Review Article

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Clinical Outcomes of Empagliflozin in the Treatment of Acute Heart Failure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Author`s Contribution

[1,3] Collection of data, conception of the study and participated in its design, final drafting of the manuscript, [2,5,6]design of the study and performed the statistical analysis along with drafting of manuscript,[4,7]literature search for the discussion

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ABSTRACT

Objective: To evaluate the effectiveness of empagliflozin in patients with acute heart failure by conducting a systematic review and meta-analysis of randomized controlled trials (RCTs).

Methodology: The recent systematic review and meta-analysis was conducted by following guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020. Four Electronic databases were used namely: PubMed, EMBASE, Clinicaltrials.gov and Cochrane library to find research articles. The Cochrane risk of bias tool was applied to assess the risk bias of included RCT's and the pooled analysis was conducted by using RevMan (Review Manager) software version 5.4.

Results: About 13 RCT's with 72,871 heart failure (HF) patients were analyzed to compare the effectiveness and safety of empagliflozin with placebo. The pooled analysis favored the experimental group as drug has controlled over first HF hospitalization among heart failure patients (Odds Ratio= 0.67; 0.52 to 0.876 Cl: 95%, p=0.13), total HF hospitalization among heart failure patients as (Odds Ratio=0.55; 0.42 to 0.74 Cl: 95%, p<0.00001), and total adverse events (fatal or non-fatal outcomes) among heart failure patients as (Odds Ratio=0.59; 0.40 to 0.88 Cl: 95%, p<0.00001). However, the levels of LVEF and NT-proBNP were reduced as reported through mean difference of LVEF (Mean difference= 0.41; -0.81 to 1.64 Cl: 95%, p<0.00001) and NT- proBNP among empagliflozin and placebo groups (Mean difference= -1.55; -7.00 to 3.91 Cl: 95%, p<0.00001).

Conclusion: The findings of recent study reported that empagliflozin, in comparison to placebo, reduced the frequency of first HF hospitalization, total HF hospitalization, and cardiovascular deaths or other adverse events among patients. The levels of LVEF and NT-proBNP were also reduced slightly among group receiving empagliflozin as compared to placebo.

Keywords: Empagliflozin, acute heart failure, LVEF, NT-proBNP, hospitalization rates.

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Introduction

Heart failure is reported as common cause of high morbidity and mortality rates globally. Approximately 64.3 million people are affected by heart failure globally. Among developed countries, the prevalence rates of heart failure (HF) were reported to be 2.5% of general adult population in 2017 and increasing gradually.[1] In other words, over 26 million people are suffering from heart failure (HF) till the day.[2] Due to increasing prevalence

rates, heart failure (HF) leads to high economic burden for developing and developed countries. Generally, heart failure (HF) is heterogeneous syndrome and characterized by symptoms of pulmonary crackles, elevated jugular venous pressure, and exercise fatigue.[3] As complex clinical syndrome, Heart failure (HF) is caused by structural or functional abnormalities such as impairments of ventricular filling and disruptions in systemic circulation. A number of different diseases can cause heart failure. [4, 5] The generally accepted opinion is that left ventricular ejection fraction, or LVEF, is a clinically valuable phenotypic trait that indicates underlying pathophysiological processes and therapeutic sensitivity. [6]

The optimal treatment options for heart failure (HF) patient are vast and controversial. According to the guidelines for HF patients, different treatment options such as aldosterone receptor antagonists, beta blockers, Angiotensin-converting enzyme inhibitors, and mineralocorticoids are recommended. [7, 8] However, new drugs such as vericiguat and sodium–glucose cotransporter 2 inhibitors (SGLT2i) are showing effective clinical outcomes for HF patients. Commonly, drug SGLT2i was being applied for treatment of type 2 diabetes.[9] Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a novel class of glucose-lowering medications that prevent the SGLT2 protein in the proximal convoluted tubule of the nephron in individuals with type 2 diabetes. [10] Examples of these medications are canagliflozin [11], dapagliflozin[12], and empagliflozin.[13] Currently, the effectiveness of SGLT2i has been demonstrated by comparing with placebo through clinical trials and major clinical outcomes are reduction in total HF hospitalization, all cause mortalities, and change in Nterminal pro-brain natriuretic peptide (NT-proBNP) among patients with type 2 diabetes mellitus regardless of presence or absence of heart failure (14). Among patients with type 2 diabetes, SGLT2i has reduced the frequency of heart failure hospitalization and incidence rates of mortalities by 23%.[15]

