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Review Article

Acute Decompensated Heart Failure: Current Role of Diuretics and Ultrafiltration

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ABSTRACT

Acute decompensated heart failure (ADHF) continues to be the leading cause of hospitalization and has a poor prognosis. Loop diuretic had been long used as cornerstone therapy for congestion and volume overload. However, several factors including diuretic resistance and declining renal function reduced the loop diuretic's effectiveness, necessitating a different treatment strategy. In ADHF, ultrafiltration (UF) could be a promising method to volume management. UF appears to be more effective at removing fluid than diuretics, according to several studies, with better quality of life and lower rehospitalization. This review highlights the current state of knowledge regarding the use of diuretics and UF in ADHF patients, as well as the challenges and questions raised associated with each approach.

1. Introduction

Acute Decompensated Heart Failure (ADHF) rather than de novo Acute Heart Failure accounts for the majority of hospitalizations in heart failure (HF).[1] An increasing number of hospital stays are being attributed to ADHF caused by volume overload. Medication non-adherence, poorly controlled risk factors, comorbidities, diet, disease progression, and/or treatment failure have all been linked to volume overload.[2] Despite the widespread use of diuretics, ADHF has a poor prognosis: 10% of patients die in the hospital, 15% within 3 months, and over half within 5 years after their first HF inpatient treatment. Re-hospitalization is also a common occurrence. The financial burden of having HF, which is mostly due to the cost of going to the hospital.[3-5]

In patients with ADHF, the standard treatment for volume overload is typically pharmacological, involving intravenous diuretics. Diuretics may cause some patients to have a reduced response. This problem has prompted the development of a number of alternative therapies, including ultrafiltration.[2]

2. Decongestive Approach for Acute Decompensated Heart Failure Therapy Goals

Congestion, defined as abnormally high cardiac filling pressures, is a significant cause of hospitalization in ADHF. Despite the wide range of phenotypes, congestion is the most common clinical sign, appearing in nearly 95% of all heart failure patients. Loop diuretics are still the treatment of choice. Volume reduction due to excessive fluid removal from the intravascular compartment combined with insufficient filling rates from the extravascular compartment is one of the disadvantages of loop diuretic therapy and may contribute to diuretic resistance.[6,7]

Because persistent congestion is a major cause of patient re-admission, pharmacological guided treatment should prioritize complete decongestion (Figure 1). Ultrafiltration should be considered if a diuretic strategy does not work.[6,7]

If the patient is discharged with persistent congestion and declining renal function, the clinical outcome is quite adverse. This could lead to an overuse of loop diuretics in patients with no residual congestion, increasing the risk of renal impairment, hypotension, and other complications. On the other hand, elevated biomarker levels may provide a false sense of security that a decongestive state has been achieved.[8]

The following are the treatment goals for patients with congestion and volume overload: 1) full decongestion without residual volume excess. However, determining the ideal time to discontinue decongestive treatment is frequently challenging. 2) Maintain an appropriate perfusion pressure in order to maintain organ perfusion. 3) Maintain medical therapy in accordance with established guidelines to improve diuretic responsiveness and long-term survival.[8]

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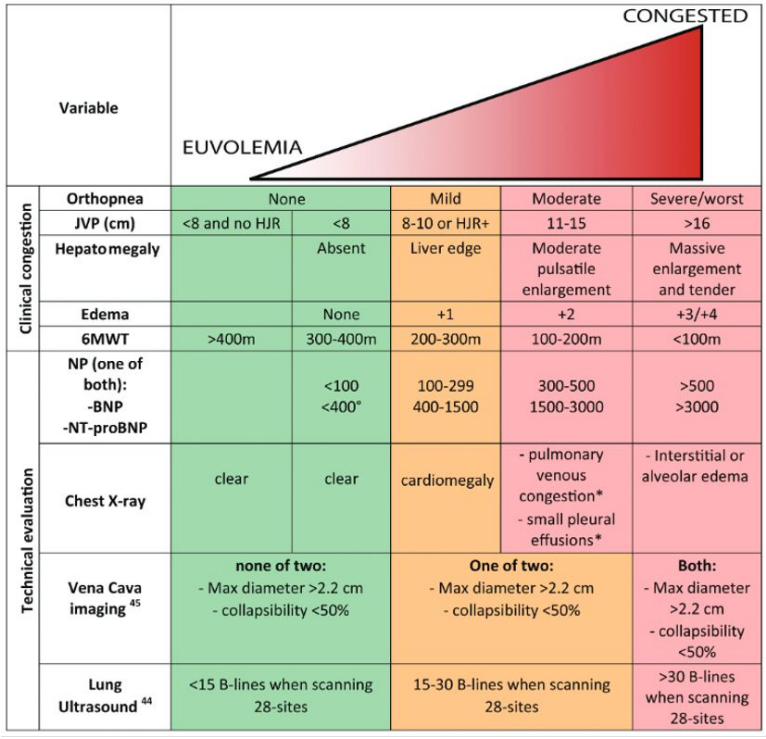

Figure 1. Integrative evaluation euvolaemia/congestion at discharge.
6MWT, 6-minute walk test; BNP, B-type natriuretic peptide; HJR, hepato-jugular reflux; HR, heart rate; JVP, jugular venous pulsation; NP, natriuretic peptide; NT-proBNP, N-terminal pro B-type natriuretic peptide; SBP, systolic blood pressure.[8]

Use of diuretics in ADHF

Chronic salt and water retention expands intravascular volume, leading to extravascular fluid accumulation. Diuretics increase the amount of sodium and water excreted by the kidneys. For diuretics to work well, it is critical to have a thorough understanding of their pharmacokinetics and pharmacodynamics. In Figure 2, the various diuretics' cellular modes of action are summarized.[8]

