Restricted Daily Sodium Intake as Heart Failure Management: A Systematic Review


Sebelas Maret University, Surakarta Indonesia, *Faculty of Medicine Tarumanagara University, Jakarta Indonesia

ABSTRACT

Objective: To evaluate mortality and morbidity in HF patients receiving sodium restriction.

Study Design: Systematic Literature Review (SLR) of RCTs and Cohort studies worldwide published between Jan 2013 to Jan 2023.

Methodology: We systematically selected RCTs and Cohort studies with sodium restriction as an intervention published within the last decade from five databases (PubMed, Scopus, Cochrane Library, Embase, and Medline). The full texts retrieved were assessed for risk of bias, and then a systematic review was performed. The endpoints analyzed were mortality and morbidity.

Result: Five RCTs and two cohort studies were included in this study, with 2,505 participants. The endpoints retrieved were mortality and morbidity (hospitalization, NYHA functional class, BNP or NT-proBNP level, quality of life, and congestion). No improvement was seen in mortality and hospitalization, but sodium restriction improved the rest of the morbidity indicators. Over-restricted and overconsumption of sodium intake might worsen HF presentation. When analyzed based on the HF groups, there was not enough evidence to recommend sodium dose based on ejection fraction; however, there was potentially more benefit for patients with higher NYHA classes. However, more evidence is still needed.

Conclusion: Sodium restriction did not benefit mortality and hospitalization but improved quality of life, systolic blood pressure, and BNP or NT-pro BNP levels in all HF classes.

Keywords: Heart failure, Hypertension, Management, New York heart association (NYHA) functional class, Sodium restriction.


INTRODUCTION

Heart failure (HF) is one of the leading health problems, affecting 26 million individuals globally. In Southeast Asia, nine million people are estimated to have HF. Baseline Health Research in Indonesia showed that cardiovascular disease in Indonesia reached 1.5% in prevalence, with HF still being the highest in number among adults; this is a concern because HF has the highest mortality risk in one year. In 2030, an estimated eight million people will develop HF and increase prevalence by 46%.

Standard HF drugs, including angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, β-adrenocceptor antagonists, and aldosterone receptor antagonists, are well-proven to improve the quality of life, symptoms, and longevity of HF patients. However, lifestyle modification is still needed to support pharmacological treatments.

Lifestyle changes help to relieve HF symptoms, improve day-to-day physical performance, and slow down the progression of the disease, especially in milder classes of HF. Physicians often recommend sodium restriction for dietary management, especially to correct congestion, a common sign and symptom in HF.

However, there are still disputes around limiting sodium intake in HF patients due to the varying data: Guideline for the Management of Heart Failure 2013 from American College of Cardiology/American Heart Association recommended sodium restriction to reduce congestion while Guidelines for the prevention, detection and management of heart failure in Australia 2018 mentioned that sodium restriction was not recommended because it led to worsening mortality as well as rehospitalization, and did not give significant difference in prognosis when compared to the non-restricted HF population. The lack of consistency regarding the efficacy of sodium restriction in HF hence called for high-quality synthesis of trials and cohort studies to fill in the gap.
METHODOLOGY

The systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guidelines (Figure-1). This systematic literature review included RCTs and Cohort studies worldwide published between January 2013 to January 2023.

Figure-1: PRISMA Flowchart

LITERATURE SEARCH

The study was performed using a wide and comprehensive search through medical databases: PubMed, Scopus, Cochrane Library, Embase, and Medline. The keywords used were heart failure, sodium, restriction, and intake. We included randomized controlled trials (RCTs) and cohort studies to analyze later. Reference lists and articles cited in the studies were also reviewed thoroughly and added to our analysis if they met the criteria.

STUDY SELECTION

Inclusion criteria

The studies included in this systematic review need to fit the inclusion criteria: 1) published between January 2013 and January 2023, 2) studying a population of stable chronic HF with standard care, 3) with the intervention of sodium restriction, and 4) with endpoints of mortality (all-cause or cardiovascular death) and morbidity (hospitalization, NYHA classes, NT-proBNP level, quality of life, and congestion).

Exclusion criteria

The exclusion criteria are 1) literature review studies, 2) studying hospitalized, unstable, or exacerbated HF patients, and 3) giving interventions outside of sodium restriction, fluid restriction, or diuretic drugs.

Data extraction and analysis

Authors analyzed each selected study and extracted the following data: 1) author, 2) publication year, 3) study characteristics (location/country, study design, sample size, length of follow-up period), 4) participant characteristics (type of heart failure), 5) intervention and control (daily sodium dose; fluid and diuretics dose if available), and 6) endpoints observed, which are mortality (all-cause or cardiovascular death), morbidity (hospitalization, NYHA classes, NT-proBNP level, quality of life, and congestion), and others (if available).

