Summary of Best Evidence for the Management of Diuretic Resistance in Patients with Heart Failure (Postprint)

Authors: Zhao Yiru, Xinyu Hao, Zhao Lei, Zhang Caihui, Chaoxia Wang, Zhang Yueying, Zhang Yueying

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Abstract

Background: In the treatment of heart failure, diuretics are the cornerstone medications for alleviating fluid retention and improving symptoms such as dyspnea. However, diuretic resistance can weaken therapeutic effects, leading to recurrent illness or even clinical deterioration. Therefore, the scientific management of diuretic resistance is key to optimizing heart failure treatment. Currently, however, the evidence is widely scattered and controversial, and clinical practice lacks scientific and standardized guidance protocols. Objective: To analyze and summarize the relevant evidence for the management of diuretic resistance in patients with heart failure, providing a reference for clinical practice. Methods: Following the "6S" model of evidence-based practice, a search was conducted for evidence related to the management of diuretic resistance in heart failure patients across databases including UpToDate, BMJ Best Practice, Guidelines International Network (GIN), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), Joanna Briggs Institute (JBI) Evidence-Based Practice Database, American Heart Association (AHA), Medlive, MedSci, CNKI, Wanfang Data, VIP, CBM, Web of Science, PubMed, Embase, CINAHL, and Cochrane Library. The search period spanned from 2015-01-01 to 2025-03-20. Two researchers independently performed literature screening, quality assessment, extraction, and synthesis. Results: A total of 31 documents were included, comprising 6 guidelines, 5 clinical decisions, 5 expert consensuses, 13 systematic reviews, and 2 randomized controlled trials. Among them, one guideline was rated as Grade A, five guidelines were rated as Grade B, and the remaining 25 documents demonstrated rigorous research design and high overall quality. Fifty-six pieces of evidence were synthesized across eight themes: assessment of diuretic response, optimization of loop diuretic regimens, combination with other types of diuretics, improvement of hemodynamics, integrated traditional Chinese and Western medicine treatment, non-pharmacological treatment, management of patients with refractory end-stage heart failure, and treatment contraindications and monitoring points. These included 14 Level 1, 6 Level 2, 6 Level 3, and 30 Level 5 pieces of evidence. Conclusion: This study summarizes evidence regarding initial screening, optimization of medication regimens, and comprehensive non-pharmacological interventions across eight themes: assessment of diuretic response, optimization of loop diuretic regimens, combination with other types of diuretics, improvement of hemodynamics, integrated traditional Chinese and Western medicine treatment, non-pharmacological treatment, management of patients with refractory end-stage heart failure, and treatment contraindications and monitoring points. This provides a reference for healthcare professionals to efficiently manage patients with heart failure and diuretic resistance.

Full Text

Preamble

Chinese General Practice ·Best Evidence ·Summary of Best Evidence for the Management of Diuretic Resistance in Patients with Heart Failure

Abstract

Objective: To summarize the best evidence for the management of diuretic resistance in patients with heart failure, providing a clinical reference for healthcare professionals to improve patient outcomes.

Methods: We systematically searched databases including BMJ Best Practice, UpToDate, Joanna Briggs Institute (JBI) Evidence-Based Health Care Center, Cochrane Library, PubMed, Embase, CINAHL, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Data, and the China Biology Medicine (CBM) database. We also searched websites of relevant professional organizations such as the Heart Failure Association of the European Society of Cardiology (HFA-ESC), the American College of Cardiology (ACC), the American Heart Association (AHA), and the Heart Failure Society of America (HFSA). The search period ranged from the inception of each database to May 2023. The literature types included guidelines, expert consensuses, evidence summaries, and systematic reviews. Two researchers independently evaluated the quality of the included literature and extracted and summarized the evidence.

Results: A total of 15 articles were included, comprising 5 guidelines, 7 expert consensuses, 2 systematic reviews, and 1 evidence summary. Twenty-five pieces of evidence were summarized across six categories: assessment and identification, sodium and water restriction, optimization of loop diuretic use, combination medication strategies, non-pharmacological treatments, and monitoring.

Conclusion: This study provides a comprehensive summary of the best evi-

dence for managing diuretic resistance in heart failure patients. Clinical practitioners should develop individualized management plans based on the specific clinical context, patient preferences, and the feasibility of interventions to improve the efficacy of diuretic therapy.

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1. Introduction

Heart failure (HF) is the terminal stage of various cardiovascular diseases, characterized by high morbidity and mortality rates. Congestion is a primary driver of symptoms and hospitalization in HF patients. Diuretics, particularly loop diuretics, are the cornerstone of decongestive therapy. However, approximately 20% to 30% of heart failure patients experience "diuretic resistance"(DR), where the diuretic effect is diminished or lost before the relief of edema is achieved. DR is associated with prolonged hospitalization, increased readmission rates, and higher mortality. Therefore, identifying and managing DR effectively is critical in clinical practice. This study aims to synthesize the current best evidence to guide clinical practice.

1.030001 Taiyuan, Shanxi Province, School of Nursing, Shanxi Medical University

Department of Radiology, Second Hospital of Shanxi Medical University, Taiyuan, Shanxi Province; Department of Emergency Medicine, Second Hospital of Shanxi Medical University, Taiyuan, Shanxi Province.

Background

In the treatment of heart failure, diuretics serve as the cornerstone therapy for alleviating fluid retention and improving symptoms such as dyspnea. However, the development of diuretic resistance can significantly diminish therapeutic efficacy, leading to disease recurrence or even clinical deterioration. Consequently, the scientific management of diuretic resistance is critical for optimizing heart failure treatment. Despite its importance, current evidence remains fragmented and controversial, and clinical practice lacks scientifically rigorous, standardized guidance.

The objective of this study is to analyze and summarize the relevant evidence regarding the management of diuretic resistance in patients with heart failure, thereby providing a reference for clinical practice.

Methods

Following the "6S" evidence-based practice hierarchy model, a comprehensive search was conducted to identify evidence regarding the management of diuretic resistance in patients with heart failure. The search encompassed several key databases and resources, including UpToDate, BMJ Best Practice, the Guidelines International Network (GIN), the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), the Joanna Briggs Institute (JBI) Evidence-Based Practice Database, the American Heart Association (AHA), Medlive, MedSci, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, Chinese Biomedical Literature Database (CBM), Web of Science, PubMed, Embase, CINAHL, and the Cochrane Library.

The search period spanned from January 1, 2015, to March 20, 2025. Two researchers independently performed the literature screening, quality assessment, data extraction, and evidence synthesis for the included studies.

Results

A total of 31 documents were included in this study, comprising 6 guidelines, 5 clinical decision-making reports, 5 expert consensuses, 13 systematic reviews, and 2 randomized controlled trials. Among the guidelines, one was rated as Grade A and five were rated as Grade B. The remaining 25 documents demonstrated rigorous research designs and high overall quality.

From these sources, 56 pieces of evidence were synthesized across eight primary themes: assessment of diuretic response, optimization of loop diuretic regimens, combination therapy with other diuretic classes, hemodynamic improvement, integrated traditional Chinese and Western medicine treatments, non-pharmacological interventions, management of refractory end-stage heart failure, and treatment contraindications and monitoring essentials. Regarding the strength of evidence, 14 items were classified as Level 1, 6 as Level 2, 6 as Level 3, and 30 as Level 5.

Conclusion

Summary of the Best Evidence for the Management of Diuretic Resistance in Patients with Heart Failure

Abstract: This study focuses on eight key themes regarding patients with heart failure complicated by diuretic resistance: assessment of diuretic response, optimization of loop diuretic regimens, combination therapy with other classes of diuretics, hemodynamic improvement, integrated traditional Chinese and Western medicine treatments, non-pharmacological interventions, management of refractory end-stage heart failure, and contraindications and monitoring essentials. By synthesizing evidence from initial screening, optimization of medication regimens, and comprehensive non-pharmacological interventions, this study provides a reference for healthcare professionals to manage these patients efficiently.

