A LITERATURE REVIEW: LOW SODIUM RESTRICTION OF PATIENTS WITH HEART FAILURE ON HOSPITAL READMISSION

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ABSTRACT

Sodium restriction effect on hospital readmission in patients with heart failure (HF) has been questioned for decades. Readmission related to low sodium intake recommendations should be changed as well as mortality. A literature review is needed to summarize the effect of low sodium, especially on readmission and mortality. This literature review aimed to summarize the prevalence of hospital readmission and mortality regarding low sodium intake in patients with HF. The searching process involved four databases; MEDLINE, Embase, EBSCO Health, Cochrane was explored for experimental studies of sodium restriction. Of 77 screened citations from 2000 to 2019 invested in patients with HF, four studies were included. Four studies from four databases were included and explained and it was found that hospital readmission was the outcome of implementing sodium restriction in patients with HF. Low sodium restriction (800 mg – 1800 mg/day) results in higher hospital readmission. Moreover, 1800 mg/day of sodium was followed by higher mortality and higher sudden death in patients with HF. Low sodium restriction did not lower hospital readmission as well as mortality of patients with HF. This article provides the reason, effect, and amount of sodium restriction in patients with HF. The recommendation from this literature review is low sodium restriction has no beneficial effect on readmission and mortality in HF conditions.

Keywords: **Heart Failure, Readmission, Sodium Restriction.**

INTRODUCTION

Heart failure (HF) is a health major problem that affected 64.34 million people around the world or can be estimated at 8.52 cases from 1.000 population in 2017 (Lippi & Sanchis-Gomar, 2020). This condition did not only happen in the high-middle countries but also increased in low-middle countries (Groenewegen et al., 2020; Lippi & Sanchis-Gomar, 2020; Lund & Savarese, 2017). HF caused an economic burden worldwide to maintain patients' health with HF (Lund & Savarese, 2017). This burden is caused by the higher cost of hospital readmission to manage HF conditions (Lippi & Sanchis-Gomar, 2020; Lund & Savarese, 2017).

The evidence of congestion is the main sign and symptom of decompensated HF in hospital admission and increasing the risk of death in patients with HF (Ponikowski et al., 2016). Congestion in HF is related to neurohormonal activity resulting in water and salt retention (Chatterjee, 2005; Hartupee & Mann, 2017). Due to this condition, patients with HF need to restrict their daily intake of sodium to reduce congestion (Ponikowski et al., 2016). Sodium restriction also benefits on maintaining HF conditions and preventing the occurrence of hypertension (d'Almeida et al., 2014). However, sodium restriction benefits on lowering mortality in patients with HF are still questioned.

Hospital readmission due to restricted sodium needs to be examined from previous studies, since, the recommendation of sodium restriction varied in several guidelines (230 – 5750 mg/day) (Gupta et al., 2012) (not excess than 6 g/day) (Ponikowski et al., 2016). Moreover, the readmission rate related to sodium restriction needs to be concluded from previous studies. Additionally, mortality will also be reviewed in this literature review. Therefore, this literature analyzes and summarizes the results of previous studies about the effect of sodium restriction related to hospital readmission and mortality in patients with HF.

METHODS

In June 2019, MEDLINE, Embase, EBSCO Health, Cochrane databases were used to search previous studies concerning sodium restriction in patients with HF with hospital readmission. Searching process is exemplified by the following PubMed/MEDLINE search strategy: ((("Heart Failure" [Mesh] AND "sodium restriction" [Mesh] OR "Diet, Sodium-Restricted" [Mesh] AND "hospital readmission"[Mesh])).

The inclusion criteria of the studies were English text, full text, randomized controlled trial (RCT), and were studied between 2000 until 2019. The exclusion of the studies included does not meet the study question, only protocol or research still in progress, and abstract only. A total of 77 studies were found with duplicated studies were 32. From title and abstract, 30 studies were excluded; and 11 studies were excluded due to their irrelevance to PICO question, non RCT, only protocol, and no full text. Finally, four studies were included in this literature review (Fig.1). Standardized critical appraisal using CONSORT 2010 Statement checklist was used.