Figure 3 shows a practical approach to treating and evaluating diuretics in ADHF. Loop diuretic must be maintained at the lowest effective dose possible to maintain euvolemia.[6,9]

Table1.Precipitating factors cause ADHF.[6]

Trigger Factor
Non-adherence with medication regimen, sodium and/or fluid restriction
Acute myocardial ischemia
Uncorrected high blood pressure
Atrial fibrillation and other arrhythmias
Recent addition of negative inotropic drugs (eg verapamil, nifedipine, diltiazem, beta blockers)
Pulmonary embolism
Initiation of drugs that increase salt retention (eg steroids, thiazolidinediones, NSAIDs)
Excessive alcohol or drug use
Endocrine disorders (eg diabetes mellitus, hyperthyroidism, hypothyroidism)
Concurrent infection (eg pneumonia, viral illness)
Additional acute cardiovascular disorders (eg valvular disease endocarditis, myocarditis, aortic dissection)

Table 2. Loop diuretic characteristics.[6]

	Furosemide	Bumetanide	Torsemide
Equivalent dose	40 mg PO	1 mg PO	20 mg PO
Bio-availability	40–70 %	80–95%	80–90 %
Influenced by food	Yes	Yes	Yes
Metabolism	Renal	hepatic	hepatic
Action duration	4–6 hours	6–8 hours	12–16 hours
Action onset	PO: 30–60 minutes IV: 5 minutes	PO: 30–60 minutes IV: 2-3 minutes	PO: 30–60 minutes
Common oral dosage	40–80 mg, 1 or 2 times daily	1-2 mg, 1 or 2 times daily	20–40 mg, 1 or 2 times daily
	Maximum dose 600 mg/day	Maximum dose 10 mg/day	Maximum dose 200 mg/day

Loop Diuretics

According to registry data, loop diuretics are given to 90 percent of ADHF patients for a median of three days. Loop diuretics work by preventing the exchange of sodium, potassium, and chloride within the loop of Henle's thick ascending branch. Table 2 summarizes the pharmacological characteristics of commonly used loop diuretics.[7,9]

Oral furosemide has a bioavailability (10-90%) determined by gastrointestinal absorption. While, oral bioavailability of bumetanide and torsemide is consistently 80-90 percent. Torsemide also has a longer half-life than furosemide or bumetanide in HF patients. The wide range of oral furosemide bioavailability makes conversion calculations difficult. Oral 40 mg furosemide is equivalent to 10-20 mg

torsemide and 0.5-1 mg bumetanide respectively. Torsemide's prolonged half-life may be beneficial in patients with renal, hepatic, and/or cardiac dysfunction.[10]

By inhibiting chloride uptake in the macula densa, loop diuretics stimulate the Renin Angiotensin Aldosterone system (RAAS). Additionally, prolonged use of loop diuretic results in compensatory distal tubular sodium reabsorption via tubular cell hypertrophy, resulting in decreased natriuresis. Loop diuretics require a low drug dose to cause sodium excretion to exceed the baseline level. Following that, a log-linear dose increase is required to reach the natriuretic response's maximum limit. Increases in loop diuretic dose above this point do not result in an increase in peak natriuresis, but do result in a prolongation of the loop diuretic period above the threshold level, resulting in an increase in total natriuresis. Multiple administrations may also increase natriuresis by lengthening the time spent above the natriuretic threshold. In the treatment of ADHF, the following recommendations are made based on these pharmacological characteristics: (i) Patients who have not previously received diuretic therapy should receive intravenous furosemide or other drugs equivalent to 20-40 mg of furosemide. Patients with pre-existing renal dysfunction should be given higher doses.

(ii) Outpatient diuretic regimens should include at least one oral diuretic. High-dose loop diuretics (2.5 times routine dose furosemide, for at least 80 mg/day) surpassed low-dose loop diuretics in the DOSE-AHF trial on secondary endpoints such as dyspnea relief, weight loss, and net fluid loss. DOSE-AHF trial found that renal dysfunction was more common in patient receiving high dose (creatinine increase >0.3 mg/dL), although higher creatinine levels were not linked to a worse outcome. When total loop diuretic dose was taken into account, the high-dose group had better results, implying that loop diuretic doses must be adequate to reach the upper threshold. Calculating an individual's top dose is difficult because it depends on previous loop diuretic treatment, body composition, volume overload, and renal function. Most experts agree that 400-600 mg intravenous furosemide is the maximum daily dose that will produce minimal additional natriuresis while increasing side effects. In order to reduce in-hospital mortality, intravenous loop diuretics must be started as soon as possible. There was no difference in term of effecitivity between continuous and bolus infusions. Due to the lack of a loading bolus dose for continuous infusion, the continuous infusion group may have failed to reach the threshold dose. A bolus infusion should be divided doses to maximize natriuretic threshold while avoiding rebound retention.[8,9]

