014.12.010

Non-osmotic and osmotic pathways of AVP release

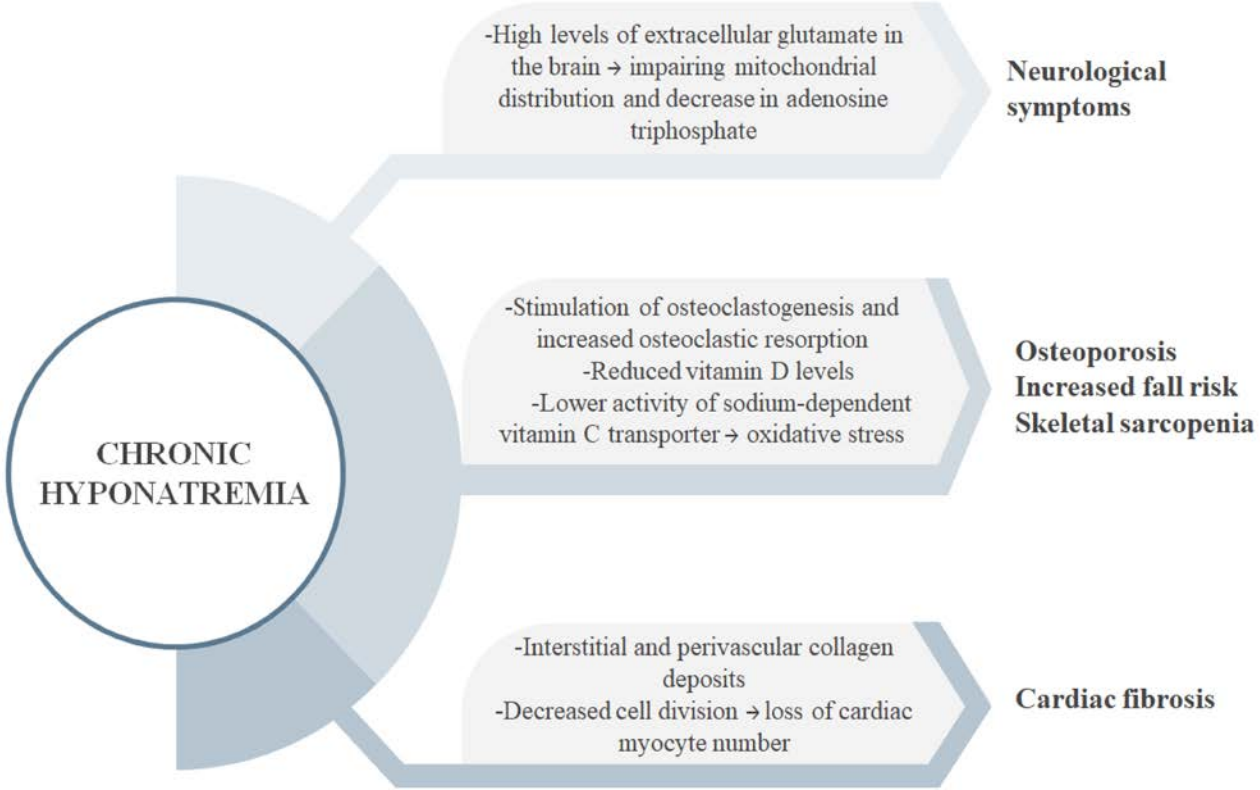
AVP secretion is modulated by both osmotic and non-osmotic pathways.

In the osmotic pathway, an increase in plasma osmolality stimulates increased production of AVP in the hypothalamus.
In the non-osmotic pathway, decreases in arterial blood pressure and circulatory blood volume diminish the sensitivity of baroreceptors, resulting in AVP release even at a lower serum osmolality.