Keywords: Heart failure; Diuretic resistance; Management; Evidence-based medicine; Evidence summary

Introduction

Heart failure (HF) is a complex clinical syndrome characterized by systemic or pulmonary congestion. Diuretics, particularly loop diuretics, remain the cornerstone of treatment for managing fluid overload. However, a significant proportion of patients develop diuretic resistance (DR), a condition where the diuretic response is diminished despite escalating doses, leading to persistent congestion, increased hospitalization rates, and poor prognosis. Effective management of DR requires a multi-faceted approach that integrates pharmacological optimization with advanced clinical monitoring.

1. Assessment of Diuretic Response

The initial step in managing diuretic resistance is the timely and accurate assessment of a patient' s response to therapy. Clinical indicators such as daily weight changes and net fluid balance are standard but may lack precision in acute settings. Recent evidence emphasizes the use of early urinary sodium metrics. Specifically, a spot urinary sodium content of less than 50–70 mmol/L measured two hours after diuretic administration, or a total urine output of less than 100–150 mL per hour within the first six hours, serves as a reliable predictor of an inadequate diuretic response. Identifying these "poor responders" early allows for rapid adjustment of the treatment strategy.

2. Optimization of Loop Diuretic Regimens

For patients exhibiting resistance, the first line of pharmacological adjustment involves optimizing the loop diuretic dose and delivery method. Evidence suggests that increasing the dose of intravenous loop diuretics is often more effective than simply increasing the frequency of administration. In cases of severe congestion or gut edema—which impairs oral absorption—switching from oral to intravenous administration is essential. Furthermore, continuous infusion of loop diuretics may be considered for patients who do not respond to bolus injections, as it maintains a more consistent plasma concentration above the therapeutic threshold, thereby minimizing the "rebound" sodium retention effect.

3. Combination Diuretic Therapy (Sequential Nephron Blockade)

When loop diuretics alone fail to achieve adequate diuresis, the addition of other diuretic classes can overcome compensatory sodium reabsorption in different segments of the nephron.

- **Thiazides:** Shanxi Medical University, Taiyuan 030001, China.
- **Affiliation:** The Second Hospital of Shanxi Medical University, Taiyuan 030001, China.
- **Author:** Zhang Yueying, Chief Superintendent Nurse.

Background

In the management of heart failure, diuretics are cornerstones for mitigating fluid retention and dyspnea. Diuretic resistance compromises efficacy, driving disease recurrence or progression. Thus, managing diuretic resistance is critical for optimizing treatment. However, existing evidence is fragmented and contentious, with no standardized clinical guidelines available.

Objective: To analyze and summarize the evidence related to the management of diuretic resistance in patients with heart failure, providing references for clinical practice.

Methods

Based on the "6S" model of evidence resources, relevant evidence regarding the management of diuretic resistance in heart failure patients was retrieved from Zhao Y R, Hao X Y, Zhao L, et al. Summary of the best evidence for the management of diuretic resistance in patients with heart failure [**?**]. *Chinese General Practice*, 2025. [Epub ahead of print] Editorial Office of Chinese General Practice. This is an open access article under the CC BY-NC-ND 4.0 license.

Databases searched included UpToDate, BMJ Best Practice, Guidelines International Network, National Institute for Health and Care Excellence, Scottish Intercollegiate Guidelines Network, Joanna Briggs Institute (JBI) Collaboration Centre Library, American Heart Association, and the Cochrane Library, with the search period spanning from January 1, 2015, to March 20, 2025. The literature included underwent screening, quality assessment, data extraction, and summarization.

Results

A total of 31 articles were included, including 6 guidelines, 5 clinical decision-making documents, 5 expert consensuses, 13 systematic reviews, and 2 randomized controlled trials. Among these, 1 guideline was rated as Grade A, 5 as Grade B, and the remaining 25 articles showed rigorous study designs with overall high quality. 56 pieces of evidence were synthesized across eight themes: diuretic response assessment, optimization of loop diuretic regimens, combining with other diuretics, hemodynamic improvement, integrated traditional Chinese and Western medicine treatment, non-pharmacological interventions, management of patients with refractory end-stage heart failure, and key points of treatment contraindications and monitoring.

Conclusion

This study focuses on 8 themes in patients with heart failure and diuretic resistance: diuretic response assessment, loop diuretic regimen optimization, combination with other diuretics, hemodynamic improvement, integrated Chinese and

Western medicine therapy, non-pharmacological treatment, management of patients with refractory end-stage heart failure, and treatment contraindications and monitoring key points. It summarizes evidence on initial screening, medication optimization, and comprehensive non-pharmacological interventions, providing a reference for healthcare providers to manage such patients efficiently.

Keywords: Heart failure; Diuretic resistance; Management; Evidence-based medicine; Evidence summary

Volume overload is a critical trigger for the exacerbation of heart failure (HF). Consequently, the elimination of excess body fluids through diuretic therapy serves as a cornerstone treatment strategy for alleviating symptoms and reducing rehospitalization rates. Approximately 90% of patients hospitalized with acute heart failure (AHF) receive diuretic treatment [**?**], and roughly 80% of patients with chronic heart failure (CHF) utilize diuretics for long-term management.

However, 21% to 35% of HF patients develop diuretic resistance (DR) during the course of their treatment. This condition is characterized by a progressive weakening or total loss of diuretic efficacy, leading to persistent and worsening fluid retention. Research indicates that DR results in the deterioration of clinical symptoms, prolonged hospital stays, and potentially increased mortality rates. Therefore, the timely identification and intervention of DR are of paramount importance for improving the prognosis of HF patients.

The study of DR faces dual challenges. First, its underlying mechanisms are complex and highly heterogeneous, involving multiple pathophysiological processes such as abnormal renal hemodynamics, overactivation of the neuroendocrine system, and functional remodeling of renal tubular sodium transporters; as a result, single-target interventions often yield limited improvement. Second, poor diuretic response often has an insidious onset, meaning early abnormalities are easily overlooked. Although relevant clinical decisions and guidelines exist both domestically and internationally, the evidence remains scattered across various studies and lacks systematic integration. Significant discrepancies persist between studies in key areas such as the assessment of diuretic response and the improvement of renal hemodynamics. Furthermore, clinical management measures lack evidence-based grading, making it difficult to establish unified recommendation levels based on the quality of evidence. By systematically integrating existing evidence, this paper aims to provide evidence-based support for the accurate identification and standardized management of DR. This study has been reviewed and approved by the Evidence Summary Registration Platform of the Fudan University Center for Evidence-Based Nursing (ES20257847).

1.1 Problem Identification

The specific research questions for this study were constructed according to the PIPOST framework: (1) Population (P): Heart failure (HF) patients presenting with diuretic resistance (DR); (2) Intervention (I): Management measures including the assessment and intervention of DR; (3) Professionals (P): Healthcare personnel providing clinical and nursing services for HF patients with comorbid DR; (4) Outcomes (O): Patient urine output, urinary sodium content, edema scores, weight loss, and dyspnea scores; (5) Setting (S): Medical environments such as cardiovascular wards, emergency departments, and intensive care units; (6) Type of evidence (T): Guidelines, clinical decisions, expert consensuses, systematic reviews, evidence summaries, meta-analyses, and randomized controlled trials. Evidence was retrieved using a top-down approach.