RESULTS

The results were summarized in Table 1. and Table 2.

Study Characteristics

Four studies were included in this literature review with three studies done in Italy (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009) and one study done in Brazil (Aliti et al., 2013). All the studies were published in 2008 – 2013.

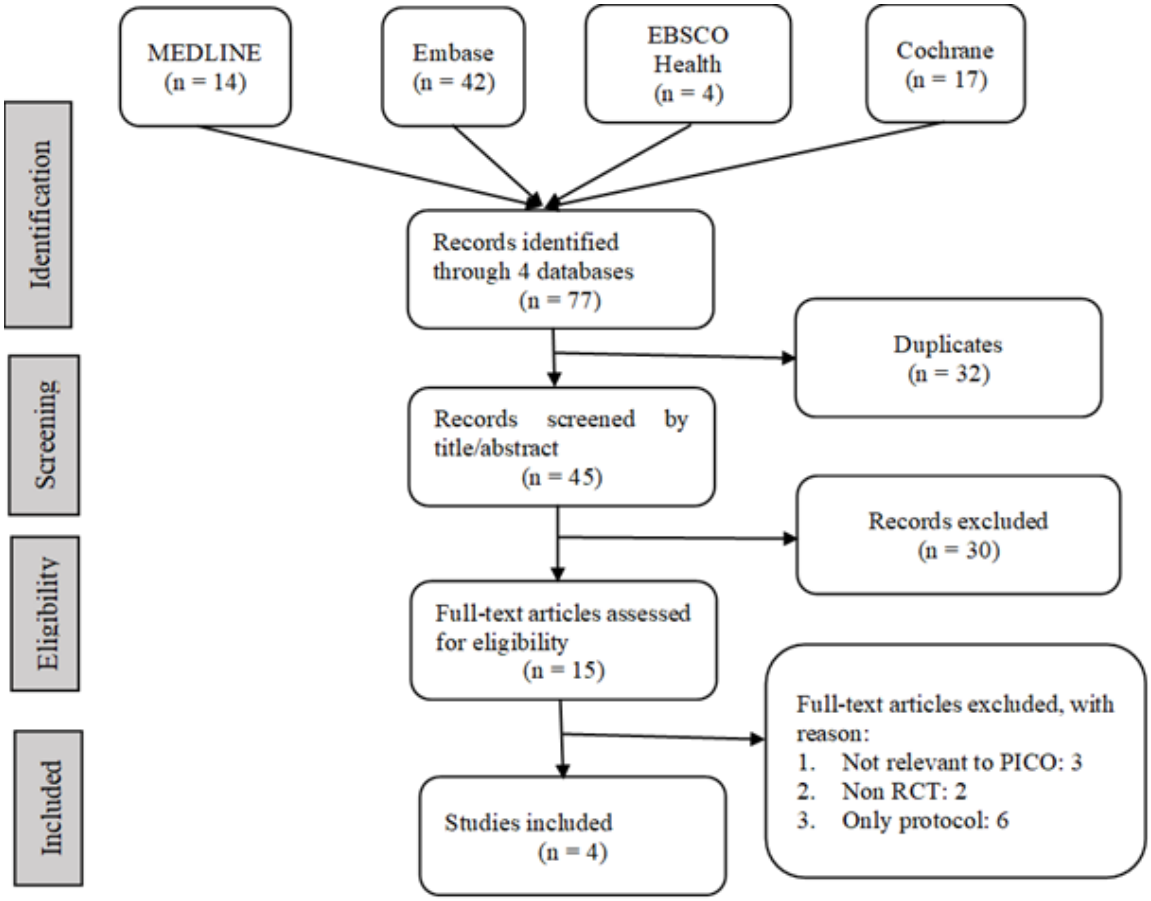

Fig.1. Article selection

Readmission was not the main outcome of (Aliti et al., 2013); three studies on brain natriuretic peptide (BNP) (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009) and two studies reported on the neurohormonal result (renin activity and aldosterone) (Paterna et al., 2008; Paterna et al., 2009).

