ESC European Society of Cardiology

European Journal of Heart Failure (2024) **26**, 730–741
doi:10.1002/ejhf.3244

POSITION PAPER

Dietary sodium and fluid intake in heart failure. A clinical consensus statement of the Heart Failure Association of the ESC

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Received 29 February 2024; revised 27 March 2024; accepted 3 April 2024; online publish-ahead-of-print 12 April 2024

Sodium and fluid restriction has traditionally been advocated in patients with heart failure (HF) due to their sodium and water avid state. However, most evidence regarding the altered sodium handling, fluid homeostasis and congestion-related signs and symptoms in patients with HF originates from untreated patient cohorts and physiological investigations. Recent data challenge the beneficial role of dietary sodium and fluid restriction in HF. Consequently, the European Society of Cardiology HF guidelines have gradually downgraded these recommendations over time, now advising for the limitation of salt intake to no more than 5 g/day in patients with HF, while contemplating fluid restriction of 1.5–2 L/day only in selected patients. Therefore, the objective of this clinical consensus statement is to provide advice on fluid and sodium intake in patients with acute and chronic HF, based on contemporary evidence and expert opinion.

Keywords Heart failure • Sodium • Fluid

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Introduction

Patient education and self-care play a pivotal role in the management of heart failure (HF).[1] The 2021 European Society of Cardiology (ESC) HF guidelines recommend avoiding excessive salt intake (>5 g/day) in all patients with HF, irrespective of ejection fraction.[2] Additionally, for patients with severe or advanced HF, restricted fluid intake (<1.5–2 L/day) may be considered to alleviate symptoms.[2] These recommendations derive from the pathophysiological changes in the sympathetic nervous system, the renin–angiotensin–aldosterone system (RAAS), the vasopressin axis, and vasodilatory/natriuretic pathways in patients with HF. Collectively, these maladaptive responses to the initial cardiac event or disorder result in increased sodium (Na^+) and water avidity.[3] It is important to note that these recommendations are based on expert consensus and have not been supported by adequately powered randomized clinical trials. Moreover, observational studies indicate that patient adherence to Na^+ and fluid restriction is generally suboptimal, as these restrictions have been associated with a poor quality of life as well as elevated plasma renin activity.[4–7] Recent data suggest that a more lenient approach to fluid and Na^+ intake may not be detrimental, while stringent restrictions may be harmful in certain conditions.

Normal physiology of sodium and fluid handling

Salt, sodium and fluids

Sodium is an essential trace element with a central role in a wide array of physiological processes within living organisms. Approximately 30% of the body's Na^+ content, which amounts to ~92 g, is sequestered within the bone as Na^+ apatite and is not fully exchangeable. A further 10% resides within the intracellular compartment, while the remaining 60% is dispersed within the extracellular fluid, which includes the plasma and interstitial fluid[8,9] (*Figure 1*). Therefore, Na^+ is the dominant extracellular electrolyte and largely determines serum osmolality and consequently, extracellular volume.[9] *Figure 1* illustrates the Na^+ and fluid distribution within the human body, a process which is tightly regulated in response to water and salt intake and aerobic, metabolic water production, as well as (mal)adaptive responses to physiological and pathological circumstances.

Salt, or sodium chloride (NaCl), constitutes the main dietary source of Na^+. The average intake in Western nations is ~4 g/day, equivalent to a salt intake of 10 g with 1 g of Na^+ corresponding to 2.54 g of salt.[10,11] To determine the quantity of Na^+ in a given mass of salt, it is essential to take into account the atomic mass units involved in the compound. The calculation involves multiplying the total mass of NaCl in grams by the Na^+ fraction, which is ~0.40, in order to obtain the Na^+ content in grams.

Gastrointestinal absorption

On a daily basis, the gastrointestinal (GI) tract effectively regulates roughly 9 L of fluids and 18 g of Na^+, primarily through secretion as an integral part of the digestive process.[12] Interestingly, oral ingestion accounts for only ~1.5–2 L of water and ~4 g of Na^+. Within an evolutionary framework, humans have adapted to limited Na^+ availability by developing a highly efficient GI system, responsible for the (re)absorption of nearly all available Na^+ and water.[11] The absorption of the majority of nutrients, Na^+ included, occurs within the small intestines through different pathways, regulated by signal transduction processes affected by neural, paracrine, and endocrine factors.[12–14] Serum levels of Na^+ and serum osmolality begin to increase within ~30 min after oral ingestion.[15] This highly efficient process can in part be attributed to the intricate microstructure of the intestinal villi, which form a plexus, representing an optimal architectural arrangement for absorption[16,17] (*Figure 2*). Key Na^+ transporters at the brush border include members of the sodium/hydrogen exchange (NHE) family, notably NHE3, as well as the sodium–glucose cotransporter 1 (SGLT1). Meanwhile, the distal part of the colon contains epithelial Na^+ channels (ENaC) responsive to mineralocorticoids.[18] The individual contribution of the specific Na^+ channels to overall Na^+ uptake can differ in the post-prandial phase (when other nutrients are available) versus the inter-prandial phase. Water follows passively driven by osmosis.[19]

Circulatory volume

Water or fluid homeostasis within the human body is controlled through two principal mechanisms. Initially, the hypothalamic thirst centre, which promptly triggers the release of vasopressin from the pituitary gland in response to an increase in serum osmolality (carefully sensed by osmoreceptors) and/or a more prominent decrease in blood pressure (monitored by baroreceptors). Subsequently, the RAAS operates to preserve a constant effective circulatory volume, predominantly through the modulation of Na^+ levels. These regulatory processes are vital for preserving the stability of the body's internal environment, responding quickly to physiological changes to ensure cellular and systemic equilibrium.