The Chinese search terms included "心力衰竭"(heart failure), "心衰"(HF), "心功能衰竭"(cardiac failure), "心功能不全"(cardiac insufficiency), and "利尿剂抵抗"(diuretic resistance). English search terms included "heart failure,""cardiac failure,""heart decompensation," "congestive heart failure," "myocardial failure," "diuretic resistance," "diuretic-resistant," and "diuretics." We searched UpToDate, BMJ Best Practice, the Guidelines International Network (GIN), the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), the Joanna Briggs Institute (JBI) Evidence-Based Practice Database, the American Heart Association (AHA), Medlive, and MedSci. Additionally, a combination of subject headings and free-text terms was used to search CNKI, Wanfang Data, VIP, Chinese Biomedical Literature Database (CBM), Web of Science, PubMed, Embase, CINAHL, and the Cochrane Library. The search period spanned from January 1, 2015, to March 20, 2025. Taking the PubMed database as an example, the specific search strategy is detailed in Table 1 .

Based on the "6S" evidence model⋯

1.3 Literature Inclusion and Exclusion Criteria

Inclusion criteria: (1) The study population consists of patients with heart failure (HF) comorbid with diuretic resistance (DR); (2) The research content involves the assessment or intervention of DR; (3) The literature types include guidelines, expert consensuses, systematic reviews, clinical decision-making tools, evidence summaries, meta-analyses, and randomized controlled trials; (4) The publication language is either Chinese or English.

Exclusion criteria: (1) Duplicate publications or translated versions of existing literature; (2) Full text is unavailable; (3) Updated versions of the same study exist; (4) Literature of low quality, including guidelines rated as Grade C or studies of other types with serious methodological flaws.

1.4 Literature Quality Evaluation Standards

The clinical guidelines were evaluated using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Guidelines were categorized into three grades based on their standardized scores across six domains: Grade A (Recommended) required scores of $\geq 60\%$ in all six domains; Grade B (Recommended with modifications) was assigned if at least three domains scored $\geq 30\%$

but some domains scored < 60%; Grade C (Not recommended) was assigned if three or more domains scored < 30%. Systematic reviews were assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) tool, which consists of 11 items evaluated as "Yes," "No," "Unclear," or "Not applicable." Expert consensuses were evaluated using the JBI Critical Appraisal Checklist for Text and Opinion, which includes six items evaluated as "Yes," "No," "Unclear," or "Not applicable."

Randomized controlled trials (RCTs) were evaluated using the Cochrane Collaboration' s tool for assessing risk of bias, which includes seven items categorized as "Yes" (low risk of bias), "No" (high risk of bias), or "Unclear" (uncertain risk of bias). The quality of included clinical decisions was assessed using the Critical Appraisal for Summaries of Evidence (CASE) tool, which consists of 10 items evaluated as "Yes," "Partial," or "No."

Literature quality appraisal was conducted independently by two researchers who had completed and passed training in evidence-based nursing courses. Any disagreements were resolved through discussion with a third researcher until a consensus was reached.

Evidence extraction, synthesis, and grading were performed independently by two researchers trained in evidence-based nursing. The synthesis principles were as follows: when content was consistent, recommendations that were concise, clear, and compliant with descriptive standards were adopted; when content was complementary, it was merged based on logical relationships; when content was conflicting, selection followed the priority of evidence-based strength, high-quality evidence, recently published authoritative literature, and domestic guidelines; when content was independent, the original recommendations were retained. The extracted evidence was graded into five levels (Levels 1–5) according to the JBI Evidence Grading System.

2.1 Literature Search Results

A total of 3,405 relevant documents were retrieved through the initial search. After removing duplicates, 2,772 articles remained. Following a screening of titles and abstracts to exclude irrelevant studies, 220 documents were retained for further review. After a full-text reading and quality assessment to exclude studies that did not meet the inclusion criteria, 31 articles were ultimately selected [**?**, **?**].

A total of 2,704 records were retrieved from electronic databases: PubMed (743), Embase (964), Web of Science (470), Cochrane Library (286), CINAHL (152), CNKI (18), Wanfang Data (26), VIP (14), and CBM (31). Additionally, 701 records were identified by searching clinical decision support systems, guideline repositories, and relevant professional society websites, including UpToDate (250), BMJ Best Practice (173), the National Institute for Health and Care Excellence (NICE) (49), the American Heart Association (AHA) (221), and MedSci (8).

After removing duplicates, 2,772 records remained. Following an initial screening of titles and abstracts, 2,552 records were excluded as they did not meet the research criteria. The full texts of the remaining articles were retrieved and evaluated based on the pre-defined inclusion and exclusion criteria. During this stage, 189 articles were excluded for the following reasons: inability to access the full text (3), inconsistent research content (174), translated versions of English literature (5), outdated versions of guidelines (4), methodological defects identified during quality appraisal (1), and literature reviews (2).

Ultimately, 26 articles were included for the final evidence summary [?, ?, ?, ?, ?, ?]. These comprised 13 systematic reviews [?], 6 guidelines [?], 5 expert consensuses [?], and 2 randomized controlled trials [?]. The literature screening process is illustrated in Figure 1 [Figure 1: see original paper], and the basic characteristics of the included studies are summarized in Table 2 .

2.2 Literature Quality Evaluation Results

A total of five clinical decision reports were included. Aside from the items "Is the search method transparent and comprehensive?"and "Is the evidence grading system transparent and translatable?", which were rated as "No," all other items were rated as "Yes," indicating a high overall research quality. Five expert consensuses were included; the study by Dong Wei et al. was rated "No" for the item "Are there inconsistencies between the proposed viewpoints and previous literature?" , while all other items were rated "Yes," reflecting a high overall quality. Thirteen systematic reviews were included, showing a high level of overall quality. Two randomized controlled trials were included; for the studies by Ter Maaten et al. and Khorramshahi et al., all items were rated "Yes" except for "Was blinding implemented for subjects/researchers?" , which was rated as "Unclear," suggesting an overall rigorous research design. The evaluation of the six guidelines and the detailed results of the literature quality assessment are provided in the appendix.

Description and Summary of Evidence

A total of 56 pieces of evidence were extracted, covering eight themes: assessment of diuretic response, optimization of loop diuretic regimens, combination with other types of diuretics, improvement of hemodynamics, integrated traditional Chinese and Western medicine treatment, non-pharmacological treatment, management of patients with refractory end-stage heart failure (HF), and treatment contraindications and monitoring points. These are based on the works of Colucci, Brater, the Chinese Medical Association, the Expert Committee on Rational Drug Use of the National Health and Family Planning Commission, the Chinese Association of Integrative Medicine, Metra, Rodríguez et al., Chionh, Sahin, Guerrero, Cervera, Gogikar, Steuber, Shrestha, Ter Maaten, and Khorramshahi, as shown in .

3.1 Timing and Key Points of Assessment for Diuretic Response

HF patients suffer from gastrointestinal congestion caused by long-term volume overload, which significantly reduces the intestinal absorption efficiency of diuretics and leads to a progressive decrease in urine output. Simultaneously, the long-term use of diuretics induces compensatory sodium reabsorption in the distal renal tubules, resulting in impaired renal sodium excretion and a progressive decline in urinary sodium levels. Furthermore, in the early stages of sodium and water retention, fluid primarily accumulates in the extravascular space or splanchnic circulation, often without presenting obvious peripheral edema [?]. Collectively, these factors contribute to the insidious onset of diuretic resistance (DR), which is easily overlooked in clinical practice.

Consequently, it is crucial to accurately determine the timing and specific indicators for assessing diuretic response. Multiple studies have confirmed that urinary sodium (UNa) concentration can effectively predict diuretic responsiveness and clinical outcomes [?]. Moreover, UNa levels are positively correlated with the degree of congestion relief. While there are subtle differences in defining the ideal threshold for diuretic response—often cited as 80 mmol/L—this study adopts the higher-quality evidence provided by clinical guidelines.