Among most used SGLT2i drugs, Empagliflozin has been proven to be effective in reducing cardiovascular mortalities, HF hospitalization, and biomarkers of HF among heart patients.[16] However, the efficacy of empagliflozin has not been well evaluated in terms of several outcomes such as change of N-terminal pro-brain natriuretic peptide (NT-proBNP) and Left ventricular ejection fraction (LVEF).[17]

The impact of Empagliflozin on heart failure patients has not been well investigated. Previous large-sample trials revealed that, when contrasted with dapagliflozin, empagliflozin produced different outcomes for an overall cardiovascular endpoint (cardiovascular deaths, non-fatal cardiac arrest, or non-fatal stroke), suggesting that different medications may have different effects.[18, 19] SGLT2i has been the main focus of previous research instead of empagliflozin [20-22] Another meta-analysis reported the outcomes of Kansas City Cardiomyopathy Questionnaire (KCCQ), cardiovascular events or hospitalization rates, and 6-min walk test (6MWT) after empagliflozin among heart failure patients by pooled analysis of seven included RCTs. [23] Hence, there is lack of comprehensive study that can evaluate the adverse events and LVEF levels along with cardiovascular events, hospitalization rates among heart failure patients. Therefore, we aimed to design a study to evaluate the effectiveness and safety of empagliflozin in patients with acute heart failure (HF) by conducting a systematic review and meta-analysis of randomized controlled trials (RCTs).

Methodology

The recent systematic review and meta-analysis was conducted by following guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020.[24] No additional ethical review was required, as the recent study was based on a systematic review and meta-analysis of already published RCT trials.

PICO Framework: Among patients with acute heart failure (HF), what are the effectiveness and safety-related outcomes of empagliflozin in comparison to placebo? The recent study used the Population Intervention Control Outcome (PICO) framework to guide the search (Table I).

Table I: PICO framework for research question of recent study.

PICO	Description
Population	Adult Patients diagnosed with acute heart failure
Intervention	Empagliflozin
Control/ comparison	Placebo
Outcome	first HF hospitalization, total HF hospitalization, reduction in LVEF, levels of NT-proBNP, and adverse cardiac events

Search Strategy: The research articles related to the study aims “Clinical outcomes of Empagliflozin in treatment of acute heart failure" were collected from different databases by using Mesh keywords. In recent systematic

review and meta-analysis, four Electronic databases were used namely: PubMed, EMBASE, Clinicaltrials.gov and Cochrane library to find research articles discussing impacts or clinical outcomes of empagliflozin among heart failure patients. The MeSH keywords used for data extraction were ("heart failure patients" OR "HF") AND ("empagliflozin" OR "Sodium–glucose cotransporter 2 (SGLT2) inhibitors") AND ("first HF hospitalization" OR "total HF hospitalization" OR "adverse events" OR "stroke"). The timeline of research was set from 2019 to June 2024.

Study Selection & Eligibility Criteria: The selection and screening of research articles were conducted in accordance with PRISMA guidelines.[25] The predefined selection criteria helped in the screening of research articles. All studies were screened independently by two authors after full text review in accordance to the selection criteria.

Inclusion Criteria: Only those research studies were included in the recent systematic review and meta-analysis that met the following criteria: 1). Discussing the study population with heart failure and cardiac risk 2). Involving the incidence of heart failure, and cardiac risks 3). Discussing the clinical outcomes of empagliflozin 4). Studies based on randomized controlled trials, 5). Studies discussing clinical outcomes of first HF hospitalization, total HF hospitalization, LVEF levels, adverse events 6). Studies with full text and published in English.