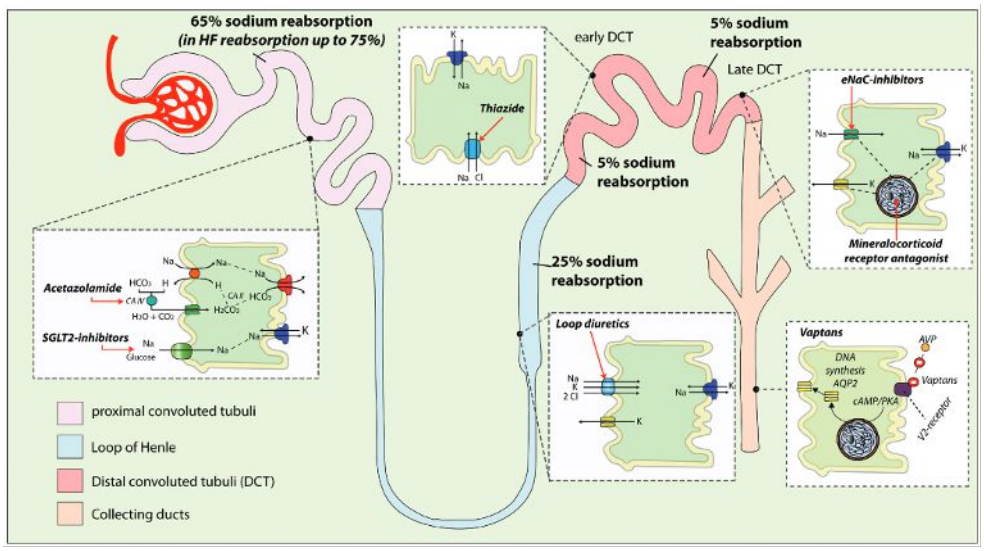

Figure 2. Site and mode of action of diuretics and effect on sodium reabsorption in the nephrons. AQP2: aquaporin-2; AVP: arginine vasopressin; cAMP: cyclic adenosine monophosphate; eNaC: epithelial sodium channel; HF: heart failure; PKA: protein kinase A; SGLT2: sodium–glucose linked transporter-2.[8]

Use of Combination Diuretics

Combining different pharmacologic classes of diuretics is one way to overcome the loop diuretics' poor diuretic response (Figure 3).

1. Thiazide

Thiazides diuretic blocked NaCl cotransporter (NCC) in the distal convoluted tubule. These diuretics can partially compensate for the increased distal sodium avidity caused by chronic loop diuretic use. Metolazone and chlorthalidone, in comparison to loop diuretics, absorbed slowly (peak time up to 8 hours). Because of its short half-life, it should be used in conjunction with a loop diuretic. Thiazides have a limited diuretic effect when used alone, producing a maximum diuretic response of 30-40% of loop diuretics. Furthermore, thiazides are bound to proteins that must be secreted into the tubules with adequate renal blood flow. Also, thiazides cause kaliuresis by excreting 2-3 potassium ions for every sodium ion lost. This effect of potassium loss is particularly pronounced in conditions characterized by elevated aldosterone levels, such as heart failure. Contrary to popular belief, thiazides work well in patients with impaired GFR.[8]

2. Mineralocorticoid receptor antagonist (MRA)

MRA natriuretic dose may be advantageous in patients suspected of having diuretic resistance. For stable heart failure, current guidelines recommend low-dose MRA. However, the beneficial effects are attributed to cardioprotective properties rather than natriuretic properties.[6] MRA has a pleiotropic effect, but its renal effect is due to its modulation