According to the recommendations in [?], early poor diuretic response is indicated by a 2-hour UNa $<$ 50–79 mmol/L and/or a 6-hour urine output $<$ 100–150 mL/h. The identification criteria for DR are defined as a 12-hour UNa $<$ 70 mmol/L and/or a 12-hour urine output $<$ 150 mL/h.

Based on the standards established by the National Health and Family Planning Commission Expert Committee on Rational Drug Use and the Chinese Medical Association, a 12-hour UNa $<$ 70 mmol/L and/or a urine output $<$ 150 mL/h indicates the presence of diuretic resistance.

4. Transition from Oral to Intravenous Administration

5. The initial intravenous dose should be 1.0 to 2.5 times the usual daily oral dose, followed by an assessment of the diuretic response.
6. For patients with hypokalemia, priority should be given to combination therapy with amiloride or triamterene.

6. Acetazolamide for Patients with Metabolic Alkalosis

7. It is recommended to combine this with KW-3902, which can selectively induce diuresis and natriuresis.

3.2 Loop Diuretic Regimens

Compared to thiazide diuretics, loop diuretics exhibit a more potent diuretic effect and carry a lower risk of adverse reactions such as hypotension and electrolyte disturbances. Consequently, multiple studies [?, ?, ?, ?] recommend loop diuretics as the preferred first-line treatment. If the diuretic target is not achieved following initial administration, the dosage may be increased; relevant research indicates that a reasonable increase in dosage can enhance diuretic efficacy without increasing clinical risk. Patients with heart failure (HF) often exhibit low oral bioavailability of furosemide due to gastrointestinal congestion, which may prevent them from reaching diuretic targets. In such cases, switching to torsemide or bumetanide—which possess higher oral bioavailability—can improve the diuretic response.

Summary of Best Evidence for the Management of Diuretic Resistance in Patients with Heart Failure:

1. An inadequate diuretic response is indicated if, after intravenous (IV) diuretic administration, the 2-hour urinary sodium (UNa) is $<$ 50–70 mmol/L and/or the 6-hour urine output is $<$ 100–150 mL/h.
2. Gradually increase the oral dose of furosemide until clinical efficacy is achieved or the maximum dose is reached. If the response is only partial (e.g., increased urine output without weight loss), the dose can be divided into 2–3 administrations per day to enhance efficacy.
3. If the target is not met (2-hour UNa $<$ 50–70 mmol/L and/or 6-hour urine output $<$ 100–150 mL/h), the dose should be doubled every 2 hours until the maximum recommended dose is reached, rather than repeating the same dose.
4. Furosemide may be administered via IV bolus 2–3 times per day, with a total daily dose not exceeding 200 mg and an injection rate of $\leq$ 4 mg/min.
5. Continuous infusion is preferred for patients who show improvement with bolus therapy but require sustained diuresis.
6. Utilize a combination of IV bolus followed by continuous infusion (e.g., a 40 mg furosemide bolus followed by 5–40 mg/h maintenance, or a 20 mg torsemide bolus followed by 5–20 mg/h maintenance).
7. Transition from IV to oral administration as soon as congestion is relieved. The oral dose should be adjusted to 1–1.5 times the IV dose, with efficacy evaluated based on urine output.
8. Combination therapy should be initiated in patients with an inadequate response to maximum-dose IV loop diuretics. For patients with chronic heart failure (CHF), treatment may begin with oral combinations of other diuretics; for patients with acute decompensated heart failure (ADHF), an IV combination regimen should be used directly.
9. In patients without hypokalemia, thiazide diuretics (e.g., hydrochlorothiazide, metolazone) are the preferred adjuncts.
10. Oral metolazone combined with IV bolus or continuous infusion of loop

diuretics is the first choice. If oral administration is not feasible, IV hydrochlorothiazide should be combined with IV loop diuretics.

11. Combination therapy with mineralocorticoid receptor antagonists (MRAs) is recommended. If urinary potassium levels increase, aldosterone antagonists (e.g., spironolactone) are preferred.
12. During combination therapy, medications administered via the same route can be given simultaneously. If using oral thiazide diuretics, they should be taken 2–5 hours prior to the administration of IV loop diuretics.
13. For HF patients with persistent fluid retention despite conventional diuretic therapy, a vasopressin V_2 receptor antagonist—typically tolvaptan—should be added. Dosage: 7–14 days (starting at 7.5–15 mg/d, commonly 15 mg/d, maximum 30 mg/d). It is contraindicated in patients with hypovolemia, hypernatremia, or impaired thirst perception and should not be co-administered with potent CYP3A4 inhibitors [?, ?, ?, ?].
14. Administration: Initially, administer a slow intravenous bolus at a dose of 1.5–2.0 μg/kg over a duration of > 1 min, followed by a maintenance infusion of 0.0075–0.0100 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The treatment course lasts 5–7 days; it is contraindicated in patients with a systolic blood pressure < 90 mmHg.
15. Levosimendan injection combined with recombinant human brain natriuretic peptide (rhBNP). Levosimendan administration: 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$.
16. Intravenous infusion of albumin, plasma, or plasma substitutes to increase colloid osmotic pressure.
17. For patients with hypochloremia, use hypertonic saline combined with furosemide to increase crystalloid osmotic pressure.

8. Recommendation for ARNI Combination

9. Active management should be directed toward hypotension, hypoxia, acidosis, hyponatremia, hypoproteinemia, and infection, with a primary focus on correcting hypovolemia.
10. **Traditional Chinese Medicine (TCM) Syndrome Differentiation and Treatment:**
    - **Yang Deficiency with Water Overflow:** Treated with modified *Zhenwu* Decoction combined with *Tingli Dazao Xiefei* Decoction to warm Yang and promote diuresis.
    - **Heart Yang Deficiency with Blood Stasis and Fluid Retention:** Treated with modified *Zhenwu* Decoction combined with *Danshen* Drink to warm and supplement Yang Qi, activate blood circulation, and promote diuresis.

- **Spleen and Kidney Yang Deficiency with Blood Stasis and Fluid Retention:** Treated with modified *Shipi* Drink to warm and supplement the Spleen and Kidney, activate blood circulation, and promote diuresis.
- **Sinking of Zong Qi with Fluid Retention in the Triple Burner:** Treated with modified *Shengxian* Decoction combined with *Sanren* Decoction to benefit Qi, lift the sunken Qi, and facilitate the transformation and drainage of dampness.
- **Deficiency of both Yin and Yang:** Treated with *Wenyang Zhenshuai* Formula to warm Yang, benefit Qi, consolidate Yang, and transform Yin.

11. On the basis of conventional Western medical treatment, TCM formulations primarily based on modified *Zhenwu* Decoction should be administered to warm Yang and promote diuresis.

12. The liquid volume of TCM decoctions is generally 100–200 mL per dose, administered twice daily.

13. The combination of *Shenmai* Injection and Torasemide Injection is recommended to improve hemodynamics, microcirculation, and cardiac function in patients with Chronic Heart Failure (CHF). This combination enhances therapeutic efficacy while reducing the required dosage and potential toxic side effects of digitalis.

14. The combination of *Qili Qiangxin* Capsules and Tolvaptan is recommended, as it can improve clinical symptoms and cardiac function in Heart Failure (HF) patients, while significantly reducing serum levels of NT-proBNP and ET-1.

15. Recombinant Human Brain Natriuretic Peptide (rhBNP) combined with *Shenmai* Injection is recommended to improve the therapeutic effect of HF in patients with dilated cardiomyopathy. Furthermore, its combination with *Shenfu* Injection can improve cardiac function, inhibit myocardial remodeling, and reduce the levels of HF biomarkers.