Exclusion Criteria: Only those studies were excluded that were: 1). Discussing population with diabetes and renal failure 2). Involving the incidence of other complications such as kidney failure, hypoglycemia and diabetic conditions, 3). Discussing the other SGLT2 drugs for treatment of heart failure, 4). Those studies were also excluded that reported outcomes rather than first HF hospitalization, total HF hospitalization, LVEF levels, adverse 5). Already published systematic reviews, meta-analyses, scoping reviews, literature reviews, conferences, and case studies 6). Studies with non-full-text papers or duplicated publications were published in other languages rather than English.

Data Extraction: A pre-made table was used to retrieve data from the listed research. Relevant data were taken from every study that two authors included. The extracted data included author names, year of publication, country, study design, study population & sample size, study follow-up or duration, and outcomes.

Primary Outcomes: In recent systematic review & meta-analysis, the primary outcomes were first HF hospitalization, total HF hospitalization, and reduction in LVEF, levels of NT-proBNP, and adverse cardiac events (e.g., severe hypoglycaemic events, number of genital infections, number of ketoacidosis events, and acute liver or renal injury) or death after intervention by empagliflozin among heart failure patients.

Risk of Bias Assessment: The Cochrane risk of bias tool was applied to assess the risk bias of included RCT's. The risk bias of included studies was evaluated on basis of seven domains; allocation concealment, blinding of participants, Selection bias, blinding of outcome assessment, selective reporting and other bias. The score or level of each included studies was categorized into Low risk, unclear and high risk.

Statistical Analysis: In recent systematic review and meta-analysis, the pooled analysis was conducted by using RevMan (Review Manager) software version 5.4. The Mantel-Hansel (M-H) random effect model was applied (26) for evaluation of mean difference of expected outcomes after empagliflozin and odd ratio of first or total HF hospitalization and adverse events (severe hypoglycaemic events, number of genital infections, number of ketoacidosis events, and acute liver or renal injury) were evaluated by pooled analysis. Furthermore, the I2 statistics was used to measure the heterogeneity. A significant difference was considered if the p-value > 0.05. If the I2 value was >50%, heterogeneity was considered significant.

Results

The selection and screening of research articles related to the study aims "Clinical outcomes of Empagliflozin in treatment of acute heart failure" was conducted by following PRISMA guidelines in recent systematic review and meta-analysis. From three prescribed electronic databases, about 2800 research articles were extracted after implication of search strategy. Only 834 papers were screened, and 214 articles were excluded before screening. The eligibility criteria was applied on only 449 articles and the final number of research articles that met inclusion criteria was 13, as mentioned in Figure no.1.

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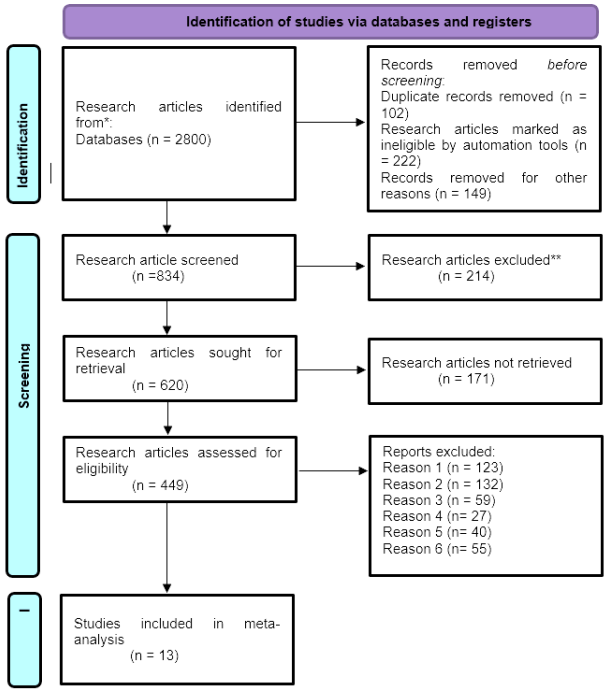

Figure 1. Screening and selection of included studies by PRISMA Guidelines.

Risk of Bias Assessment: The Cochrane risk of bias tool was used to assess the studies, and the findings are presented in Figure 2 and 3. All our studies were considered to have minimal risk of bias, indicating a high level of reliability.