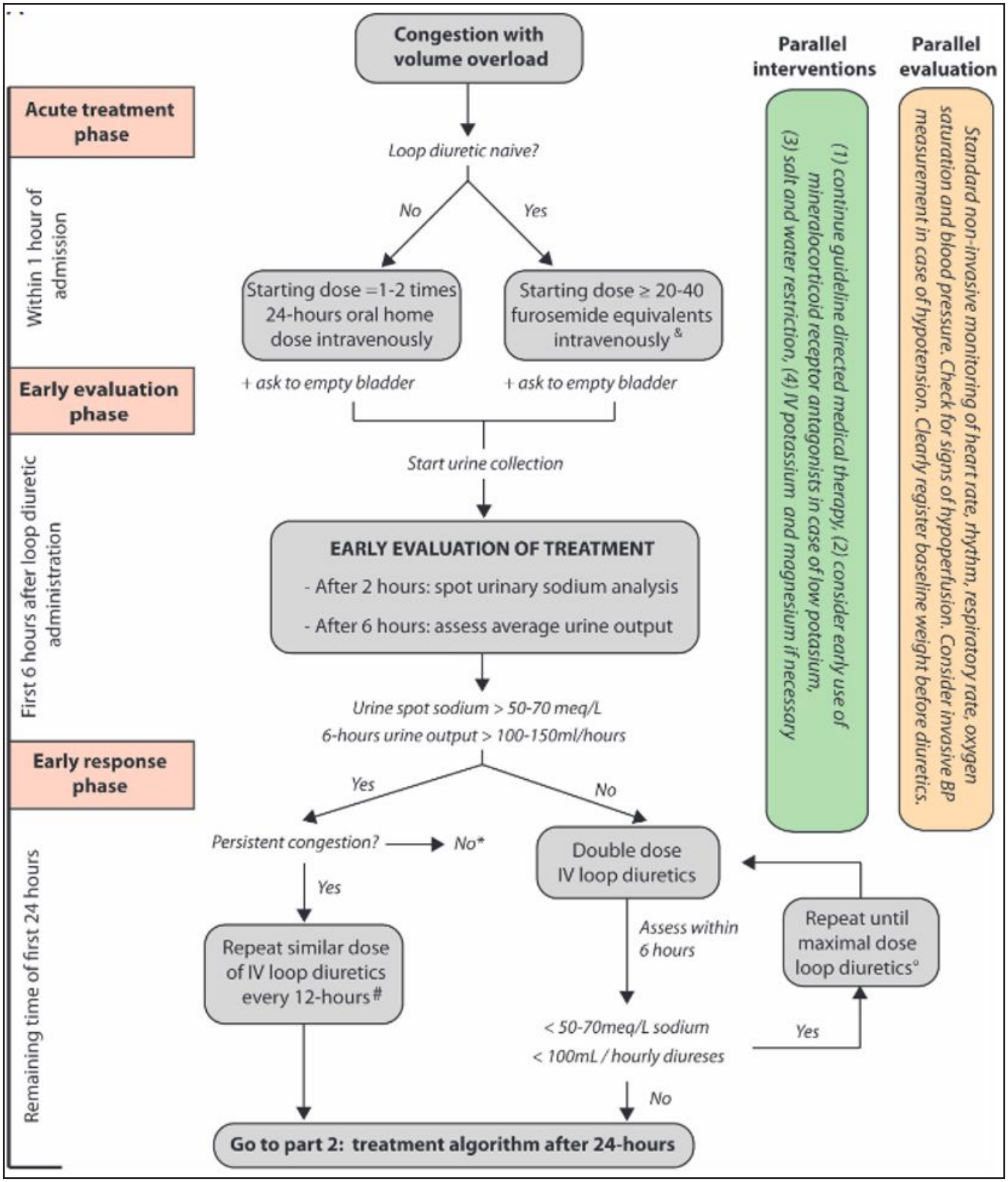

Figure 3. (A) Congestion with volume overload

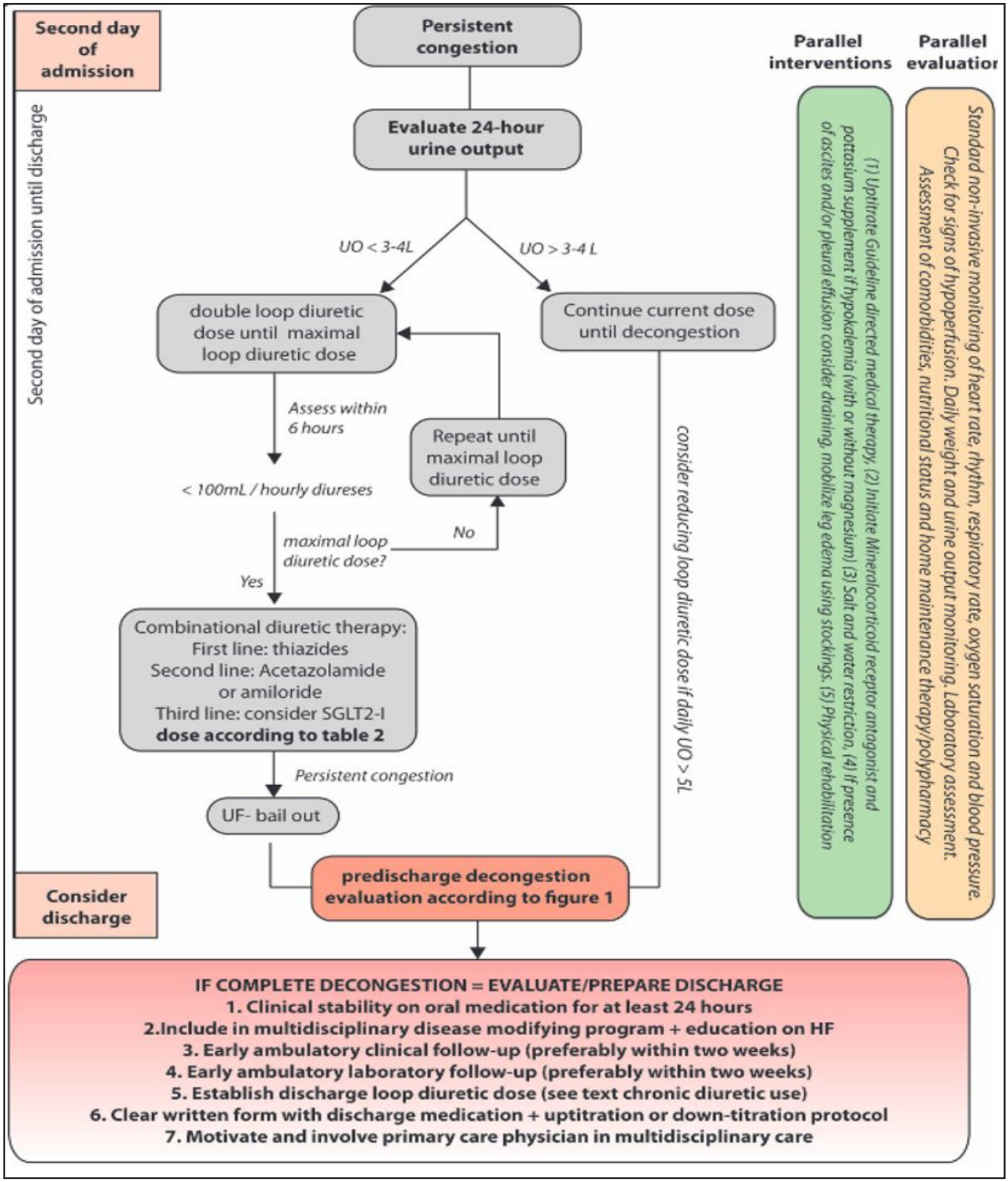

Figure 3. Flow chart to diuretic use in acute heart failure.
(A) Congestion with volume overload. (B) Treatment algorithm after 24 h. Total loop diuretic dose can be administered either as continuous infusion or bolus infusion. BP, blood pressure; HF, heart failure; IV, intravenous; SGLT2-I, sodium–glucose linked transporter 2 inhibitor; UF, ultrafiltration; UO, urine output.[8]

Table 3. Diuretics Limitations Ultrafiltration Loops and Advantages.[32]