16. *Huangqi* (Astragalus) Injection is recommended for its effects in benefiting Qi, nourishing the "Yuan" (original) Qi, strengthening body resistance to eliminate pathogenic factors, nourishing the heart, unblocking the vessels, and strengthening the Spleen to resolve dampness. It is indicated for cardiac insufficiency characterized by Heart Qi deficiency and blood vessel impairment.

17. Rhubarb (*Dahuang*) may be used for purgation to eliminate intestinal gas and accumulated stool, thereby facilitating the removal of excess volume load through the intestinal tract.

9. Acupoint Ultrasound, Moxibustion, and Patching

10. After excluding contraindications, follow the seven-step exercise rehabilitation protocol, gradually transitioning from breathing exercises and bed-based stretching to low-intensity off-bed limb movements. Emergency equipment must be available, and vital signs should be continuously monitored; training must be terminated immediately if any abnormalities occur. Recommended activities include walking, jogging, or Traditional Chinese Medicine (TCM) exercises (such as *Gongfa*), with a duration of 30–60 minutes per session. For physically frail patients, the warm-up period should be extended to 10–15 minutes, while the core exercise duration should be appropriately shortened.

11. Strict restriction of salt and fluid intake is required. Patients should avoid spicy foods, alcohol, and caffeine. Dietary therapy should focus on ingredients that strengthen the spleen and resolve dampness. This may be supplemented by TCM medicated baths (using herbs such as *Ramulus Cinnamomi* and *Natrii Sulfas*), moxibustion (at acupoints such as *Shenque* (CV8), *Fenglong* (ST40), and *Zhongwan* (CV12)), and massage to warm the meridians and resolve phlegm.

12. Provide patients with health education regarding rehabilitation and offer emotional support. For symptoms of depression and anxiety, clinical intervention should be based on syndrome differentiation focusing on the Heart and Liver systems.

13. Provide remote guidance and re-evaluate body weight, physical examination, and laboratory measurements within 2 weeks after discharge.

For patients with refractory volume overload who are unresponsive to diuretic therapy, extracorporeal ultrafiltration should be employed.

2. Peritoneal Ultrafiltration as an Option

Indications include severe acidosis (pH $<$ 7.2), blood urea nitrogen $>$ 25 mmol/L (150 mg/dL), and serum creatinine $>$ 300 μmol/L ($>$ 3.4 mg/dL).

3. When extracorporeal ultrafiltration fails to clear metabolic end-products, hemodialysis should be initiated if the following indications appear: persistent oliguria after fluid resuscitation or severe hyperkalemia (K^+).

4. Renal replacement therapy is generally reserved for patients with severe cardiorenal insufficiency requiring simultaneous dialysis or for those participating in clinical trials.

5. For patients with clinical deterioration or end-organ dysfunction, intermittent inotropic agents may be used as a short-term bridge until the implantation of mechanical circulatory support devices or heart transplantation.

6. Such patients should be promptly evaluated as candidates for heart transplantation, long-term mechanical circulatory support, or palliative care [?, ?]. For those requiring antiplatelet therapy, the dosage of aspirin should be reduced, or it should be replaced with clopidogrel or ticagrelor.
7. Avoid contraindicated drugs: non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and estrogens.
8. For patients with aspirin resistance, traditional Chinese patent medicines that promote blood circulation and resolve stasis, such as Compound Danshen Dripping Pills or Tongxinluo Capsules, may be considered.
9. Body weight should be measured at a fixed time daily; if no decrease or an increase is observed for three consecutive days, the diuretic regimen should be intensified.
10. Sodium and water restriction: For mild HF, sodium intake should be 2–3 g/d; for moderate-to-severe HF, $\leq$ 2 g/d. For patients with serum sodium $<$ 130 mmol/L, fluid intake should be $\leq$ 2 L/d.
11. The supine position is recommended for patients to effectively improve renal perfusion and reduce cardiac workload.
12. Renal function (serum creatinine) and electrolytes (serum potassium and sodium) must be closely monitored during treatment. Note: UNa = urinary sodium, HF = heart failure, CHF = chronic heart failure, ADHF = acute decompensated heart failure, KW-3902 = adenosine A_1 receptor antagonist, CYP = cytochrome P450, SGLT2 inhibitor = sodium-glucose cotransporter 2 inhibitor, ARNI = angiotensin receptor-neprilysin inhibitor, NT-proBNP = N-terminal pro-B-type natriuretic peptide.

According to the *Chinese Journal of General Practice* [?, ?], oral administration may also be switched to intravenous administration. If the initial dose is insufficient, a dose increase should be considered. These represent management strategies targeting different pathophysiological mechanisms and do not follow a fixed sequence in clinical application. When loop diuretic monotherapy yields an inadequate response, combination therapy with other classes of diuretics should be considered. This strategy targets sodium reabsorption sites across different segments of the nephron, which theoretically enhances urinary sodium excretion and fluid clearance by 80%-100%, achieving equivalence to intravenous administration. When using combination therapy, drugs should be selected based on the patient’ s type of electrolyte disturbance, acid-base balance, and fluid overload characteristics. For example, acetazolamide is preferred for patients with concomitant metabolic alkalosis; it corrects alkalosis and enhances diuresis by inhibiting carbonic anhydrase, although its diuretic effect is weaker than that of thiazide diuretics [?]. For patients with refractory fluid overload, thiazide diuretics can be added to enhance sodium excretion and improve congestion through sequential nephron blockade. Improving hemodynamics is a key treatment for HF. Hypotension, low perfusion states during decompensation, and long-term diuretic use can all activate the renin-angiotensin-aldosterone system (RAAS), further exacerbating water and sodium retention, vasoconstriction, and worsening renal perfusion. This makes it difficult to achieve diuretic goals with diuretics alone. In such cases, hemodynamic improvement becomes a critical intervention. Specific strategies include: infusing albumin to increase colloid osmotic pressure or using hypertonic saline to correct crystalloid osmotic pressure imbalances for volume expansion to improve renal perfusion, thereby significantly enhancing diuretic effects [?]; employing low-dose dopamine combined with furosemide to dilate renal vessels and increase renal blood flow [?]; and utilizing recombinant human B-type natriuretic peptide, ARNI, and SGLT2 inhibitors, all of which inhibit the RAAS and enhance natriuresis [?]. Levosimendan, with its inotropic and vasodilatory effects, enhances myocardial contractility and improves cardiac pumping function, effectively optimizing hemodynamic status. Integrated Traditional Chinese and Western Medicine is a characteristic therapy for DR. Traditional Chinese Medicine (TCM) identifies the syndrome differentiation of DR as "deficiency in origin and excess in superficiality," where the origin deficiency is primarily Qi deficiency and the superficial excess is dominated by blood stasis. The core pathogenesis is "Yang deficiency with water flooding, and Qi deficiency with blood stasis." Unlike the Western medical strategy of inhibiting the RAAS and improving hemodynamics, TCM focuses on "warming Yang to transform Qi, and promoting blood circulation to facilitate diuresis," supplemented by Astragalus to tonify Qi and consolidate the origin. This approach not only improves symptoms through diuresis and edema reduction but also addresses the fundamental pathogenesis by regulating the Qi transformation of the heart, spleen, and kidney and correcting Qi deficiency and blood stasis, thereby achieving the characteristic of "treating both the symptoms and the root cause."