An increase in serum osmolality by even a small margin, measured in milliosmoles per L, prompts the kidneys to conserve free water. This response is crucial due to the brain's sensitivity to osmotic fluctuations. Notably, the body expels water at a faster rate compared to Na^+. This is because Na^+ excretion involves additional physiological processes, as depicted in *Figure 3*, which outlines the sequence of events following the consumption of 1 L of NaCl 0.9%.[20]

Splanchnic veins ordinarily store approximately 25% of the total blood volume, which is essential for maintaining and adapting cardiac preload, influenced by neurohormonal pathways (given their high density of α_1 and α_2 receptors).[21,22] Part of the GI absorbed serum Na^+ and fluids eventually drain from the capillaries into the tissues and interstitium, determined by the intricate balance of oncotic and hydrostatic pressures according to the Starling principle.[23] It has been hypothesized that part of total body Na^+ is eventually bound to the negative electrostatic glycosaminoglycan (GAG) networks in the gel-like interstitium mostly in the skin, bone and cartilage which may acts as a storage reservoir.[9] These

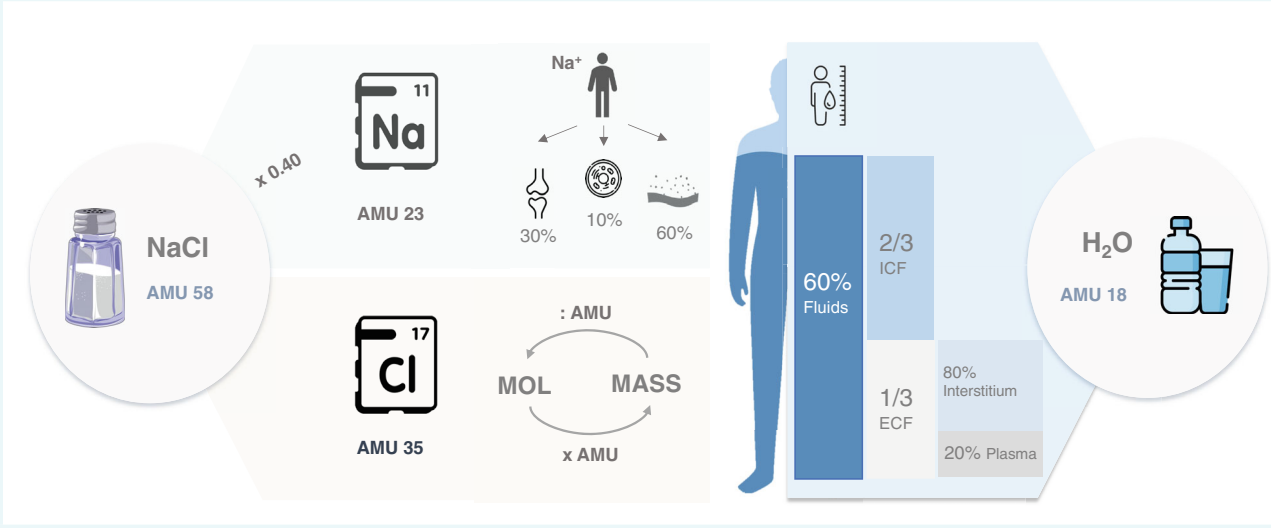

Figure 1 Salt, sodium and fluid distribution in the human body. AMU, atomic mass unit; Cl, chloride; ECF, extracellular fluid; H_2O, water; ICF, intracellular fluid; Na, sodium.