Limitations of Loop Diuretics	Ultrafiltration Advantage
Hypotonic urine elimination	Isotonic plasma water output
Diuretic resistance: lack of dosing guidelines	Precise control of the rate and amount of liquid discharge
Electrolyte abnormalities	No effect on plasma electrolyte concentration
Decreased glomerular filtration rate	Improved glomerular filtration rate
Direct neurohormonal activation	No direct neurohormonal activation
Neither safety nor efficacy was demonstrated in an RCT	RCTs demonstrate safety, efficacy, and improvement in outcomes
Photosensitivity	
skin rash	
Deaf	
Bone loss	

of Na+ and K+ channel activity in the distal tubule. MRA is recommended as a class I disease-modifying therapy for HFrEF for it mechanism that inhibits the release of aldosterone caused by neurohormonal overactivity. ATHENA-HF trial recently evaluated additional diuretic effect of high-dose MRA therapy in conjunction with standard therapy.[11] After 96 hours, 100 mg of spironolactone was not proven to be beneficial to 25 mg. Spironolactone is a prodrug with a half-life of 48-72 hours following oral administration, which may account for the observed lack of effect. MRA at high doses, on the other hand, is considered safe because it does not cause hyperkalemia or deteriorate renal phisyiology. MRA therapy may also help to compensate for the hypokalemic effects of other class diuretics.[11-13]

3. Acetazolamide

Physiologically, increased proximal sodium reabsorption predicts sodium retention, justifying targeting the proximal nephron in heart failure patients. Acetazolamide inhibits the carbonic anhydrase associated with the brush border, resulting in decreased intracellular hydrogen that worked in Na-H exchanger. This Na-H exchanger contributes significantly to proximal sodium reabsorption. Interestingly, it becomes more involved during arterial hypoperfusion due to its response to the neurohormone angiotensin II. Increased natriuresis is associated with elevated luminal bicarbonate concentrations.[6]

There is a significant increase in proximal nephron sodium avidity as a result of the hemodynamic changes in HF, which include decreased renal blood flow and an increased filtration fraction. From a pathophysiological standpoint, there are several benefits in heart failure. First, most of sodium is reabsorbed in the proximal renal tubule, which is especially important in patients with ADHF. Second, a higher chloride delivery to macula densa cells reduces renin level and thus neurohumoral modulation. Finally, endogenous natriuretic peptides (which act in the distal nephron) may resume their original function. In the proximal tubule, acetazolamide inhibits sodium reabsorption.14 it also enhances the diuretic effect when used with loop diuretics.[8]

4. Other Potential Agents

A novel class of diabetes medications known as sodium-glucose linked transporter-2 (SGLT2 inhibitors) inhibits proximal sodium absorption.[15-17] In two trials of diabetic patients with a high prevalence of cardiovascular disease, SGLT2 inhibitors reduced HF hospitalization and reduced GFR decline.[23,24]

Amiloride inhibits the distal epithelial sodium channel (ENaC), result in channel decongestion and decreased filling pressure. Chronic ENaC overexpression has also been linked to thiazolidinedione-mediated volume retention in diabetics.[15]

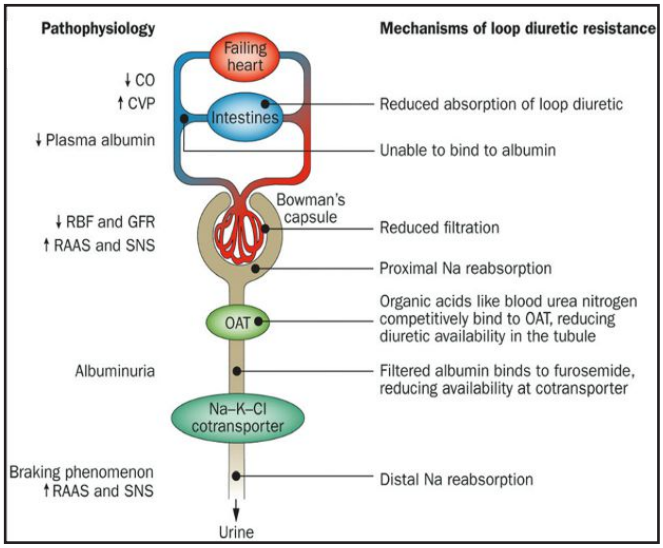

Figure 4. Overview of diuretic resistance in ADHF.[21]

Vasopressin antagonists inhibit arginine vasopressin, thereby decreasing the supply of luminal aquaporin aqueducts in collecting tubule. This causes an increase in aquaresis without significantly impairing natriuresis response. EVEREST trial report that tolvaptan did not decrease morbidity or mortality in HF patients when used in combination with standard therapy. Extracellular volume change is primarily a result of sodium retention, which precludes its use in congestive heart failure. In advanced heart failure, however, high levels of arginine vasopressin causing plasma expansion and dilutional hyponatremia.[8] According to recent research, tolvaptan causes decreased body weight without significant clinical improvement in dyspnea in patients with renal impairement, diuretic resistance, or hyponatremia.[18,19] Tolvaptan is an option in Europe for patients who have persistent hyponatraemia and congestion.[20]

Diuretic resistance in ADHF

The response to diuretics, which is defined as the ability to achieve natriuresis, diuresis, and ultimately clinical decongestion following appropriate diuretic doses, is determined by a number of factors. Loop diuretics requires active sodium secretion from the proximal sodium pool via protein transporters that are dependent on renal blood flow. While the thick ascending branch reabsorbs 25% of filtered sodium, residual sodium reabsorption occurs in the proximal and distal convoluted tubules, limiting the amount of sodium excreted via loop diuretics and eventually leading to hypotonic urine.[15,21]