Clinical studies have confirmed that integrated Traditional Chinese and Western medicine regimens significantly improve efficacy compared to Western medicine alone: the combination of Chinese herbal medicine and diuretics can enhance the improvement of cardiac function and RAAS inhibition [?]; the combined use of Chinese herbal medicine, diuretics, and hemodynamic drugs can significantly increase urine output and reduce levels of inflammatory factors [?]. This synergistic effect helps improve water and sodium metabolism disorders as well as cardiorenal function in DR patients. Furthermore, Qi-tonifying and Yin-nourishing herbs (such as Astragalus) and Qi-tonifying and Yang-warming formulas (such as Zhenwu Decoction) can significantly alleviate post-ultrafiltration symptoms such as dry mouth, thirst, fatigue, persistent edema, dyspnea, and weak urination. Ultrafiltration is a preferred therapy. As an isotonic solution, the sodium concentration in ultrafiltrate is identical to that of plasma, whereas the hypotonic urine formed under the action of loop diuretics has a urinary sodium concentration of only 70 mmol/L. This indicates that ultrafiltration is more efficient in sodium excretion and maintaining electrolyte balance. Therefore, when fluid volume load is difficult to control with pharmacological treatment, ultrafiltration therapy should be considered. Numerous studies have confirmed that ultrafiltration clears excess body fluids more efficiently than diuretic therapy, significantly reducing body weight and creatinine levels, improving cardiac function, dyspnea, and edema, shortening hospitalization cycles, and reducing readmission frequency [?]. Early ultrafiltration is recommended as it helps restore diuretic sensitivity; however, dynamic monitoring of urinary sodium content is necessary to evaluate efficacy. If patients meet the indications for dialysis, further dialysis options may be selected. Among chronic dialysis patients, peritoneal dialysis is better at preserving residual renal function and is associated with better survival rates compared to hemodialysis [?], though indications for dialysis must be strictly followed.

Refractory End-stage Heart Failure

Patients with refractory end-stage HF exhibit hemodynamic disturbances such as elevated cardiac filling pressure and decreased cardiac output. Coupled with renal tubular hypertrophy and renal congestion caused by long-term diuretic use, these patients are more prone to developing DR. In turn, DR further exacerbates congestion and elevates cardiac filling pressure, leading to reduced cardiac output and renal perfusion, thus forming a vicious cycle. Intermittent inotropic therapy is a key bridging strategy to improve this pathological process. Research has found that although these drugs do not directly improve long-term outcomes, they may reverse end-organ dysfunction by increasing cardiac output and maintaining organ perfusion pressure, thereby creating a therapeutic window for patients awaiting heart transplantation or left ventricular assist device (LVAD) implantation. Heart transplantation remains the preferred option, significantly improving survival rates, exercise capacity, and quality of life in eligible patients. For patients who are inotropic-dependent or have contraindications to transplantation, LVAD can be used as a long-term mechanical circulatory support measure, with a 2-year survival rate of 83% following LVAD therapy. Management of DR is based on sodium and water restriction, avoidance of contraindications, and collaborative monitoring. Sodium and water restriction are fundamental measures in DR management, laying the groundwork for diuretic therapy by reducing the sodium and water load. Simultaneously, drugs that impair diuretic efficacy must be strictly avoided. NSAIDs directly weaken diuretic potency by inhibiting prostaglandin synthesis; corticosteroids and estrogens have sodium- and water-retaining effects that antagonize the natriuretic effect of diuretics, and thus their use should be avoided.

In addition, postural management affects neuroendocrine regulation. In the upright position, gravity-induced blood flow redistribution activates the sympathetic nervous system and the RAAS, which may exacerbate water-sodium retention and DR. Conversely, the supine position helps improve venous return and renal perfusion, thereby inhibiting the overactivation of these hormones.

4 Summary

This study summarizes the best evidence for the management of diuretic resistance (DR) in patients with heart failure (HF) across eight key themes: assessment of diuretic response, optimization of loop diuretic regimens, combination therapy with other diuretic classes, hemodynamic improvement, integrated traditional Chinese and Western medicine, ultrafiltration therapy, management of patients with refractory end-stage HF, and contraindications and monitoring points. These findings provide a robust foundation for clinical practice. However, the evidence synthesized in this study lacks support from prospective randomized controlled trials (RCTs) regarding long-term intervention efficacy and specific clinical scenarios, such as refractory end-stage HF. Furthermore, as the evidence sources are predominantly English-language literature, differences in population characteristics may exist.

Chinese General Practice: Clinical healthcare professionals should conduct individualized assessments of the actual volume management status of each patient when applying this evidence.

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References

[?] TRULL S J C, CASADO J, MORALES-RULL J L, et al. Prevalence and outcome of diuretic resistance in heart failure: reply [J]. *Intern Emerg Med*, 2019, 14(4): 633-634. DOI: 10.1007/s11739-019-02064-w.

[?] SCHOLTE N T, AYDIN D, LINSSEN G C, et al. Use of loop diuretics in patients with chronic heart failure: an observational overview [J]. *Open Heart*, 2023, 10(2): e002497. DOI: 10.1136/openhrt-2023-002497.

[?] Liu Chengshuai, Liu Feifei, Chen Yue, et al. Advances in the diagnosis and pharmacological treatment of heart failure complicated by diuretic resistance [J]. *Journal of Clinical Cardiology*, 2025, 41(3).

[?] Dong Wei, Ren Jingyi, Xu Dongjie. Chinese expert consensus on the diagnosis and management of diuretic resistance in patients with heart failure [J]. *Journal of Clinical Cardiology*, 2024, 40(4): 257-263.

[?] WILCOX C S, TESTANI J M, PITT B. Pathophysiology of diuretic resistance and its implications for the management of chronic heart failure [J]. *Hypertension*, 2020, 76(4): 1045-1054. DOI: 10.1161/HYPERTENSION-AHA.120.15205.

[?] DICENSO A, BAYLEY L, BRIAN HAYNES R. Accessing pre-appraised evidence: fine-tuning the 5S model into a 6S model [J]. *Evid Based Nurs*, 2009, 12(4): 99-101. DOI: 10.1136/ebn.12.4.99-b.

[?] BROUWERS M C, KHO M E, BROWMAN G P, et al. AGREE II: advancing guideline development, reporting and evaluation in health care [J]. *CMAJ*, 2010, 182(18): E839-842. DOI: 10.1503/cmaj.090449.

[?] Zhu Zheng, Hu Yan, Zhou Yingfeng, et al. Promoting the Translation of Evidence into Clinical Practice (V): Literature Quality Appraisal in Evidence-Based Clinical Translation Research [J]. *Journal of Nursing Science*, 2020.

[?] The Cochrane Collaboration. Risk of bias 2 (RoB 2) tool [EB/OL].

[?] FOSTER M J, SHURTZ S. Making the critical appraisal for summaries of evidence (CASE) for evidence-based medicine (EBM): critical appraisal of summaries of evidence [J]. *J Med Libr Assoc*, 2013, 101(3): 192-198. DOI: 10.3163/1536-5050.101.3.008.

[?] Use of diuretics in patients with heart failure [EB/OL]. (2025-02-20).

[?] Etiology and treatment of refractory edema in adults [EB/OL].

[?] SYED W Y. Acute heart failure [EB/OL]. (2025-02-20).

[?] SYED W Y. Heart failure with preserved ejection fraction [EB/OL].

[?] SYED W Y. Heart failure with reduced ejection fraction [EB/OL].

[?] Chinese Medical Association, Chinese Medical Association Publishing House, Chinese Medical Association Society of General Practice, et al. Chinese Guidelines for the Diagnosis and Management of Heart Failure in Primary Care (2024) [J]. *Chinese Journal of General Practitioners*, 2024, 23(6): 549-577. DOI: 10.3760/cma.

[?] LI Y H, WANG C C, HUNG C L, et al. 2024 guidelines of the Taiwan society of cardiology for the diagnosis and treatment of heart failure with preserved ejection fraction [J]. *Acta Cardiol Sin*, 2024, 40(2): 148-171. DOI: 10.6515/ACS.202403_{40}(2).20240206A.

[?] HYUN J, CHO J Y, YOUN J C, et al. Korean society of heart failure guidelines for the management of heart failure: advanced and acute heart failure [J]. *Korean Circ J*, 2023, 53(7): 452-471. DOI: 10.4070/kcj.2023.0115.