RESULTS

Search results

At the start of our search, we selected five electronic databases that included a total of 9,046 research articles, consisting of 472 articles from PubMed, 3,043 articles from Scopus, 349 articles from Cochrane Library, 3,511 articles from Embase, and 1,671 articles from Medline. Several 8,978 studies were removed from the title and abstract exclusion. Five duplicate records were obtained and were immediately excluded. Of the remaining 66 records assessed for eligibility, 61 were excluded during screening; these records consisted of 18 studies with irrelevant outcomes and 43 with incompatible study designs. Finally, seven studies met our inclusion and exclusion criteria, comprised of 5 RCT studies and two prospective cohort studies.

For quality assessment of the studies, we used Version 1 of the Cochrane risk-of-bias tool for randomized trials (RoB) and the Newcastle-Ottawa Scale for cohort studies. The scoring of the RoB tool was separated into individual elements. Each study was judged by "high", "low", or "unclear" risk of bias.10 The scoring of the Newcastle-Ottawa Scale is based on three domains: selection, comparability and exposure.11

The quality of the studies, as shown in Figure-2 and Table-I, was then categorized according to the overall number of stars.
The populations included in this study were from China, Mexico, the United States of America, Canada, South Korea, and Sweden, as shown in Table-III. The follow-up period ranged from three months to three years. A total of 2,505 patients were included in this analysis. All participants were adults with stable heart failure with standard therapy. Four studies used the New York Heart Association (NYHA) functional classification to classify participants, while three other studies used ejection fraction (heart failure with reduced ejection fraction, HFrEF; heart failure with preserved ejection fraction, HfP EF).

**Intervention and Control Group Characteristic**

The intervention given was sodium restriction; in one out of seven studies, the intervention included fluid restriction as well. Five studies compared two groups of intervention and control groups; one study compared three groups with high, moderate, and low sodium intake; and one study used cooking salt scores to measure daily salt intake in teaspoons.

**Mortality**

Mortality was observed in three studies, as shown in Table-IV. Doukky et al.,\textsuperscript{15} showed that, although non-significant, there was an increase in cardiac death with a hazard ratio [HR]: 1.62; 95% CI: 0.70 to 3.73; \(P=0.257\) and all-cause mortality of \(P=0.074\) in the sodium-restricted group. In accordance with that, one study by Song et al. (2014) showed a significantly lower death rate in the group with higher sodium intake in NYHA class I-II patients (HR=0.39, 95% CI 0.16 to 0.98, \(P=0.047\)). However, based on the same study by Song et al. (2014), it differed with the higher class of the NYHA (III-IV) population, which showed higher consumption of sodium had a 2.1 times risk of hospitalization (\(P=0.044\)).\textsuperscript{17} While one study by Li et al.,\textsuperscript{12} signified that there was no significant increase in all-cause mortality (HR=0.838, 95% CI 0.684 to 1.027, \(P=0.088\)) or cardiovascular death (HR=0.782,
Endosequence Root Repair Material as Pulp Capping Agent

95% CI 0.598 to 1.020, \( P=0.071 \) in lower or higher sodium intake groups.

**Morbidity**

**Hospitalization**

Results varied for the hospitalization endpoint. Hospitalization was observed in five out of seven studies, signifying that it was the most observed endpoint. Three studies showed that the non-restricted sodium group posed a significantly lower risk for HF hospitalization, in research by Doukky et al.\(^{15} \) (32.3% vs 20.0%; HR: 1.82; 95% CI: 1.11 to 2.96; \( P=0.015 \)); Li et al.\(^{12} \), that showed that patients with cooking salt score