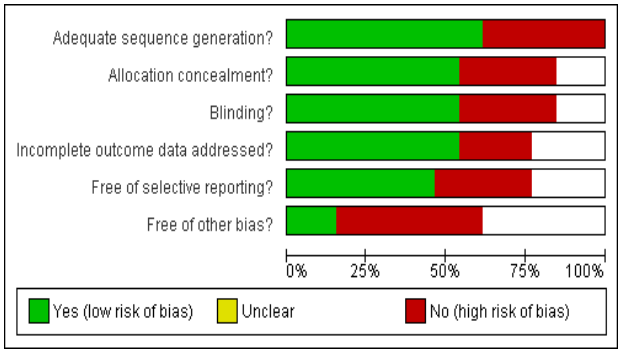

Figure 2. Graph of Risk of bias among included studies

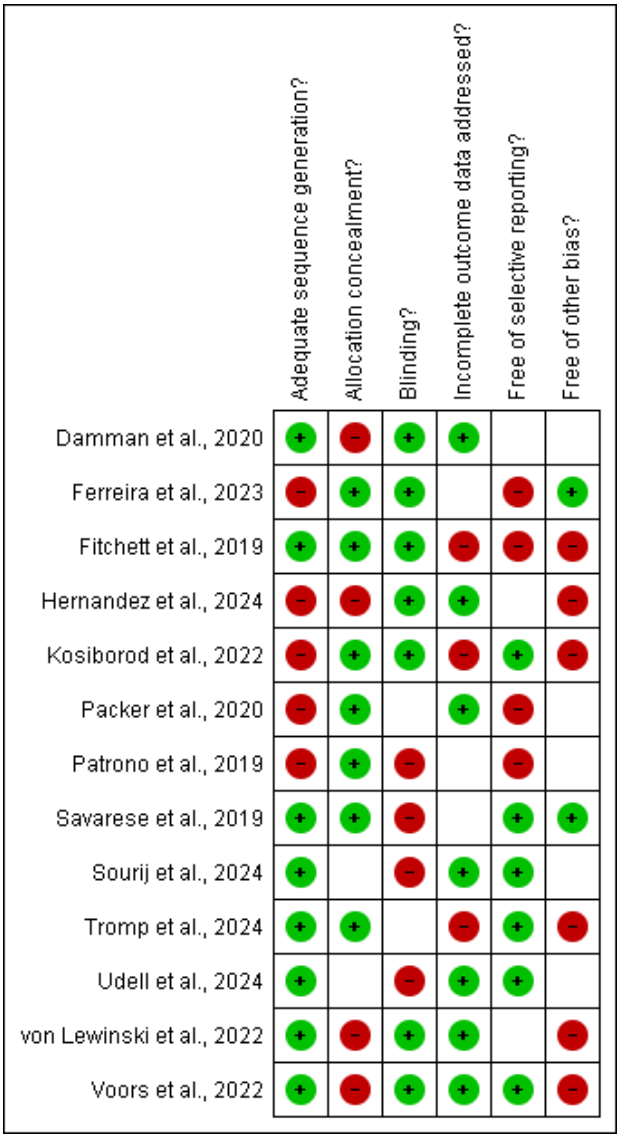

Figure 3. Graph of risk bias summary of included studies.

In recent systematic review and meta-analysis, the interventions used to reduce the rates of heart failures, was empagliflozin among patients with acute cardiac risk to evaluate its clinical outcomes. This study analyzed 13 RCTs and 72,871 heart failure (HF) patients to meet research aims. The median follow up of all included studies varied from 30 days to 18 months. To produce heterogeneity, 13 RCT's were taken from 9 different countries such as 2 from England [27, 30], 2 from Austria [28, 38], 2 from Canada [35, 37] , 2 from Netherlands ([29, 31], 1 from USA [32], 1 from Sweden [33], 1 from France [34], 1 from Australia [36] and 1 from Singapore.[39]