Mortality was measured in three studies (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009). Sudden death during follow-up also was measured in three studies. All of the studies were done after discharge from the hospitalization. One study investigated patients with acute decompensated heart failure (ADHF) (Aliti et al., 2013) and three studies investigated patients with compensated heart failure (CHF) (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009). Patients with HF were followed up in 30 days until 57 months. The study design of every study was randomized and blinded. The number of total participants in each study ranged from 75 to 1927 participants. The smallest number of participants was in Brazil (Aliti et al., 2013) and the largest was in Italy (Paterna et al., 2011).

Sodium Restriction

Three studies applied low sodium restriction in the intervention group as much as 80 mmol/day (1.8 g/day) (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009), and one study applied 800 mg/day (Aliti et al., 2013). In another hand, in the control group, three studies applied 120 mmol/day (2.7 g/day) (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009) and one study applied 3-5 g/day (Aliti et al., 2013).

Demographic characteristics

The age of patients with HF in one study was younger (60 ± 11.0) (Aliti et al., 2013) than in three studies with over 70 years old (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009).

These studies had more males compared to females (Aliti et al., 2013; Paterna et al., 2011; Paterna et al., 2009). The percentage of male was 61.86% - 74% whereas one study had a lesser percentage of males < 50% (Paterna et al., 2009).

Disease-Related Characteristics

All studies provided various disease-related characteristics; however, this literature review focuses on major findings related to HF including ejection fraction, new york heart association (NYHA) class, and medications. The ejection fraction of all studies was < 40% with the lowest being 24.6% (Aliti et al., 2013). Related to NYHA class, most of the studies had participants in NYHA class III and IV, nevertheless, one study was done involving NYHA class II participants (after hospital discharge) (Paterna et al., 2009). In the medications part, in every study, there was a different medication used the most. Angiotensin-converting enzyme (ACE) inhibitors were received by all participants in the study by Paterna et al (2008), and alfa and beta-blockers were received by all participants in the study by Paterna et al (2011). Aldosterone antagonists were received by over 89% of participants in the study by Paterna et al (2009) and beta-blockers were

Table 1. Summarize the four studies on salt restriction and relationship with hospital readmission in patients with heart failure

No	Author/Design	Study Outcome	Duration of Intervention	Natrium	Major Findings
1	(Aliti et al., 2013) Randomized, blinded, parallel group	1. Weight loss 2. Clinical stability 3. Perception of thirst 4. Readmissions within 30 days. 5. Clinical result	3 and 30 days follow up	IG: 800 mg/day CG: approximately 3-5 g	1) Bodyweight is similar between two groups 2) The thirst is significantly higher on IG, (5.1 [2.9]) than in the CG (3.44 [2.0]) 3) Readmission in 30 days was similar in both group (29% vs. 19%, p = .41)
2	(Paterna et al., 2008) Randomized, blinded	1. Readmission 2. Mortality 3. Sudden death 4. Plasma BNP 5. Aldosterone levels 6. Plasma renin activity 7. Clinical result	180 days	IG: 80 mmol CG: 120 mmol	1) Readmission for worsening CHF was higher in the intervention group compared to the control group (26.32% vs. 7.63%, p < 0.05) in the primary endpoint 2) Readmission and mortality were higher in the intervention group compared to the control group (39.47 % vs. 12.71%) in the secondary endpoint 3) Sudden death was numerically higher in the intervention group than in the control group (4 vs.1)
3	(Paterna et al., 2009) Randomized, blinded	1. Readmission 2. Mortality 3. Sudden death 4. Plasma BNP 5. Plasma renin activity 6. Aldosterone levels 7. Clinical result	180 days	8 groups IG: 80 mmol (4 groups) CG: 120 mmol (4 groups)	1) Readmission in groups with sodium restriction 80 mmol had the percentage of readmission 49%, 54.9%, 71.1%, and 78.4 %. These were significantly higher than 120 mmol groups 7.69%, 29.4%, 51.9%, and 58%. 2) Mortality in 80 mmol groups were significantly higher (9.8%, 13.7%, 11.5% and 15.7%) than in 120 mmol groups (1.9%, 3.9%, 9.6%, and 12%). 3) Sudden death in 80 mmol groups were significantly higher (1.96%, 3.9%, 1.9%, and 3.9%) than in 120 mmol groups (1.9%, 0%, 1.9%, and 0%)
4	(Paterna et al., 2011) Randomized, blinded	1. Readmission 2. Mortality 3. Sudden death 4. BNP 5. Clinical result 6. Hospital time	Every week for the first month, every month for the first 6 months, and thereafter, every 3 months (57 ± 15 months)	IG: 80 mmol (4 groups) CG: 120 mmol (4 groups)	1) Readmission was significantly higher in the intervention group (34.2%) compared to control groups (18.5%) 2) Mortality was significantly higher in the intervention group (23.8%) than in the control group (12.9%) 3) Sudden death was higher in the intervention group (5.1%) than in the control group (3.5%)