### Table-III: Study Characteristics

<table>
<thead>
<tr>
<th>No.</th>
<th>Study design</th>
<th>Daily sodium dose</th>
<th>Observed variables</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Li et al. (2022)(^{12} )</td>
<td>Cooking salt score was used (with scoring, which was no table salt consumption= 0, 1/8 tsp= 1/4 tsp= 2, ≥1/2 tsp= 3) with 1 tsp of table salt= 2235.5 mg sodium</td>
<td>Primary endpoint: composite of cardiovascular death, HF hospitalization, and cardiac arrest. Secondary endpoint: all-cause death, cardiovascular death, HF hospitalization.</td>
<td>Patients with the score of &gt;0 had significantly lower primary endpoints and HF hospitalization, but there was no difference for cardiovascular death or all-cause death</td>
</tr>
<tr>
<td>2.</td>
<td>Ivey-Miranda et al. (2021)(^{13} )</td>
<td>Restricted (2 grams/day) vs non-restricted (3 grams/day)</td>
<td>NT-proBNP, quality of life, and blood pressure</td>
<td>There were no differences of NT-proBNP and quality of life between both groups; but it was found that consumption of ≤2.5 grams/day still improved NT-proBNP level and quality of life. Blood pressure was found lower in restricted patients (2 grams/day).</td>
</tr>
<tr>
<td>3.</td>
<td>Kalogeropoulos et al. (2020)(^{14} )</td>
<td>Restricted (1.5 grams/day) vs non-restricted (3 grams/day)</td>
<td>Food satisfaction, adherence, quality of life, NT-proBNP, hospitalization, blood pressure, and serum creatinine</td>
<td>Both groups felt satisfied with their food, with consumption of either 1.5 grams or 3 grams per day. Quality of life improved for the restricted group (1.5 grams/day). Serum creatinine was found better in the restricted group (1.5 grams/day) and was elevated from the baseline in the non-restricted group (3 grams/day). Adherence, NT-proBNP, hospitalization rate, and blood pressure were not found different between both groups.</td>
</tr>
<tr>
<td>4.</td>
<td>Doukky et al. (2016)(^{15} )</td>
<td>Restricted (&lt;2.5 grams/day) vs non-restricted (22.5 grams/day)</td>
<td>Death and HF hospitalization</td>
<td>Sodium restriction (&lt;2.5 grams/day) significantly correlated with higher risk of death and HF hospitalization.</td>
</tr>
<tr>
<td>5.</td>
<td>Colin-Ramirez et al. (2015)(^{16} )</td>
<td>Low (1.5 grams/day) vs moderate (2.3 grams/day)</td>
<td>Quality of life and BNP level</td>
<td>There was an improvement of quality of life on both intervention groups; BNP level was lower on the low sodium intake group (1.5 grams/day). There were no differences on the NYHA class between both groups.</td>
</tr>
<tr>
<td>6.</td>
<td>Song et al. (2014)(^{17} )</td>
<td>&lt;2 grams/day, 2-3 grams/day, or &gt;3 grams/day</td>
<td>Hospitalization, death, and event-free survival.</td>
<td>In NYHA I/II patients, patients who consumed &lt;2 grams/day had higher risk and patients who consumed &gt;3 grams/day had lower risk for hospitalization and death compared to 2-3 grams/day. Meanwhile, for NYHA III/IV patients, consumption of &gt;3 grams/day had shorter event-free survival; there was no differences between &lt;2 grams/day and 2-3 grams/day.</td>
</tr>
<tr>
<td>7.</td>
<td>Philipson et al. (2013)(^{18} )</td>
<td>The intervention group was given instructions on sodium diet of &lt;5 grams/day; and fluid restriction (&lt;1.5 L/day). The control group was not given restriction instruction.</td>
<td>Composite of NYHA class, hospitalization, peripheral edema, quality of life</td>
<td>The intervention group had better composite, which was mainly due to NYHA class improvement and leg edema; and there was no bad effect on thirst, hunger, or quality of life.</td>
</tr>
</tbody>
</table>

Based on NYHA functional class

<table>
<thead>
<tr>
<th>Study design</th>
<th>Daily sodium dose</th>
<th>Observed variables</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location: China; Multicenter, international, randomized, double-blind, and placebo-controlled trial; 2:3-years follow-up; 1.713 samples (propensity-matching) with HFpEF.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
>0 significantly had a lower number of HF hospitalization (HR=0.737, 95% CI 0.603 to 0.900, P=0.003); and Song et al. signified that NYHA I-II patients with lower sodium intake had lower HF hospitalization rate (HR=0.39, 95% CI 0.16 to 0.98, P=0.047). However, hospitalization was higher in the NYHA III-IV group with higher sodium intake intervention.17

However, the restricted group posed a better composite endpoint in 51% of patients, with hospitalization being one of the endpoints (P<0.001) in a study by Philipson et al. (2013)18, while Kalogeropoulos et al.14 showed that the number of hospitalizations between control and intervention group did not differ significantly.