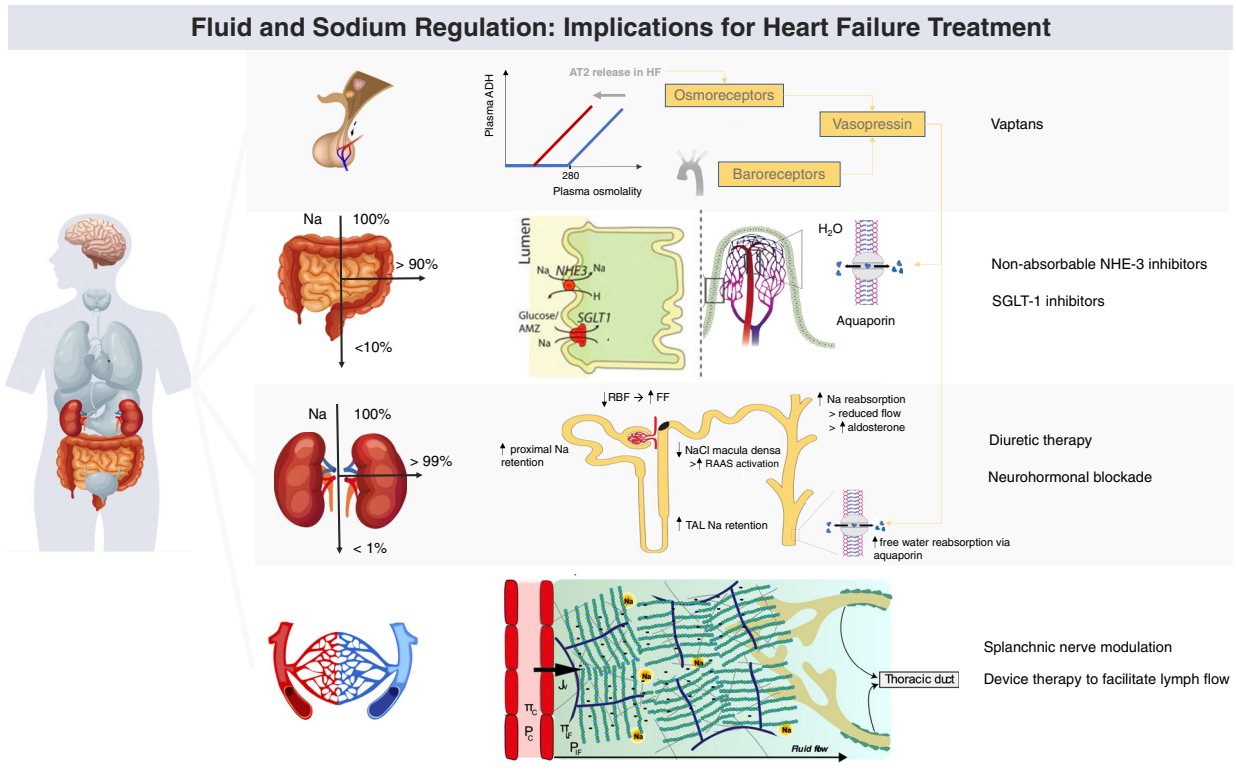

Figure 2 Sodium and fluid handling with therapeutic implications in the context of heart failure (HF). FF, filtration fraction; Na, sodium; NHE, sodium/hydrogen exchange; RAAS, renin–angiotensin–aldosterone system; RBF, renal blood flow; SGLT-1, sodium–glucose cotransporter 1; TAL, thick ascending limb.

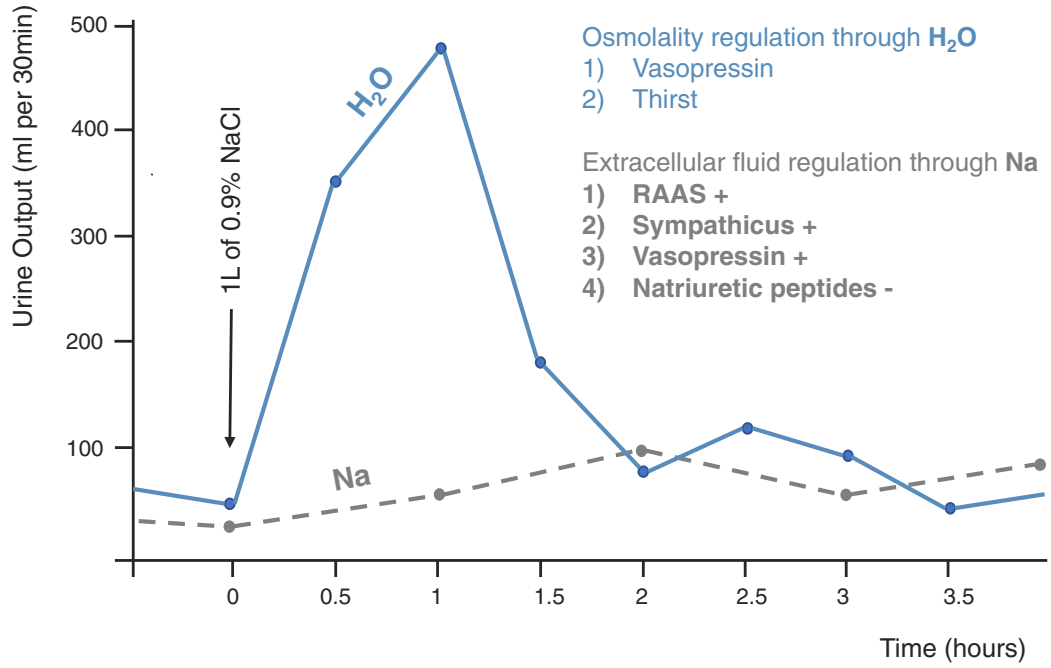

Figure 3 Response to drinking of 1 L of 0.9% NaCl by a healthy man. After 2 h, all the water but limited sodium has been eliminated. ADH, antidiuretic hormone; Cl, chloride; H_2O, water; Na, sodium; RAAS, renin–angiotensin–aldosterone system. Adapted from Levick.[20]

GAG networks may play an important role in overall Na^+ balance, fluid homeostasis and endothelial function.[9,24] Given the low compliance of the interstitium and the bipolar structure of H_2O, any additional water is pushed out of the interstitium towards the lymphatic vessels while the positive Na^+ cations potentially remain electroneutral-trapped by the negative GAG structure.[9,18,25] Lastly, the lymphatic system is responsible for clearing and returning interstitial fluid to the vasculature, and the thoracic duct flow is estimated to be ~1.5 L/day.[25,26]

Renal sodium and water balance

Sodium undergoes unimpeded filtration at the renal glomerulus. The renal tubules receive daily ~25 500 mmol of Na^+ (or ~600 g Na^+), a result derived from a normal glomerular filtration rate (GFR ~180 L/day) and serum Na^+ concentration (~142 mmol/L) – a number dramatically greater than the daily Na^+ intake.[27] Thus, only a tiny fraction of Na^+ – called the fractional Na^+ excretion (FeNa normally <1%) – is ultimately excreted in the urine, as tubular Na^+ reabsorption exceeds 99%. Importantly, the urinary Na^+ concentration is usually lower than the serum Na^+ concentration, especially in HF patients with increased neurohumoral activation. As such, water (diuresis) is needed to be able to excrete Na^+ (natriuresis) in the urine. Considering that nearly all ingested Na^+ is reabsorbed in the GI tract, a sophisticated regulatory mechanism is in place to ensure that net renal Na^+ excretion mirrors dietary intake over longer periods of time.[11] Intrinsic autoregulation aims to maintain the GFR within narrow limits in each functionally active nephron.