Table 2. Summarize the four studies on Demographic and Diseases-Related Characteristics

Author/Characteristics	Total Sample	Intervention group	Control Group
(Aliti et al., 2013)	N = 75		
Age mean (± SD)	60 (± 11.0)	60.6 (± 10.5)	59.3 (± 12.2)
Male (%)	69	74	65
LVEF mean (SD) (%)	26.0 (± 8.7)	27.4 (± 8.9)	24.6 (± 8.4)
NYHA class III (%)	47	47	46
NYHA class IV (%)	45	42	49
Medication (beta-blockers) (%)	56	79	76
(Paterna et al., 2008)	N = 232		
Age, mean (SD)	72.6 (± 8)	73.3 (± 9)	72.1 (± 7)
Male (%)	62.06	62.28	61.86
LVEF	<35%	<35%	<35%
NYHA Class	III	III	III
Medication (ACEi) (%)	100	100	100
(Paterna et al., 2009)	N = 410		
Age, range	NA	74.3 (± 8), 75.6 (± 10), 75.7 (± 8), 75.6 (± 7)	75.6 (± 8), 76.5 (±9), 75.4 (± 8), 76.5 (± 7)
Male (%)		37.2, 35.2, 38.4, 39.2	34.6, 37.2, 38.4, 36.0
LVEF	NA	<35%	<35%
NYHA Class	<35%	II*	II*
Medication (aldosterone antagonist) (%)	II*	89.1	91.2
	NA		
(Paterna et al., 2011)	N = 1927		
Age, mean (SD)	NA	74.7 (± 11)	73.4 (± 13)
Male (%)	62.94	63.06	62.83
Left ventricular ejection fraction mean	<40%	33.7 (± 4)	34.4 (± 5)
NYHA Class	III	III	III
Medication (alfa and beta blockers) (%)	100	100	100

received by 56 participants in the study by Aliti et al (2013).

Readmission

Three studies found readmission was significantly higher on patients with HF who received low sodium restriction compared to normal sodium (Paterna et al., 2011; Paterna et al., 2008; Paterna et al., 2009), however, one study found readmission numerically higher in the group with low sodium restriction

The readmission status varied from 30 days, 180 days, and over 6 months. The readmission percentage of patients with ACHF with low sodium restriction was 29% on 30 days follow-up. In patients with CHF with low restricted sodium, the percentage of readmission was 26.325% to 78.4% on 180 days of follow-up. Moreover, the readmission percentage of patients with CHF who received low sodium restriction was 34.2% in over 54 months follow up.

Mortality

Three studies revealed the mortality rate of patients with HF who received low sodium restriction was significantly higher than patients with HF who did not receive low restricted sodium. Paterna et al (2018) revealed that the percentage of readmission and mortality in 180 days follow-up in the intervention group was 39.47%; Paterna et al (2009) found mortality in the intervention group was 9.8% - 15.7%) in 180 days of follow-up, and over 3 years of follow up, the mortality of patients who received low sodium restriction was 23.8% (Paterna et al., 2011).