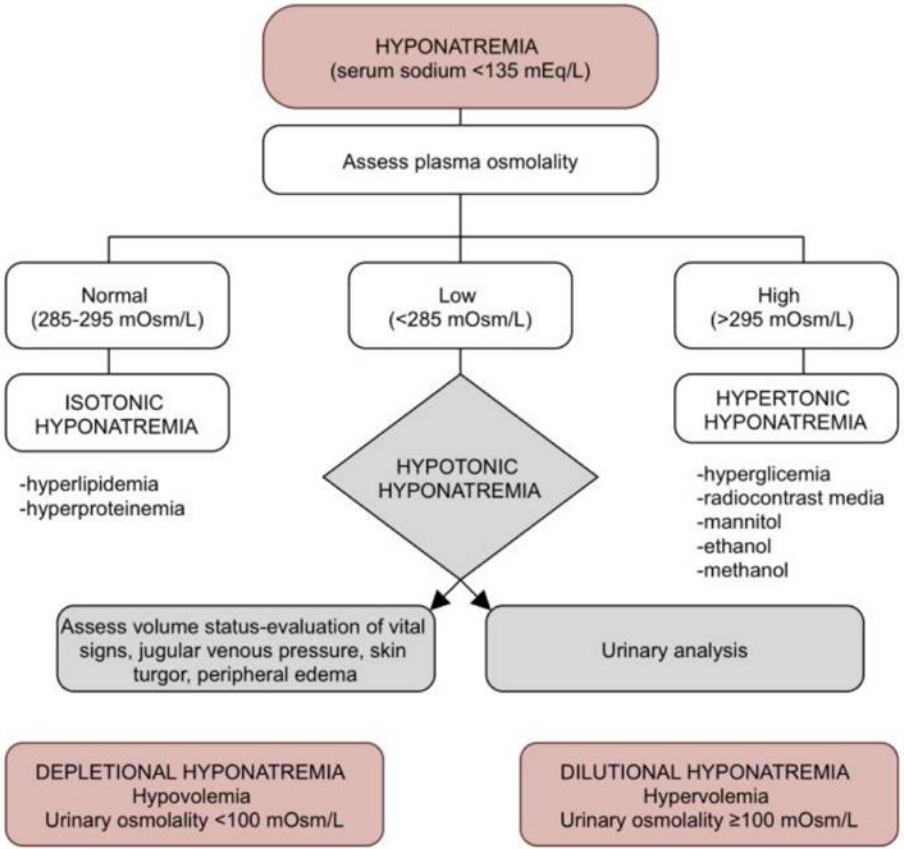


Tee et al. https://doi.org/10.1111/imj.14624

Symptoms of hyponatremia

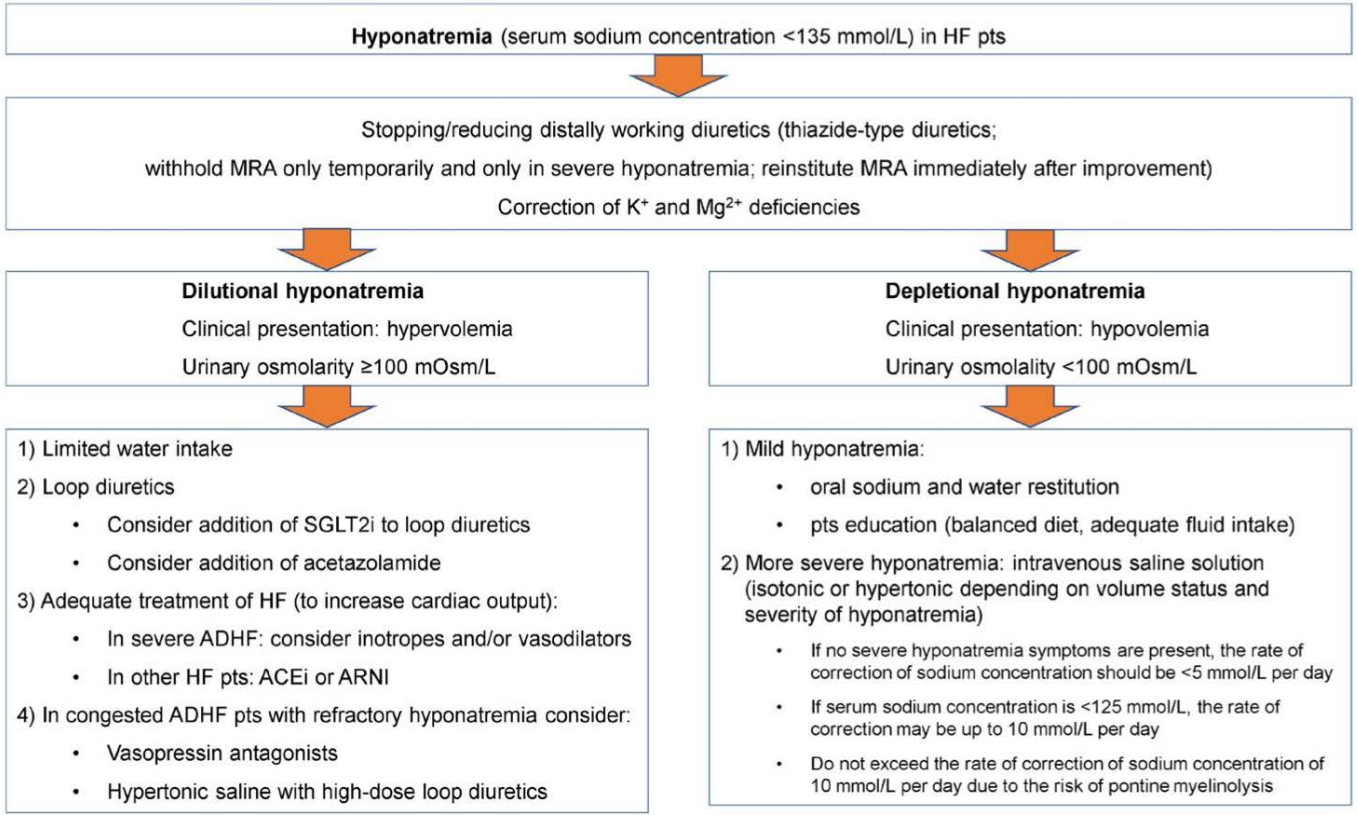


Diagnostic algorithm in HF associated hyponatremia



J. Pers. Med. **2023**, 13(1), 140

Algorithm for the hyponatremia management



Kapłon-Cieślicka A, et al. Heart 2021;0:1–7. doi:10.1136/heartjnl-2021-320277

Management of dilutional hyponatraemia in HF

Known and potential mechanisms		Drug
Reduced AVP secretion	▶ Indirect effect through immediate improvement of cardiac output.	▶ Inotropes. ▶ Vasodilators. ▶ Dual AVP antagonists.
	▶ Indirect effect through reverse cardiac remodelling and subsequent improvement of cardiac output.	▶ ACEi. ▶ ARNI. ▶ SGLT2 inhibitors.
	▶ Direct inhibition of AVP release.	▶ ACEi. ▶ ARNI.
Antagonising AVP effects in the collecting ducts		▶ ACEi. ▶ ARNI. ▶ Dual and selective V2 receptor AVP antagonists.

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▶	Preservation of the urine-diluting properties of the distal nephron by increasing distal nephron flow	▶ Increasing proximal (but not distal) sodium excretion.	▶ Loop diuretics. ▶ Acetazolamide. ▶ SGLT2 inhibitors.
▶		▶ Other mechanisms increasing sodium delivery to the Henle's loop and distal nephron.	▶ Hypertonic saline solution.
Antagonising AVP effects in th		▶ Improved renal blood flow through afferent arterioles (increased glomerular filtration).	▶ Hypertonic saline solution.
		antagonists.	

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▶		▶ Other mechanisms increasing sodium delivery to the Henle's	▶ Hypertonic saline solution.
Antagonising AVP effects in th		Reduced osmotic gradient of the renal medulla (reduced driving force for AVP-dependent free water reabsorption)	▶ Improved renal blood flow through the vasa recta (increased 'washout'). ▶ Dual AVP antagonists. ▶ ACEi. ▶ ARNI.
			▶ Decreased sodium reabsorption in the Henle's loop. ▶ Loop diuretics.
			▶ Decreased urea reabsorption in the collecting ducts. ▶ Dual AVP antagonists.
		Osmotic diuresis	▶ SGLT2 inhibitors. ▶ Hypertonic saline solution.

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