In short, blood flow is kept constant by mediating arteriolar resistance.[28] Tubuloglomerular feedback regulates filtration by maintaining a constant chloride load passing the macula densa cells at the end of the thick ascending loop of Henle. An increase in chloride concentration (glomerular hyperfiltration) promptly lead to vasoconstriction of the afferent arteriole via the release of adenosine and a decrease in release of renin, overall leading to less vasoconstrictive effects of angiotensin II (ATII) on the efferent arteriole.[27] Additionally, the glomerulus and proximal tubules operate in tandem (glomerulotubular balance) to maintain a relatively constant amount of iso-osmotic ultrafiltrate to be processed by more distal regions of the nephron. The distal convoluted tubules and collecting ducts reabsorb ~10% of the total Na^+, with tight regulations based on tubular flow rate, aldosterone levels, and vasopressin which explains the concentrating and diluting capacity of the kidneys.

Achieving maximal free water clearance (resulting in a urine osmolality down to 30 mOsm/kg) involves two distinct processes: (i) active Na^+ and chloride absorption in the distal diluting segments, and (ii) suppression of vasopressin to prevent the reabsorption of free water in the collecting ducts.[29] In general, the human body must eliminate approximately 600 mOsm of renally cleared solute daily. Considering the kidneys' concentration or dilution capacity, the typical human body accomplishes this by producing a minimum urine volume of 500 ml/day (a volume <500 ml/day is referred to as oliguria, which the kidney is easily capable of producing), up to an impressive 20 L/day in situations requiring maximal urine dilution. This underscores the remarkable capacity of the kidneys to excrete excess free water.

Sodium and fluid handling in patients with heart failure and potential treatment targets

Gastrointestinal absorption

As in healthy persons, there is nearly complete intestinal Na^+ and fluid absorption in patients with HF. Therefore, differential Na^+ uptake in HF is not a major contributing mechanism leading volume overload and congestion in HF.[18] Nevertheless, the microstructure of the intestinal villus is prone to (i) congestion, resulting in malabsorption, and (ii) shunting of oxygenated blood towards its base, making the villus tip vulnerable to ischaemia. In the context of HF, the presence of splanchnic congestion and reduced flow might thus induce anaerobic conditions, subsequently precipitating intracellular and regional acidosis.[16,17] This acidosis is a recognized trigger for further upregulation of NHE3, the primary ion channel responsible for controlling Na^+ absorption in the intestines.[16] Indeed, impaired Na^+ absorption has been observed in NHE3 knockout mice, leading to the therapeutical hypothesis that non-absorbable NHE3 inhibitors may have potential benefits in addressing congestion.[30,31] However, in the short term, GI adverse events, especially diarrhoea, were frequently documented in animal and small-scale human studies, and the effectiveness appeared to decline over time due to the activation of alternative pathways, including increased aldosterone production and the up-regulation of the specific ENaC.[12,14,31–34] The ultimate impact of decongestive strategies designed to target GI absorption, which includes potential effects on the gut microbiome, is still uncertain.[12,31,35]

Despite the limited impact of Na^+ uptake through the SGLT1 receptor, potent inhibitors of SGLT1, such as phlorizin – a dihydrochalcone compound first isolated in 1835 from apple tree bark – have been associated with various GI adverse effects. These include diarrhoea, dehydration, and malabsorption, underscoring the biological relevance of this pathway.[36,37]

Circulatory volume

Importantly, cardiac filling pressures usually rise days to weeks prior to hospital admission for acutely decompensated HF, even though many patients gain less than 1 kg in weight during this time frame.[38–40] This challenges the notion of subacute salt and water overload with consequent volume overload as the major contributing factor. Transient venoconstriction, induced by increased sympathetic stimulation, may lead to the redistribution of blood from splanchnic venous capacitance beds (reservoir function) to the effective circulatory volume.[41] This may exert a more prominent influence on the observed pressure elevation than simple volume overload. Recent evidence suggests that blocking neural activity of the greater splanchnic nerve could have benefits, but long-term effects remain unknown.[42–44]

In the context of Na^+ and fluid retention, merely 25% remains within the intravascular compartment, whereas the remaining 75% is sequestered within the extravascular space, comprising the interstitium and the third space.[45] HF leads to structural alterations in the lymphatics and increased flow in the enlarged thoracic duct up to eight-fold higher than normal, reaching 8 ml/min in HF patients.[25,45,46] Nevertheless, at a given point, the lymphatic system might become insufficient to cope with this increased capillary filtration, especially in states of increased central venous pressure further impeding the outflow, leading to a volume-overloaded interstitium. These observations evoked interest into devices that might facilitate lymphatic decompression and increase lymphatic flow.[26,47] Additional research is needed in the interplay between microcirculation, interstitium and the lymphatic system and how therapies in this space can be used to mitigate signs and symptoms of volume overload and congestion in our patients with HF.[25]