Sudden death was identified in two studies (Paterna et al., 2011; Paterna et al., 2009). The trend was similar with mortality rate, with sudden death was significantly higher in intervention group control group. In 180 days of follow-up, the sudden death rate was 1.9% - 3.9%) and in over 3 years of follow-up it was 5.1%. Additionally, in Paterna et al (2008), sudden death was higher for 180 days of follow-up (4 patients in IG and 1 patient in CG).

DISCUSSION

Low sodium restriction on the intervention group in this literature review was from 800mg/day up to 1.8 g/day from four studies. This was associated with the recommendation of sodium restriction for patients with HF from the various association in the world (including the National Heart Foundation of Australia, Heart Failure Society, European Society of Cardiology, American Heart Association, Royal College of Physicians, Heart Failure Society of America, Scottish Intercollegiate Guidelines Network and American Dietetic

Association) which was between 1.4 g - < 3 per day (Gupta et al., 2012). The lower sodium restriction (< 2 g/day) was addressed for severe HF symptoms in all guidelines (Gupta et al., 2012).

Increasing neurohormonal activity in patients with HF provokes congestion due to increased sympathetic activity, elevating angiotensin II, renin, and vasopressin (Hartupee & Mann, 2017). Congestion especially pulmonary congestion as the worsening signs of HF is the reason patients with HF are admitted to the hospital (Ponikowski et al., 2016). Therefore, low sodium intake impact is not only lowering the congestion of HF, decreasing neurohormonal activity (aldosterone and renin-angiotensin), reducing blood pressure, but also decreasing pulmonary capillary wedge pressure and reducing oxidative stress (Patel & Joseph, 2020).

From the analysis of four articles, low sodium restriction did not reduce the frequency of hospital admission. Interestingly, patients with restricted sodium had higher readmission frequency in the follow-up of 30 days, 180 days, and over 3 years. However, most of the articles showed lower readmission hospitals in the usual diet of sodium (2.7 g/day and 3-5 g/day). Low sodium restriction had an adverse effect on HF conditions by activation of antidiuretic and anti-natriuretic systems. The activation of diuretic and anti-natriuretic systems elevates neurohormonal activity which contributes to increasing signs and symptoms especially congestion (Patel & Joseph, 2020). This adverse effect may contribute to readmission frequency on patients with HF.

Mortality and sudden death have a similar trend with hospital readmission from literature analysis. Patients with CHF who received low sodium restriction had higher mortality and sudden death compared to those who received the usual sodium diet. This mortality was followed up in 180 days and over 3 years after discharge from the hospital. This analysis was supported by a previous study that found that mortality was associated with cardiovascular diseases from a data survey (Cohen et al., 2006).

However, this was in contrary to a previous study suggesting that no different mortality rate in patients with HF in the community setting (Kalogeropoulos et al., 2015). The higher mortality in the lower intake of sodium group may be influenced by the direct or indirect aggravation of neurohormonal activity caused by low sodium intake. As mentioned above, aggressive sodium restriction can lead to

activating neurohormonal activity resulting in deteriorating signs and symptoms of HF condition.

CONCLUSION

Sodium restriction is recommended to lowering HF signs and symptoms especially severe HF conditions. The included articles showed those who received 2.7 -3 g/day of sodium had lower hospital readmission and mortality. The effect of sodium restriction with the exact amount has not been established yet. However, this literature has shown the effect and reason that can be used in clinical reference.

This literature has several limitations including (1) obtained articles were only from MEDLINE, Embase, EBSCO Health, and Cochrane databases (2) outcome variables were only readmission and mortality (3) the intervention was not only sodium restriction but also other intervention e.g., fluid restriction, furosemide (4) the participants were mostly in NYHA classes III and IV. Thus, the result can be generalized onto similar characteristics with this study related to the total number of participants (2664 patients with HF) and the homogeneity (demographic and HF-related factors of the participants).

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