Table 4. Diuretic comparison characteristics single loop and ultrafiltration.[33]

Loop Diuretics	Ultrafiltration only
Direct neurohormonal activation	No direct neurohormonal activation
Hypotonic urine elimination	Isotonic plasma water output
Unpredictable sodium and water elimination	Precise control of the rate and amount of liquid discharge
Development of diuretic resistance with prolonged administration	Restoration of diuretic response
Risk of hypokalemia and hypomagnesemia	No effect on plasma concentrations of potassium and magnesium
Peripheral venous access	Peripheral or central venous catheter
No need for anticoagulants	Anticoagulant requirement
No extracorporeal circuit	The need for extracorporeal circuits

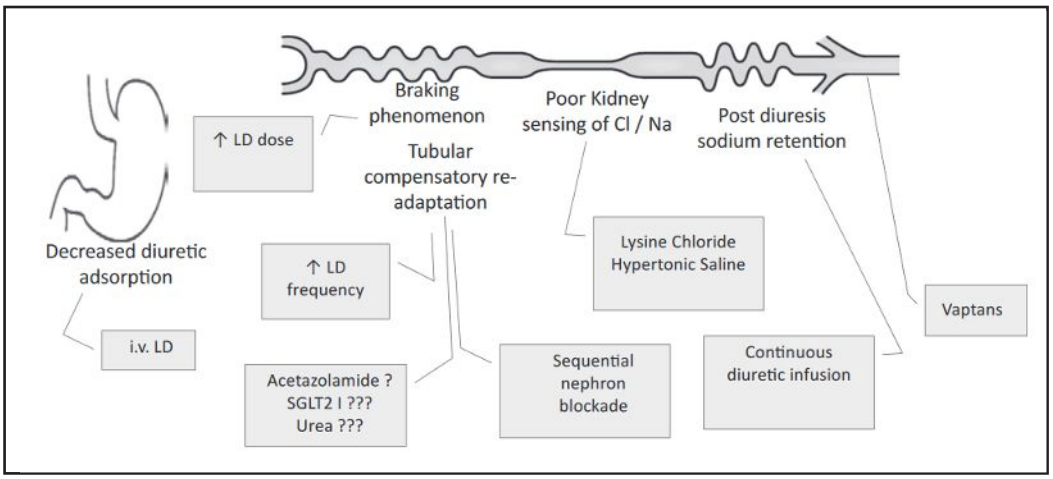

Figure 5.Pathways involved in diuretic resistance and therapeutic options (grey box) aimed at addressing these mechanisms.LD: loop diuretic.[24]

Diuretic resistance is defined as a failure to increase fluid and sodium (Na+) output sufficiently to relieve congestion despite escalating doses of diuretic to a ceiling level.[22] Diuretic resistance is characterized by reduced in natriuresis and diuresis, which limits the ability to attain euvolemia. Always consider the dose and type of diuretic agent used, as well as the degree of volume overload, body composition, and renal function when interpreting the diuretic response. The terms net fluid output and weight change are commonly used at the moment. While weight assessment appears to be a simple procedure, it is technically demanding, and weight fluctuations may not be indicative of volume redistribution changes. Additionally, there is a biased causality between weight loss and urine output.[8]

Numerous studies have established a link between inadequate diuretic response and an increased risk of hospitalization and death. Diuretic resistance can be driven by a range of mechanisms (Figure 4), including impaired intestinal absorption, transport defect due to hypoalbuminemia, decreased renal filtration (caused by decreased renal blood flow and/or increased CVP), proximal sodium reabsorption, competitive binding by organic acids, distal sodium reabsorption due to braking phenomena, and activation of the RAAS. The glomerular filtration rate decreases as intravascular volume expands and venous pressure rises, exacerbating renal dysfunction, diuretic resistance, and volume accumulation.[21]

Strategies in Dealing with Diuretic Resistance

In general, the first step toward overcoming diuretic resistance is to ensure that patients adhere to recommended sodium restriction. This is primarily based on the theoretical premise that dietary salt restriction aids in the management of fluid overload.[22] However, extremely low sodium diets are associated with adverse outcomes and can result in hyponatremia and hypochloremia, both of which may contribute to diuretic resistance.[23]

Additionally, chronically low sodium diets can result in sodium deficiency in the extracellular matrix and bone, which can lead to osteoporosis. As a result, dose adjustment of the loop diuretic should be patient-specific. Additionally, to maintain a stable plasma concentration of diuretics, the drug-free interval must be reduced by increasing the daily dose frequency.[23]

When excessive fluid retention persists despite diet and medication adjustments, clinicians have several options: (a) switching to combination oral diuretic therapy or intravenous drug administration; (b) initiating high saline infusion in combination with loop diuretics in cases of hyponatremia; (c) initiating vaptans in cases of hyponatremia; and finally (d) initiating ultrafiltration when medical therapy fails to improve clinical outcomes (Figures 5 and 6).[24]

Role of Ultrafiltration in HF management

Long-term diuretic therapy has been linked to RAAS activation, electrolyte abnormalities, renal insufficiency, and ADHF progression. Furthermore, over 20% of patients had diuretic resistance, and over 30% do not improve after diuretic therapy.[8]

This management challenge has resulted in the development of alternative strategies, including ultrafiltration. A meta-analysis of nine RCTs found that, when compared to the diuretic group, ultrafiltration group had a 90-day readmission rate for heart failure and a tendency to decrease readmissions. There is concern that ultrafiltration may affected renal function and increase the risk of serious adverse events such as renal failure, bleeding, and procedural complications. CARRESS-HF25 reported that patients with HF who also had impaired renal function had a decreased tolerance for ultrafiltration. As a result, the use of early ultrafiltration appears to be more effective.