Table II: Characteristics of included Studies

Author, Year	Country	study population	Sample size		Study follow up	Study design	Dose of Intervention (Empagliflozin)	First HF hospitalization	Total HF hospitalization	Change in NT-proBNP	LVEF	Adverse events (>2)
Hernandez et al., 2024 (27)	England	6328 heart patients	3260 in Empagliflozin group	3262 in placebo group	17.9 months	EMPACT-MI, double-blind, randomized, placebo-controlled Trial	10 mg daily	T: 118 P: 153	T: 148 P: 207			T: 15 P: 27
von Lewinski et al., 2022 (28)	Austria	476 heart patients	237 in Empagliflozin group	239 in placebo group	26 weeks	EMMY, Randomized controlled trial	10 mg daily		T: 31 P: 32	T:-15% P: -4.4 %	T: 4.7 (3.6; 5.8) P: 2.8 (1.8; 3.9)	T: 3 P: 0
Damman et al., 2020 (29)	Netherland	80 acute HF patients	40 in treatment group	39 in placebo	30 days	Randomized multicenter double blind trial	10 mg daily	T: 2 P: 13	T: 6 P: 25	T: −46 ± 32% P: −42 ± 31%		T: 9 P: 17
Packer et al., 2020 (30)	England	3730 patients of heart failure	1863 patients in the empagliflozin group	1867 patients in placebo	52 weeks	Randomized multicenter double blind trial	10 mg daily		T: 361 P: 462	T: -12 % P: -7%		T: 187 P: 202
Voors et al., 2022 (31)	Netherland	566 HF patients	260 in empagliflozin	264 in placebo	90 days	Randomized multicenter double blind trial	10 mg daily	T: 28 P: 39	T: 36 P: 52	T: 24.07 (22.61–25.62) P: 26.77 (25.15–28.48)		T: 11 P: 22
Patrono et al., 2019 (32)	Massachusetts, USA	39063 HF patient	18 880 in empagliflozin	201 839 in placebo	5.3 months	EMPRISE Study, Randomized multicenter double blind trial	10 mg daily		T: 1482 P: 31758			
Savarese et al., 2019 (33)	Sweden	7020 HF patients	4687 in empagliflozin	2333 in placebo	6 months	EMPA-REG OUTCOME trial	10 or 25 mg daily		T: 221 T: 95			T: 520 P: 551
Ferreira et al., 2023 (34)	France	530 HF patients	114 in empagliflozin	140 in placebo	90 days	EMPULSE, randomized controlled trial	10 mg daily	T: 17 P: 27	T: 34 P: 42		T: −1.9 (−2.3, −1.5) P: −1.0 (−1.6, −0.5)	T: 7 P: 11
Fitchett et al., 2019 (35)	Canada	7020 HF patients	3048 in empagliflozin	1518 in placebo	12 month	EMPA-REG OUTCOME Trial	10 mg daily	T: 3 P: 4	T: 191 P: 358			T: 3 P: 7
Kosiborod et al., 2022 (36)	Australia	530 HF patients	265 in treatment	265 in placebo	90 days	EMPULSE Trial	10 mg daily			T: 22 % P: 13%		T:19 P: 21
Udell et al., 2024 (37)	Canada	6,522 HF patients	2,648 patient	2,181 in placebo	17.9 months	EMPACT-MI, randomized controlled trial	10 mg daily	T: 118 P; 153	T: 153 P: 297		T: -9.7 P: -0.5	
Sourij et al., 2024 (38)	Austria	476 HF patients	42 patients in empagliflozin	195 in placebo	26 weeks	EMMY, randomized controlled trial	10 mg daily				T: −0.469 C: -0.67	
Tromp et al., 2024 (39)	Singapore	530 HF patients	182 in treatment	172 in placebo	90 days	EMPULSE Randomized controlled trial	10 mg daily		T: 19 P: 31	T: 27% P: 23		T: 8 P: 11

Primary Outcomes

First HF hospitalization: Among the 13 included studies, 6 studies discussed the first heart failure hospitalization rates during varying follow up (max. 18 months and min. 30 days) after empagliflozin in comparison to placebo. [27, 29, 31, 34, 35, 37] The pooled analysis favored the experimental group as drug has controlled over first HF hospitalization among heart failure patients as (Odds Ratio=0.67; 0.52 to 0.876 Cl: 95%, p=0.002) and heterogeneity was found (df = 5; I2 = 42%), as shown in figure 4. The symmetrical distribution in funnel plot showed the low risk bias among included studies as shown in Figure 5.