Renal sodium and water balance

Neurohormonal activation, reduced renal perfusion (low cardiac output and elevated venous pressure), and a pre-existing lower amount of functionally active glomeruli, contribute to the reduced GFR observed in HF patients.[11,48,49] The subsequent higher filtration fraction in the setting of a decreased renal blood flow (in order to preserve the GFR) and increased venous pressures raises peritubular capillary oncotic pressure which facilitates proximal Na^+ and water reabsorption (glomerulotubular balance).[50,51] This leads to a substantial reduction in the delivery of Na^+ (and chloride) to the distal nephron, posing challenges for the distal tubules to regulate the concentration of urine.[11] ATII, whether autocrine or paracrine, plays a central role by binding to angiotensin type 1 receptors in the proximal tubules and cortical collecting ducts. Excess of ATII induces vasoconstriction, relatively increased resistance in efferent over afferent arterioles, mesangial cell contraction, elevated levels of aldosterone and endothelin, and ATII is a potent non-osmotic trigger for thirst, even when serum osmolality is usually low.[52,53] Moreover, vasopressin release driven by angiotensin and baroreceptors in context of low blood pressure hinders the production of diluted urine by making the collecting ducts leaky to water through given the insertion of aquaporin-2 channels.[51] In addition, the set point for vasopressin release for any given serum osmolality is reduced in patients with HF.[54–56] This results in gradual expansion of total body fluid, lower osmolality, and dilutional hyponatraemia in the evolving course of HF (*Figure 2*). The kidney serves as the primary target of diuretic therapy. A more comprehensive understanding of renal physiology and the initiation of diuretic therapeutic interventions has been addressed previously by this working group.[50]

Effects of guideline-recommended heart failure medical therapy on sodium and fluid avidity

The physiological processes outlined above (*Figure 2*) in untreated HF patients result in the retention of Na^+ and water. This retention serves as the foundation for the dietary intake restrictions recommended in all clinical guidelines.[2,57] Increased Na^+ avidity was also elegantly demonstrated by McKie *et al.*[58] in patients with early (untreated) stages of HF, showing that they were already susceptible for volume overload as administration of normal saline resulted

in reduced natriuresis compared to healthy individuals, which could be partially restored by the administration of exogenous natriuretic peptides. However, most aforementioned physiological studies have been conducted prior to the introduction of contemporary guideline-recommended medical therapy. In a cohort of 12 treated and stable HF patients, the renal, haemodynamic, and neuroendocrine responses to alterations in Na^+ intake (70 mmol/day vs. 250 mmol/day) closely resembled those observed in healthy individuals.[7] Therefore, it appears that the neuroendocrine mechanism responsible for sensing intravascular volume expansion triggered by increased Na^+ intake and subsequently facilitating renal Na^+ excretion is at least partially intact in patients with medically well-managed and 'stable' disease.[7] Additionally, too strict dietary salt and water restrictions are often associated with reduced intake of other healthy food substances, reduced caloric intake, persistent thirst, paradoxical increases in renin release, increase in sympathetic nervous system activity and disruptions in immune and lipid homeostasis.[59–62] Furthermore, adherence to Na^+ restriction is generally poor, as indicated by studies collecting urinary Na^+ levels (though challenging to assess in patients on diuretics).[63] Therefore, the question arises as to whether the need for restrictions are still applicable to contemporary HF management. In the context of this document, we categorize the HF population into 'acute' and 'chronic' groups. The 'chronic' category refers to those with chronic *stable* HF, under guideline-recommended HF therapy, without signs and symptoms of congestion, and without or minimal loop diuretic requirement. The 'acute' category is characterized as acute HF, during the up-titration phase of guideline-recommended HF therapy, presence of residual congestion, and/or the need for maintenance on loop diuretics.

Recent evidence for fluid restriction in heart failure

There are limited studies with small patient numbers that specifically focus on fluid intake in the context of HF; randomized trials including major adverse cardiovascular events are summarized in *Table 1*.[64–72] These studies exhibit significant variability in their designs, patient groups, intervention methods, and settings.[64,65,73] Overall, none of these have reported a significant effect or association with reduced fluid intake and cardiovascular mortality or HF-related hospitalizations.

Acute heart failure

In the setting of acute HF, Aliti *et al.*[66] randomized 75 patients to either restricted fluid and Na^+ intake (<800 ml/day and 800 mg/day, respectively) or a liberal intake (>2.5 L/day and 3–5 g/day, respectively). No significant differences were observed between the two groups in terms of intravenous diuretic administration rates, weight changes, or clinical stability during the 3-day follow-up period. Applying a similar approach but concentrating solely on fluid restriction, Travers *et al.*[73] observed no significant difference in the time to clinical stabilization in patients with acute decompensated HF between those with restricted fluid intake and those with liberal fluid intake. However, the between-group difference in fluid intake was only 392 ml/day. In the case of hyponatraemic patients (<135 mmol/L), the implementation of fluid restriction may have a positive impact on the quality of life based on a randomized controlled pilot study (SALT-HF [Strict Allowance of Fluid Therapy in Hyponatremic Heart Failure] trial).[64,65,73] However, thirst is a very common issue in up to 50% of (acute) HF patients, even more so in cases of hyponatraemia, significantly impacting quality of life and correlating with prescribed fluid restrictions.[74,75] Xerostomia, altered taste, dry skin and itching are other side effects of stringent fluid restriction.[18,64]