Other studies, such as RAPID-CHF26 and UNLOAD Trial27 have reported that early ultrafiltration (within 24 hours of admission) is superior to diuretics in terms of weight loss and fluid removal. Additionally, numerous clinical trials conducted reported that early ultrafiltration can improve diuretic sensitivity in patients with heart failure. At 90 days, the UNLOAD trial discovered that patients treated with UF experienced a 52 percent reduction in unscheduled visits, a 44 percent reduction in HF readmissions, and a 63 percent reduction in readmission days when compared to standard care. Early ultrafiltration also can improve diuretic sensitivity.[27]

CUORE study discovered that despite similar weight loss at discharge, 27 patients treated with UF had fewer heart failure-related readmissions over a one-year period than 29 patients treated with standard care. Diuretics are chose to continue during UF because it is presumed that boosting urinary sodium excretion increases diuretic sensitivity.[28]

AVOID-HF study tested the hypothesis that patients hospitalized for heart failure who received UF had a longer time to develop first heart failure within 90 days than those who received IV diuretics. Patients in the UF group developed first heart failure more slowly than those in the diuretic-adjusted group (62 versus 34 days; p=0.106), although this difference was not statistically significant. However, there is insufficient evidence to suggest that patients in the UF group experienced fewer heart failure and cardiovascular events within 30 days of discharge than patients in the diuretic-adjusted group.[29]

According to the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, Ultrafiltration may be considered in patients with volume overload refractory to diuretic therapy (Class IIb, Level of Evidence: C).20 Likewise with the European guidelines, ACC/AHA 2013 recommends ultrafiltration for patients with marked volume overload to relieve congestive symptoms and weight gain (Class IIb, Level of Evidence: B).30 Through the update of guidelines for the management of heart failure in 2022, the ACC/AHA opens the discourse on the use of early ultrafiltration with the aim of increasing decongestion and decreasing rehospitalization, although it does pay attention to many aspects such as patient selection, fluid expenditure speed, venous access, prevention of complications related to therapy, and costs. which still requires further study.[31]

Comparison of Ultrafiltration and pharmacological therapy in HF

Loop diuretics have a number of drawbacks, as detailed in Table 3. Resistance to diuretics is common, contributing to the large intra- and intraindividual dose response. Loop diuretics have an effect on hemodynamics and stimulate the sympathetic nervous system and RAAS. By lowering the glomerular filtration rate, these hemodynamic and neurohormonal changes reduce the effectiveness of subsequent loop diuretic doses.[32]

In contrast to loop diuretics, UF activates neurohormones only when fluid loss exceeds plasma filling rate, resulting in intravascular volume depletion (Table 4). Plasma water movement from the interstitial space to the vasculature varies according to serum albumin concentration, i.e., serum oncotic pressure and capillary permeability. Although a UF rate of 250 mL/hour is less likely to exceed the plasma refill rate, the rate of fluid loss should be adjusted to maintain blood volume and hemodynamic stability based on the patient's vital signs, serum creatinine, and urine output (Figure 2).[33]

UF therapy effectively removes greater volumes of fluid while maintaining stable serum creatinine levels.[34] UF has the same effect as diuretics in terms of improving quality of life. Bart et al. discovered that UF therapy improved dyspnea scores and congestive heart failure symptoms.[26] Kabach et al. found that UF was associated with a decreased risk of clinical deterioration and an increased likelihood of clinical decongestion; however, UF had no effect on readmission or mortality rates.[35] Wobbe et al. established a sustained advantage for UF treatment over standard care in terms of HF-related readmissions between 30 days and 12 months after therapy. Agostoni et al. also described the long-term benefits of UF therapy in patients with congestive heart failure, reporting improvements in exercise performance lasting three months, as well as improvements in lung function and decreased resting norepinephrine levels lasting up to six months following UF therapy. Between 30 days and 12 months after therapy, UF treatment demonstrated a sustained advantage over standard care in terms of the number of HF-related readmissions.[28]