### Quality of life (QoL)

QoL was measured in four studies. Sodium restriction significantly improved the quality of life in the restricted group when measured with the Kansas City Cardiomyopathy Questionnaire (KCCQ) score in two studies by Kalogeropoulos et al. (P<0.001) and Colin-Ramirez et al. (P=0.006)14,16. A study by Ivey-Miranda et al. might exhibit no differences between the 2-gram sodium/day group vs 3 grams/day (P=0.04) when measured with The Minnesota Living with Heart Failure Questionnaire (MLHFQ), but the scores improved when the consumption was <2.5 gram/day13. The study conducted by Philipson et al. showed an improvement in QoL scores in both restricted and non-restricted groups when measured with the Life Satisfaction Questionnaire (LiSat-11)18. However, Colin-Ramirez et al. (2015) also showed that there was an improvement in QoL in the non-restricted group, although not significant (P=0.07)16.

#### NT-proBNP or BNP Level

Two studies signified that there was no difference in NT-pro BNP level between groups, both in a study by Ivey-Miranda et al. (2021) (95% confidence interval -27 to -73%; p=0.002) and Kalogeropoulos et al. (2020) (with P=0.70 and P=0.69 for between-groups change).13,14 Colin-Ramirez et al. (2015) presented a differing result, with the low-sodium group showing a lowered BNP level (P=0.06).16

#### NYHA Class and Congestion

One study presented no significant NYHA difference between the intervention and control group (P=0.87).16 But Philipson et al. (2013) showed improved NYHA class (P=0.01) and oedema (P=0.01) in the intervention group that received <5 grams of sodium/day and fluid intake no higher than 1.5 L/day.18

### Other Endpoints

Other endpoints were observed in the seven studies included in this research. The first was blood pressure, which was used to measure the safety of the intervention. If the intervention of sodium restriction

### Table IV: Outcome Variables Observed in the Studies

<table>
<thead>
<tr>
<th>Sr</th>
<th>Studies</th>
<th>CVD death</th>
<th>All-cause mortality</th>
<th>Hospitalization</th>
<th>QoL</th>
<th>NYHA class</th>
<th>Peripheral edema</th>
<th>BNP or NT-proBNP</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Li et al. (2022)12</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Ivey-Miranda et al. (2021)13</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Kalogeropoulos et al. (2020)14</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Doukky et al. (2016)15</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Colin-Ramirez et al. (2015)16</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Song et al. (2014)17</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Philipson et al. (2013)18</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number of studies</td>
<td>2 3 5</td>
<td>4 2 1 3 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: Favoring sodium restriction group (✓)
Favoring non-sodium restriction group (✓✓)
Not showing difference between sodium restriction and non-sodium restriction groups (✓)
Notes (2): * = in HF NYHA I-II
** = in HF NYHA III-IV
*** = composite endpoint
Notes (3): CVD= cardiovascular risk; QoL= quality of life; NYHA class= New York Heart Association functional classification; BPN= blood pressure; Cr= creatinine
caused SBP to drop below 90 mmHg, the patients would be withdrawn. One study showed no significant SBP drop in the intervention \((P=0.24)\) and control group \((P=0.29)\). Another study by Ivey-Miranda et al. (2021) showed that blood pressure decreased significantly in the intervention group \((P=0.05)\) but not any lower than <90 mmHg. The second observed endpoint was creatinine level, which showed a decrease in the sodium-restricted group \((P=0.001)\).

**DISCUSSION**

Among the selected studies, the recommended dose of daily sodium consumption for HF patients is difficult to conclude due to the widely varying results. There are several reasons for the inconsistency of the result: 1) the diverse characteristics and comorbidities of the HF patients included in the studies; 2) the most used method to measure sodium intake was with diet recall, which was not a precise technique to estimate sodium consumption; 3) the lack of homogeneity of daily sodium consumption classification; and 4) not all studies considered to measure daily fluid intake and furosemide dose.

The variabilities in the results also derived from the paradox of limiting sodium consumption in HF patients. Sodium restriction initially aims to break the vicious cycle in HF that leads to excessive water retention, as shown in Figure-3. In contrast, the excessive water retention in HF that later increases circulating volume is a compensation mechanism for the low cardiac output (CO) in HF. However, this mechanism, combined with maladaptive RAAS, commonly causes congestion in HF patients that worsens morbidity and mortality.

**The recommendation based on the Ejection Fraction:**

**Heart failure with reduced ejection fraction (HFrEF)**

Two studies by Ivey-Miranda et al. (2021) and Kalogeropoulos et al. comprised of HFrEF patients. Sodium restriction of 1.5 to 2 grams/day posed no harm and even showed a possible benefit for HFrEF patients, especially for: QoL improvement; the reduction of NT-proBNP level, although insigni-ficant; and the decline of systolic blood pressure. Patients also expressed satisfaction with consuming 1.5 grams of sodium/day. In relevance to the systolic blood pressure finding, hypertension is one of the most common comorbidities in HF. Another perspective to look at sodium restriction in HF is aimed at relieving congestion and controlling blood pressure.