Chronic heart failure

Studies on fluid restriction in the setting of chronic HF patients are scarce. The pilot study of Holst *et al.*[64] indicated that a daily fluid intake of <1.5 L was not linked to any discernible benefits compared to liberal intake (30 ml/kg/day) in HF patients post-discharge but water restriction proved to be very challenging to adhere. Encouragingly, the FRESH-UP (Fluid REStriction in Heart failure vs. liberal fluid UPtake) trial is a randomized, controlled, open-label, multicentre trial investigating the effects of a 3-month period of liberal fluid intake versus fluid restriction (1500 ml/day) on quality of life in 506 ambulatory patients with HF and New York Heart Association (NYHA) class II–III class symptoms.[76]

Recent evidence for sodium restriction only in heart failure

Chronic heart failure

A meta-analysis in chronic ambulatory patients with HF indicates a tendency towards increased all-cause mortality and a higher rate of HF hospitalization with limited Na^+ consumption.[77] Additionally, a synthesis of data from all trials concerning Na^+ restriction in HF up to 2 April 2022 (17 trials including 1683 patients) demonstrated neutral results for all-cause mortality and cardiovascular hospitalization.[67,77] These findings were consistent across different types of studies, including randomized controlled trials and observational studies, irrespective of left ventricular ejection fraction, follow-up duration, and Na^+ restriction intensity but lack however statistical power.[78,79] Of note, an association was observed between earlier year of publication and the impact of Na^+ restriction on mortality reduction in both meta-analyses which might be explained by progressive uptake of more and better neurohumoral blockers over time.[77,78] Finally, the SODIUM-HF (Study of Dietary Intervention under 100 mmol in Heart Failure) trial, which is the largest randomized controlled trials to date ($n = 806$) showed that a long-term dietary intervention to reduce Na^+ intake (<1500 mg/day) in ambulatory HF patients did not reduce clinical events including all-cause mortality or hospitalization, although modest improvements were seen in quality of life. However, the latter should be interpreted with care given the open-label design with patient's awareness of allocated intervention, rather small difference in Na^+ intake between groups (only 415 mg) and the lack of statistical power (estimated vs. observed effect size 20% vs. 11% and event rate 21.3% vs. 16.1%).[67] Furthermore, it is important to note that (i) 80% were on RAAS inhibitor,

Table 1 **Randomized trials on sodium and/or fluid intake in heart failure patients including major adverse cardiovascular events**

Study	Design	Patient population	Sample size	Intervention	Comparator	MACE
Fluid intake						
Holst *et al.*[64]	Cross-over	HFrEF without clinical signs of congestion	74	Maximum fluid intake of 1.5 L/day	Fluid intake based on 30 ml/kg body weight/day	Readmission rate: NS
Albert *et al.*[65]	Parallel-group, single-blind	ADHF, serum sodium ≤137 mg/dl	52	Maximum fluid intake of 1 L/day	Usual care discharge instructions and education	60-day mortality or readmission rate: NS
Sodium and fluid intake						
Aliti *et al.*[66]	Parallel-group with blinded outcome assessments	Inpatients with ADHF, HFrEF	75	Sodium to 800 mg/day and fluid to 0.8 L/day during hospital stay	Unrestricted sodium and fluid intake	30-day readmission rate: NS
Machado d'Almeida *et al.*[68]	Parallel-group with blinded outcome assessors	Inpatients with ADHF, HFpEF	53	Sodium to 800 mg/day and fluid to 0.8 L/day during hospital stay	Unrestricted sodium and fluid intake	30-day mortality or readmission rate: NS
Fabricio *et al.*[69]	Single-blind	Patients hospitalized with ADHF	44	Low-sodium diet (3 g/day dietary salt) and fluid to 1 L/day	Normal-sodium diet (7 g/day salt) and fluid to 1 L/day	30-day readmission rate: NS
Sodium intake						
Hummel *et al.*[70]	Single-blind, multicentre	Discharged from hospital with ADHF	66	Home-delivered sodium-restricted food (1500 mg/day sodium)	Usual care discharge instructions and education	30-day mortality or readmission rate: NS
Kalogeropoulos *et al.*[71]	Double-blind	HFrEF with recent hospitalization on optimal GRMT	27	Sodium-restricted diet (1.5 g/day sodium)	Sodium-restricted diet (3 g/day sodium)	30-day readmission rate: NS
Ivey-Miranda *et al.*[72]	Double-blind	HFrEF on optimal GRMT	70	Sodium-restricted diet (2 g/day sodium)	Sodium-restricted diet (3 g/day sodium)	30-day mortality or readmission rate: NS
Ezekowitz *et al.*[67]	Multicentre open-label with blinded outcome assessments	Adult patients with chronic HF (NYHA class II–III) on optimal GRMT	806	Sodium-restricted diet (1.5 g/day sodium)	Usual care according to local guidelines	30-day mortality or readmission rate: NS

ADHF, acute decompensated heart failure; GRMT, guideline-recommended medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MACE, major adverse cardiovascular event; NS, not significant; NYHA, New York Heart Association.

87% received beta-blockers, and 60% were on mineralocorticoid receptor antagonists, and (ii) the control group's daily Na^+ intake was 2073 mg, falling below the recommended threshold.

Acute heart failure

In contrast, there are some observational data which indicate that patients on diuretics with NYHA class III/IV symptoms had significant reductions in hospital visits, readmissions, and even mortality if they were on a self-proclaimed lower Na^+ diet.[80] Moreover, ambulatory patients who were admitted with acute HF exhibited a chronically lower urinary Na^+ concentration and a further drop in urinary Na^+ concentration during the week preceding hospitalization.[63] In more symptomatic/congestive patients with recurrent worsening episodes with high diuretic needs that may have long-term nephron remodelling and advanced Na^+ avidity, the effectiveness of diuretics may diminish, making Na^+ restriction a potential necessary measure that outweighs the associated risks.[81] Certainly, an expanding body of research has examined urinary Na^+ concentration (including spot samples and continuous collections) in the context of both acute and chronic HF. Associations have been observed between low urinary Na^+ levels and reduced diuretic efficacy, persistent congestion, and an elevated risk of HF readmission or cardiovascular mortality.[63,82–84] Further research building upon these insights may inform more individualized and dynamic clinical recommendations in the future.