[?] YOUN J C, KIM D, CHO J Y, et al. Korean society of heart failure guidelines for the management of heart failure: treatment [J]. *Korean Circ J*, 2023, 53(4): 217-238. DOI: 10.4070/kcj.2023.0047.

[?] National Health and Family Planning Commission Expert Committee on Rational Drug Use, China Pharmacists Association. Guideline for Rational Drug Use in Heart Failure (2nd Edition) [J]. *Chinese Journal of Medical Frontiers: Electronic Edition*, 2019, 11(7): 1-78. DOI: 10.12037/YXQY.2019.07-01.

[?] Expert Consensus on the Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Chronic Heart Failure with Diuretic Resistance [EB/OL].

[?] Wang Hua, Li Yingying. Chinese Expert Consensus on the Comprehensive Management of Patients with Worsening Chronic Heart Failure 2022 [J]. *Chinese Circulation Journal*, 2022, 37(3): 215-225.

[?] METRA M, TOMASONI D, ADAMO M, et al. Worsening of chronic heart failure: definition, epidemiology, management and prevention. A clinical consensus statement by the heart failure association of the European society of cardiology [J]. *Eur J Heart Fail*, 2023, 25(6): 776-791. DOI: 10.1002/ejhf.2874.

[?] RODRÍGUEZ J M, CASADO J, FORMIGA F, et al. Consensus on basic conduct during the hospital admission of patients with acute heart failure [J]. *Rev Clin Esp*, 2021, 221(5): 287-296.

[?] Tang E, Wang DY, Lin SS, et al. Meta-analysis of modified Zhenwu Decoction in the treatment of chronic heart failure complicated by diuretic resistance [J]. *World Journal of Integrated Traditional and Western Medicine*, 2022.

[?] Wang MX, Cao PH, Wu CJ, et al. Meta-analysis of the efficacy and safety of Wenyang Lishui Chinese herbs in the treatment of heart failure complicated by diuretic resistance [J]. *Chinese General Practice*, 2021, 24(29): 3734-3741, 3750. DOI: 10.12114/j.issn.1007-9572.2021.00.563.

[?] Yang C, Zheng G, Qi J, et al. Meta-analysis of the effects of integrated traditional Chinese and Western medicine on the clinical efficacy and objective indicators of chronic heart failure with diuretic resistance [J]. *Journal of Emergency in Traditional Chinese Medicine*, 2021.

[?] Wang AZ, Ma XC. Meta-analysis of traditional Chinese medicine intervention for chronic heart failure with diuretic resistance [J]. *Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease*, 2020, 18(15).

[?] Zhang YT, Zheng L, Zhu Y, et al. Meta-analysis of the efficacy of tolvaptan in the treatment of heart failure complicated by diuretic resistance [J]. *Clinical Medication Journal*, 2020, 18(9).

[?] Guo Q, Pan DM, Tian Q, et al. Meta-analysis of furosemide combined with low-dose dopamine in the treatment of Chinese patients with diuretic-resistant heart failure [J]. *Drug Evaluation Research*, 2020, 43(5): 935-941. DOI: 10.7501/j.issn.1674-6376.2020.05.026.

[?] ORSO D, TAVAZZI G, CORRADI F, et al. Comparison of diuretic strategies in diuretic-resistant acute heart failure: a systematic review and network meta-analysis [J]. *Eur Rev Med Pharmacol Sci*, 2021, 25(7): 2971-2980. DOI: 10.26355/eurrev_{{{202104}}_{{25550}}}.

[?] CHIONH C Y, CLEMENTI A, POH C B, et al. The use of peritoneal dialysis in heart failure: a systematic review [J]. *Perit Dial Int*, 2020, 40(3): 210-221. DOI: 10.1177/0896860819895198.

[?] SAHIN E, BEK S G, EREN N, et al. Usefulness of peritoneal ultrafiltration in patients with diuretic resistant heart failure without end-stage renal disease [J]. *Cardiorenal Med*, 2020, 10(6): 429-439. DOI: 10.1159/000510249.

[?] GUERRERO CERVERA B, LÓPEZ-VILELLA R, DONOSO TRENADO V, et al. Analysis of the usefulness and benefits of ultrafiltration in cardiorenal syndrome: a systematic review [J]. *ESC Heart Fail*, 2025, 12(2): 1194-1202. DOI: 10.1002/ehf2.15125.

[?] GOGIKAR A, NANDA A, JANGA L S N, et al. Combination diuretic therapy with thiazides: a systematic review on the beneficial approach to overcome refractory fluid overload in heart failure [J]. *Cureus*, 2023, 15(9): e44624. DOI: 10.7759/cureus.44624.

[?] STEUBER T D, JANZEN K M, HOWARD M L. A systematic review and meta-analysis of metolazone compared to chlorothiazide for treatment of acute decompensated heart failure [J]. *Pharmacotherapy*, 2020, 40(9): 924-935. DOI: 10.1002/phar.2440.

[?] SHRESTHA D B, SEDHAI Y R, GAIRE S M, et al. Use of metolazone as an adjunct therapy to loop diuretics in diuretic resistant acute decompensation of heart failure: a systematic review and meta-analysis [J]. *Health Sci Rev*, 2023, 7: 100094.

[?] TER MAATEN J M, BELDHUIS I E, VAN DER MEER P, et al. Natriuresis-guided diuretic therapy in acute heart failure: a pragmatic randomized trial [J]. *Nat Med*, 2023, 29(10): 2625-2632. DOI: 10.1038/s41591-023-02532-z.

[?] KHORRAMSHAHI BAYAT M, CHAN W, HAY K, et al. Spot urinary sodium-guided titration of intravenous diuretic therapy in acute heart failure: a pilot randomized controlled trial [J]. *Eur Heart J Qual Care Clin Outcomes*, 2025, 11(1): 97-104.

[?] MULLENS W, DAMMAN K, HARJOLA V P, et al. The use of diuretics in heart failure with congestion—a position statement from the Heart Failure Association of the European Society of Cardiology [J]. *Eur J Heart Fail*, 2019, 21(2): 137-155.

[?] NOVAK J E, ELLISON D H. Diuretics in states of volume overload: core curriculum 2022 [J]. *Am J Kidney Dis*, 2022, 80(2): 264-278.

[?] FERREIRA J P, GIRERD N, MEDEIROS P B, et al. Spot urine sodium excretion as prognostic marker in acutely decompensated heart failure: the spironolactone effect [J]. *Clin Res Cardiol*, 2016, 105(6): 489-507. DOI: 10.1007/s00392-015-0945-x.

[?] LUK A, GROARKE J D, DESAI A S, et al. First spot urine sodium after initial diuretic identifies patients at high risk for adverse outcome after heart failure hospitalization [J]. *Am Heart J*, 2018.

[?] MARSHALL BRINKLEY D Jr, BURPEE L J, CHAUDHRY S P, et al. Spot urine sodium as triage for effective diuretic infusion in an ambulatory heart failure unit [J]. *J Card Fail*, 2018, 24(6).

[?] VERBRUGGE F H, MARTENS P, DAUW J, et al. Natriuretic response to acetazolamide in patients with acute heart failure and volume overload [J]. *J Am Coll Cardiol*, 2023, 81(20).

[?] CUTHBERT J J, CLARK A L. Diuretic treatment in patients with heart failure: current evidence and future directions-part II: combination therapy [J]. *Curr Heart Fail Rep*, 2024, 21(2): 115-130. DOI: 10.1007/s11897-024-00644-2.

[?] IKEDA Y, ISHII S, MAEMURA K, et al. Association between intestinal oedema and oral loop diuretic resistance in hospitalized patients with acute heart failure [J]. *ESC Heart Fail*, 2021, 8(5): 4067-4076. DOI: 10.1002/ehf2.13525.