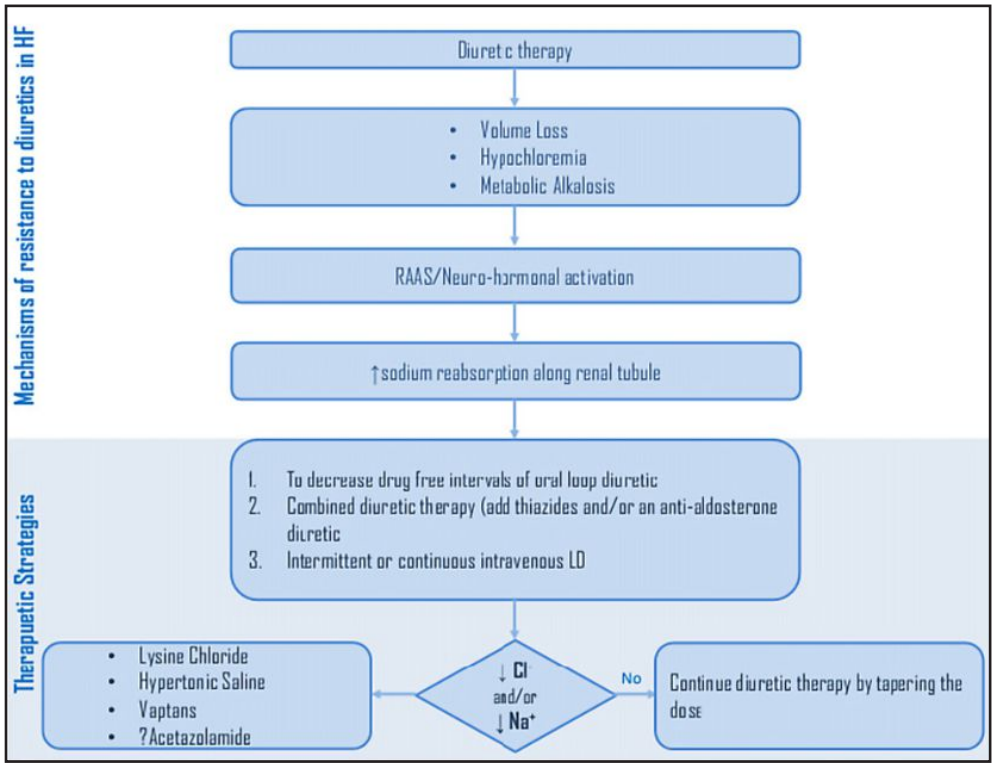

Figure 6.Therapeutic algorithm for the treatment of diuretic resistance.[24]

While chronic diuretic therapy appears to have a detrimental effect on neurohormonal activation, UF may reduce rehospitalization rates by inhibiting neurohormonal activation, although available data are inconsistent. Agostoni et al. found that UF therapy significantly decreased plasma renin activity, as well as serum norepinephrine and aldosterone levels. Giglioli et al. discovered similar aldosterone levels, but Seker et al. discovered no between-group differences in renin or aldosterone levels.[31] Additionally, an analysis of the CARRESS-HF trial discovered that patients treated with UF had significantly higher plasma renin activity than those treated with diuretics.[36] UF may allow for a reduction in the dose of diuretics required to maintain euvolemia in the patient. Costanzo et al. explained that the dose required in the UF group was significantly less than the dose required in the diuretic alone group 10 days after discharge.[29] Marenzi et al. similarly reported that the UF group required significantly lower diuretic doses at the 12-month follow-up.[28,37]

Hu et al. demonstrated that after three days of ultrafiltration therapy alone, the congestive state improved significantly more than with diuretic infusion alone. On day 8, urine production increased and weight loss was significantly greater in patients receiving early filtration and sequential torsemide or tolvaptan than in those receiving torsemide and tolvaptan. Additionally, patients who received early ultrafiltration and sequential therapy had a higher urine output than patients who received only ultrafiltration therapy. These results suggest that ultrafiltration enhances the patient's sensitivity to diuretics.[38]

The disadvantages of UF include higher costs when compared to intravenous diuretics. On the other hand, the decrease in heart failure hospitalizations resulted in a decrease in overall costs. The most expensive component of UF is the single-use disposable filters required for the UF system and the length of hospital stay.[38] Clotting of the UF filter, temporary discomfort at the venous access site, central venous catheter infection, catheter malfunction, hypotension, bleeding events, and kidney injury are all possible side effects of UF. Volume overload refractory to UF occurs in a very small percentage of patients. Siddiqui et al. concluded in a recent systematic review and meta-analysis that UF was safe and effective in ADHF and had no significant side effects when compared to IV diuretics. UF is associated with fewer bleeding events than standard therapy. The study found no clinically significant increase in the incidence of hypotension in UF. Additionally, the incidence of acute kidney injury is comparable between UF and diuretic therapy. The CARRESS-HF study25 compared the effect of UF on renal function versus diuretic therapy in patients with chronic volume overload and decreased renal function. Although UF was associated with higher serum creatinine levels initially, serum creatinine levels were found to be lower in the long term when compared to patients receiving standard diuretic therapy. Reduced renal function during decongestion in heart failure was found to be a stronger predictor of mortality than baseline creatinine values and was associated with subsequent use of high-dose diuretics. This study compared the effect of UF versus diuretic therapy on renal function in heart failure patients with persistent volume overload and decreased renal function.[25]

When these two treatment strategies were compared, there was no difference in all-cause mortality. According to a meta-analysis, UF and diuretics both have a similar effect on kidney function (creatinine elevation), which may result in similar mortality. While there was a trend toward improvement in rehospitalization and emergency department visits, there was no statistically significant difference between the two therapies. As with death, this could be the result of a complex interaction between impaired renal function, decongestion, and outcome in patients with ADHF. Long-term studies and larger clinical trials are needed to shed additional light on these findings. However, the lack of improvement in re-hospitalization, a significant economic burden, may call this strategy into question.[30]

Conclusion

Congestion is the primary cause of ADHF. The ultimate goal of therapy in the setting of ADHF hospitalization is complete decongestion. Although many questions about the optimal approach to using diuretics remain unanswered, their demonstrated efficacy in reducing congestion and extensive clinical experience suggest that diuretics will continue to play a significant role in the management of ADHF.

Resistance to diuretics is common and contributes to the high dose response individual level. By lowering the glomerular filtration rate, hemodynamic and neurohormonal changes limit the effectiveness of subsequent loop diuretic doses. As a result, alternative methods are critical.

Ultrafiltration enables more efficient sodium and fluid removal without the electrolyte imbalances or neurohormonal activation associated with diuretics, resulting in improved quality of life and decreased readmission rates. The optimal methods for successfully decongesting while minimizing changes in renal function and neurohormonal activation continue to be a focus of intense research, which will provide additional insight into best practices for ADHF management.

4. Declarations

4.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involvement in the study.

4.2. Consent for publication
Not applicable.

4.3. Availability of data and materials
Data used in our study were presented in the main text.

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