Recent evidence for liberal sodium intake in most heart failure patients

Chronic heart failure

In contrast to limiting Na^+ intake, studies have also explored the potential therapeutic benefits of administering salt to individuals with HF.[85] A mechanistic study focused on examining Na^+ regulation in ambulatory euvolaemic HFrEF patients receiving guideline-recommended medical therapy. This study involved age-matched volunteers and entailed a modest increase in daily Na^+ intake by 1.2 g (equivalent to 51 mmol) over a period of 4 weeks.[86] Patients with well-treated HF and reduced ejection fraction tolerated a prolonged increase of Na^+ intake without signs and symptoms of HF, congestion or blood volume increase, and the increase of Na^+ intake led to a significant decrease in neurohumoral stimulation and increased natriuresis.

Acute heart failure

In the acute HF setting, it has been postulated that salt loading along with diuretics might potentially facilitate diuresis and decongestion. The SMAC-HF trial (short-term effects of hypertonic saline solution in acute HF and long-term effects of a moderate Na^+ restriction in patients with compensated HF with NYHA class III), involving NYHA class III HF patients, suggested that the infusion of hypertonic saline (150 ml of 1.4–4.6% NaCl) twice daily, alongside more liberal Na^+ intake, led to significant increases in urine output, weight loss and reduced hospitalization time but the impact on net negative Na^+ balance was not assessed.[87] Several other studies and/or meta-analyses with hypertonic saline have reported similar results.[88–92] Conversely, the OSPREY-AHF (Oral Sodium to Preserve Renal Efficiency in Acute Heart Failure) trial, conducted in acute congested HF cases requiring intravenous diuretics, reported that adding up to 6 g of oral NaCl per day on top of liberal Na^+ and fluid intake, compared to placebo, did not result in a significant difference in the combined endpoint of weight change and creatinine change at 96 h or discharge.[85] In conclusion, based upon the current studies, there is no convincing evidence for a clear benefit of the addition of hypertonic saline during the treatment of acute decompensated HF. However, there is a need for more rigorous research to find the mechanisms through which salt supplementation may confer benefits in a selected subset of patients with acute decompensated HF.

How to approach fluid and sodium intake

Fluid intake

The 2021 ESC HF guidelines recommend avoiding large volumes of fluid intake for all patients with HF.[2] In general, a normal fluid intake falls within the range of 1.5 to 2.5 L/day, corresponding to 15–30 mL/kg/day. A more liberal fluid policy is considered to involve an intake of more than 2.5–3.0 L/day, whereas a restrictive fluid policy typically entails an intake of less than 1–1.5 L/day (*Figure 4*).

For both chronic and acute HF, a normal fluid intake is suggested, primarily guided by the sense of thirst. This requirement may vary depending on environmental factors suggesting more liberal intake in hot and humid conditions and/or excessive (GI) losses. Patients with chronic HF do not seem to be adversely affected by a more liberal fluid intake policy. In patients with acute HF, a restrictive fluid intake policy, following shared decision-making with the patient to enhance adherence, may aid in managing Na^+ levels in instances of dilutional hyponatraemia. However, the primary objective in acute HF is generally to achieve an overall net negative fluid balance, primarily reliant on an adequate diuretic response. Uncertainty persists following a recent hospitalization, and if avoiding a liberal fluid intake can be justified in unstable patients with HF on high-dose diuretics.

Sodium intake

The ESC HF guidelines recommend limiting salt intake to <5 g/day.[2] A normal Na^+ intake falls within the range of 1.5–4 g/day (equivalent to 3.75–10 g of salt per day). A liberal approach involves intake exceeding 4 g/day, while a more restrictive approach limits intake to <1–1.5 g/day. Most salt intake originates from processed foods, and it is obligatory for every food product in Europe to list the content on the package, which should enable a personalized approach. As explained in the 2021 ESC guidelines on cardiovascular disease prevention in clinical practice, salt reduction can be achieved by dietary choices which contain fewer processed foods and the reformulation of foods by lowering their salt content.[93]

For patients with chronic HF, a normal Na^+ intake is suggested, with more liberal intake being permissible up to 5 g/day. Importantly, a diet with normal Na^+ intake, compared to a restrictive