Sodium restriction may benefit because the serum sodium can draw and hold water intravascularly and further worsen the congestion, as shown in Figure-3. Hence, sodium restriction is one of the most common recommendations for HF patients. The argumentation behind the recommendation is that sodium restriction also acts as a diuretic, reducing intravascular volume by decreasing fluid retention in the kidney.

**Heart failure with Preserved Ejection Fraction (HFpEF)**

One study by Li et al. (2022) comprised of HFpEF patients. The study showed that overstrict sodium restriction (with a cooking salt score of 0) was proven unbeneficial by increasing the rate of HF hospitalization, although it did not significantly affect mortality. This is because low sodium diet leads to lower filtrated sodium and higher uptake of sodium in proximal tubules that cause a reduction of the sodium amount going through macula densa, stimulating the release of renin and later activating the RAAS) as shown in Figure-3. Hence, an over-strict sodium diet may trigger a counter-regulatory mechanism that decreases CO and worsens HF patients’ hemodynamics.
The recommendation based on NYHA Functional Classification

Two studies observing mortality and HF hospitality classified the participants based on their NYHA functional classification. One study with the NYHA II-III population signified that daily sodium consumption of <2.5 grams/day was associated with a higher risk of mortality or HF hospitalization. In contrast to that, the NYHA II-III population in a study by Colin-Ramirez et al. (2015) had better QoL and BNP levels outcomes in the group with lower sodium consumption of 1.5 grams/day. The varying results might be due to the need for studies to run subgroup analyses between each NYHA group.

One study by Song et al. (2014) showed that patients reacted differently to daily sodium doses based on their NYHA severity. NYHA I-II patients had better outcomes with higher sodium consumption; >3 grams of sodium/day lowered the risk of hospitalization and death, while in contrast, a dose of <2 grams of sodium/day caused a higher risk of hospitalization and death. On the contrary, NYHA III-IV patients with >3 grams of sodium/day had shorter event-free survival. Hence, low sodium intake tends to trigger a counter-regulatory mechanism (Figure-3) in lower NYHA classes. Sodium restriction is better advised for higher NYHA classes patients, especially when their congestion does not improve significantly despite being given standard HF treatment.

However, Philipson et al. (2013) showed that >5 grams of sodium/day in NYHA II-IV patients showed worse composite outcomes when compared to <5 grams/day, be it the NYHA functional class, hospitalization, peripheral oedema, and QoL. Hence, daily sodium consumption in all NYHA classes should not exceed 5 grams/day.

Our study showed that the recommendation of sodium daily dose could only be generalized among some HF patients since each HF group reacted differently to different sodium doses. Hence, physicians should tailor the sodium dose based on the HF type instead, whether based on the ejection fraction or the functional type.

Strengths and Limitations

This systematic review concluded the last decade's most recent trials and prospective cohorts. In comparison to other existing systematic reviews on the same subject, the authors discussed and analyzed endpoints based on 1) specific HF classification to reduce biased analysis due to the diverse characteristics of the HF patients included in this study and 2) sodium dosing instead of sodium grouping to limit the bias due to the inhomogeneity of the sodium restriction grouping.

However, the authors only concluded studies published in English, and the follow-up period between studies also varied widely (between three months and three years), which might contribute to endpoint bias.

CONCLUSION

Sodium restriction did not improve mortality and hospitalization in HF patients. However, it may benefit the quality of life (due to the relief of congestion and NYHA class improvement), systolic blood pressure, and BNP or NT-proBNP levels. Either very low (0 gram) or very high (>5 gram) daily sodium intake is not recommended for all HF types. The dose of daily sodium intake recommendation is still inconclusive, but the sodium restriction approach is more beneficial for HF with higher NYHA functional classes. More evidence is needed to recommend sodium dose for HF patients based on ejection fraction. For future research, we suggest running subgroup analyses so sodium recommendations can be given in an individualized manner based on HF characteristics.

Conflict of Interest: None.

Authors’ Contribution
Following authors have made substantial contributions to the manuscript as under:
1,2: Conception, study design, drafting the manuscript, approval of the final version to be published.
3,4: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.
5,6: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES


22. Yancy CW. The Uncertainty of Sodium Restriction in Heart Failure: We Can Do Better Than This. JACC Heart Fail 2016; 4(1): 39-41. https://doi.org/10.1016/j.jchf.2015.11.005