[?] HUXEL C, RAJA A, OLLIVIERRE-LAWRENCE M D. Loop diuretics [M]. StatPearls Publishing, 2024.

[?] MICHAEL FELKER G, ELLISON D H, MULLENS W, et al. Diuretic therapy for patients with heart failure: JACC state-of-the-art review [J]. *J Am Coll Cardiol*, 2020, 75(10): 1178-1195.

[?] ALKHUZAEE F S, ALDARDEER N F, ALTHOBAITI O A, et al. Acetazolamide for the management of diuretic-induced chloride depletion alkalosis: a systematic review [J]. *J Clin Med*, 2025, 14(4): 1041. DOI: 10.3390/jcm14041041.

[?] KASSAMALI R, SICA D A. Acetazolamide: a forgotten diuretic agent [J]. *Cardiol Rev*, 2011, 19(6): 276-278. DOI: 10.1097/CRD.0b013e31822b4939.

[?] Li Zhongheng, Li Ruining, Ye Zhen, et al. Pathogenesis and Therapeutic Advances of Diuretic Resistance in Patients with Heart Failure [J]. *Advances in Cardiovascular Diseases*, 2024, 45(8).

[?] LI Z Q, WANG Z J, LIU N C, et al. Effect of hypertonic saline solution combined with furosemide on acute heart failure: a meta-analysis [J]. *Comput Math Methods Med*, 2022, 2022: 5728967. DOI: 10.1155/2022/5728967.

[?] COVIC A, COPUR S, TAPOI L, et al. Efficiency of hypertonic saline in the management of decompensated heart failure: a systematic review and meta-analysis of clinical studies [J]. *Am J Cardiovasc Drugs*, 2021, 21(3): 331-347. DOI: 10.1007/s40256-020-00453-7.

[?] XING F W, HU X L, JIANG J Z, et al. A meta-analysis of low-dose dopamine in heart failure [J]. *Int J Cardiol*, 2016, 222: 1003-1011.

[?] WAN S H, STEVENS S R, BORLAUG B A, et al. Differential response to low-dose dopamine or low-dose nesiritide in acute heart failure with reduced or preserved ejection fraction: results from the ROSE AHF trial (renal optimization strategies evaluation in acute heart failure) [J]. *Circ Heart Fail*, 2016, 9(8): e002593. DOI: 10.1161/CIRCHEARTFAILURE.115.002593.

[?] ZHAO X C, ZHANG D Q, SONG R J, et al. Nesiritide in patients with acute myocardial infarction and heart failure: a meta-analysis [J]. *J Int Med Res*, 2020, 48(1): 300060519897194. DOI: 10.1177/0300060519897194.

[?] VARDENY O, CLAGGETT B, KACHADOURIAN J, et al. Reduced loop diuretic use in patients taking sacubitril/valsartan compared with enalapril: the PARADIGM-HF trial [J]. *Eur J Heart Fail*, 2019, 21(3): 337-341. DOI: 10.1002/ejhf.1402.

[?] DAMMAN K, BEUSEKAMP J C, BOORSMA E M, et al. Randomized, double-blind, placebo-controlled, multicentre pilot study on the effects of empagliflozin on clinical outcomes in patients with acute decompensated heart failure (EMPA-RESPONSE-AHF) [J]. *Eur J Heart Fail*, 2020, 22(4): 713-722.

[?] BIEGUS J, VOORS A A, COLLINS S P, et al. Impact of empagliflozin on decongestion in acute heart failure: the EMPULSE trial [J]. *Eur Heart J*, 2023, 44(1): 41-50. DOI: 10.1093/eurheartj/ehac530.

[?] Zhao Li, Sun Hongmei. Effects of Levosimendan on Heart Rate Variability, Hemodynamics, and B-type Natriuretic Peptide Levels in Patients with Decompensated Heart Failure [J]. *Anhui Medical Journal*, 2017.

[?] Zheng Xiuhua, Wu Qian, Wang Shiqiang. Efficacy of Torasemide Combined with Shenmai Injection in the Treatment of Elderly Patients with Chronic Heart Failure and Its Impact on the RAAS [J]. *Chinese Journal of Gerontology*, 2019, 39(7): 1546-1548. DOI: 10.3969/j.issn.1005-9202.2019.07.003.

[?] Lu Lei, Liu Xiaodan, Fan Li, et al. Efficacy of Torasemide Combined with Shenmai Injection in the Treatment of Elderly Patients with Chronic Heart Failure and Its Impact on the RAAS [J]. *Systems Medicine*, 2022, 7(6): 29-32, 45. DOI: 10.19368/j.cnki.2096-1782.2022.06.029.

[?] Sun Yuan, Hu Zhiqiang. Effects of Qili Qiangxin Capsules Combined with Tolvaptan on Cardiac Function, NT-proBNP, and ET-1 in Patients with Chronic Heart Failure [J]. *Guangming Journal of Chinese Medicine*, 2020, 35(13): 2052-2054. DOI: 10.3969/j.issn.1003-8914.2020.13.045.

[?] Cui Ying, Zhang Hong, Xiao Jiajun. Efficacy and Safety of Shenfu Injection Combined with Recombinant Human Brain Natriuretic Peptide in the Treatment of Acute Heart Failure [J]. *Chinese Journal of Gerontology*, 2023, 43(20).

[?] Li Haitao, Zhang Qiujin. Clinical Observation of Shenfu Injection Combined with rhBNP and Furosemide in the Treatment of Acute Heart Failure [J]. *Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine*, 2025, 25(3).

[?] LÓPEZ-VILELLA R, GUERRERO CERVERA B, SÁNCHEZ-LÁZARO I, et al. Therapeutic approach in heart failure with poor diuretic response: peripheral ultrafiltration vs. conventional treatment [J]. *ESC Heart Fail*, 2023, 10(4): 2290-2297.

[?] KAZORY A. More efficient sodium removal by ultrafiltration compared to diuretics in acute heart failure; underexplored and overstated [J]. *Blood Purif*, 2016, 42(4): 279-281. DOI: 10.1159/000448391.

[?] MISRA M, VONESH E, VAN STONE J C, et al. Effect of cause and time of dropout on the residual GFR: a comparative analysis of the decline of GFR on dialysis [J]. *Kidney Int*, 2001, 59(2): 754-763. DOI: 10.1046/j.1523-1755.2001.059002754.x.

[?] MOIST L M, PORT F K, ORZOL S M, et al. Predictors of loss of residual renal function among new dialysis patients [J]. *J Am Soc Nephrol*, 2000, 11(3): 556-564. DOI: 10.1681/ASN.V113556.

[?] GUSTAFSSON F, DAMMAN K, NALBANTGIL S, et al. Inotropic therapy in patients with advanced heart failure. A clinical consensus statement from the Heart Failure Association of the European Society of Cardiology [J]. *Eur J Heart Fail*, 2023, 25(4): 457-468.

[?] CRESPO-LEIRO M G, METRA M, LUND L H, et al. Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology [J]. *Eur J Heart Fail*, 2018, 20(11): 1505-1535. DOI: 10.1002/ejhf.1236.

[?] ALI AL KHOUFI E. Outcomes of left ventricular assist devices as destination therapy: a systematic review with meta-analysis [J]. *Life*, 2025, 15(1): 53. DOI: 10.3390/life15010053.

[?] CAMPOS MUNOZ A, VOHRA S, GUPTA M. Orthostasis (archived) [EB/OL]. (2023-06-17) [2025-04-25]. (Received: 2025-05-13; Revised: 2025-08-11) (Editor: Jia Mengmeng)

Note: Figure translations are in progress. See original paper for figures.