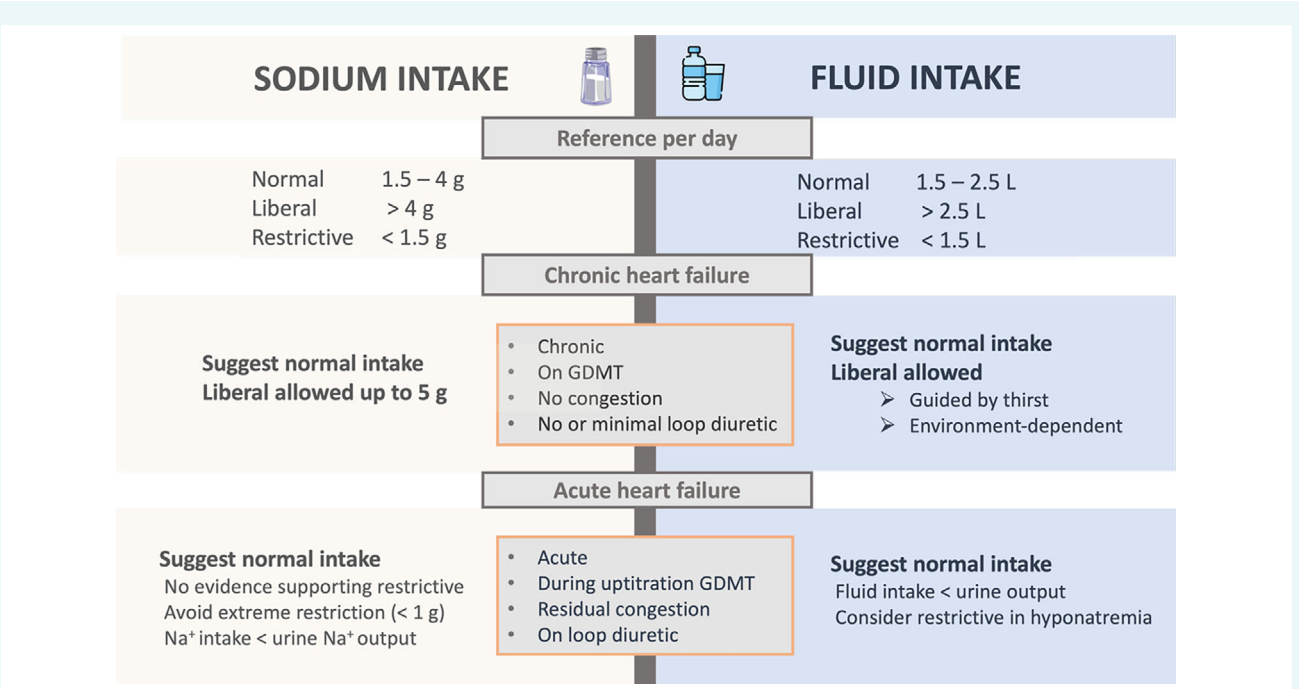

Figure 4 Advice on fluid and sodium intake in patients with acute and chronic heart failure, based on contemporary evidence and expert opinion. GDMT, guideline-directed medical therapy; Na^+, sodium.

approach, improves the quality of life, and ensures that patients are adhering to a healthy diet. The objective is to maintain a neutral Na^+ balance, and to prevent decompensation and volume overload. Recent evidence suggests a regained ability to enhance renal Na^+ excretion in well-treated patients with HF not needing maintenance diuretics. However, in patients with acute HF, a liberal intake may not be tolerated. During an episode of acute decompensated HF treated with intravenous diuretics, regardless of the ejection fraction, there are no data supporting the benefits of a restrictive Na^+ intake policy, and it may even be linked to harmful effects. A normal Na^+ intake is likely the best strategy, as long as the overall net Na^+ balance (intake vs. output) remains negative during the acute decongestion phase. Extreme salt restriction (<0.5–1 g/day) is potentially detrimental in most scenarios and should be avoided.

Sodium and fluid intake on the intensive care unit

Similar principles apply in patients with HF who are unable to eat and drink independently and receive salt and fluids through intravenous or gastric tube administration. In stable patients, the aim is to achieve a daily intake consistent with a normal Na^+ and fluid regimen. Ventilated patients with HF may require increased fluid intake during fever or acute illness. Moreover, it is essential to consider the fluids administered concurrently with medications and flushes (fluid creep) and the occurrence of extravascular volume collections. However, the balance may be more delicate, with insufficient intake potentially leading to significant haemodynamic consequences, and excessive intake primarily predisposing to respiratory issues. Monitoring of diuresis is possible, allowing for tracking the net effect over multiple days and making necessary adjustments when required.

Gaps in evidence

Clinical studies examining the impact of Na^+ intake on HF outcomes, particularly in perceived high-risk populations such as right-sided HF, HF with preserved ejection fraction (especially in the setting of arterial hypertension) and patients with high utilization of loop diuretics, remain limited and inconsistent. In SODIUM-HF, the population with ejection fraction >40% exhibited a lower risk of cumulative events (hazard ratio 0.82 vs. 1.05 for ejection fraction >40% vs. <40%) associated with Na^+ restriction diet.[67] However, this difference did not reach statistical significance and was based on relatively small subpopulations, rendering the trial underpowered for this analysis.

Additional data focusing on fluid intake in patients with HF are highly awaited. The variability in study protocols, fluid regimen and variations in clinical and therapeutic characteristics among studies complicates data comparison and the attainment of definitive conclusions. Encouragingly, new studies such as the FRESH-UP trial are underway, and hold promise for shedding further light on this topic.[76]

Patients with HF do not uniformly exhibit the same level of renal Na^+ avidity, and the precise influence of disease-modifying, guideline-recommended medical therapy remains unclear. Further complexity is added by the fact that sodium avidity in an individual patient likely fluctuates over time. Further research is required to

determine the optimal methods, for instance through urinary Na^+ sampling, for assessing and quantifying inherent renal Na^+ avidity, as well as to investigate potential distinctions between acute and chronic HF.

As most of the regulation of fluid and Na^+ balance is done by the kidneys, it is unclear if analysis of urine composition can aid in the selection of a patient cohort likely to benefit from dietary Na^+ and fluid interventions. Also, any potential effect of salt intake on diuretic response remains to be elucidated.

Conflict of interest: none declared.

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