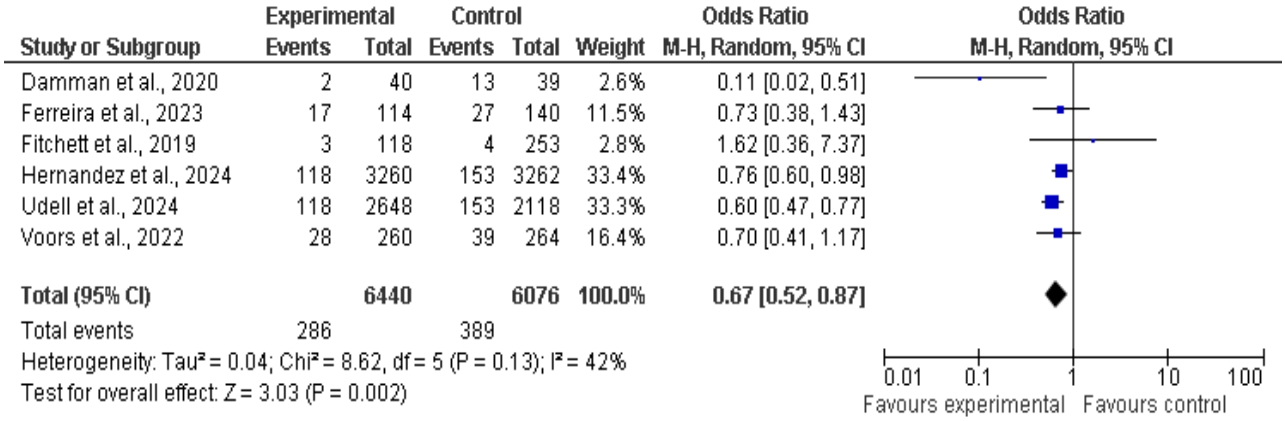

Figure 4: Forest plot of first HF hospitalization among empagliflozin and placebo groups

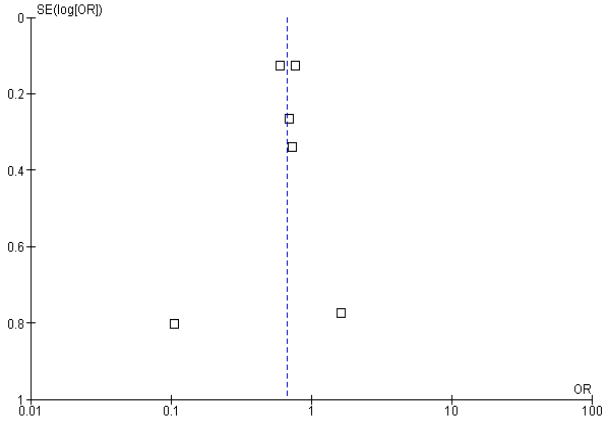

Figure 5: Funnel plot of first HF hospitalization among empagliflozin and placebo groups

Total Hospitalization rates

Among the 13 included studies, 11 studies discussed the total HF hospitalization rates during varying follow up (max. 18 months and min. 30 days) after empagliflozin in comparison to placebo.[27-35, 37, 39] The pooled analysis favored the experimental group as drug has controlled over total HF hospitalization among heart failure patients as (Odds Ratio=0.55; 0.42 to 0.74 Cl: 95%, p<0.0001) and heterogeneity was found (df = 10; I2 = 95%), as shown in figure 6. The slight symmetrical distribution in funnel plot showed moderate risk bias in included studies in Figure 7.

Change in NT-proBNP

Among the 13 included studies, 6 studies discussed the change in NT-proBNP levels during varying follow up (max. 18 months and min. 5 months) after empagliflozin in comparison to placebo (28-31, 36, 39). There was slight difference in NT- proBNP among empagliflozin and placebo groups (Mean difference= -1.55; -7.00 to 3.91 Cl: 95%, p=0.58), and heterogeneity was found (df = 5; I2 = 100%), as shown in figure 8. The symmetrical distribution in funnel plot showed low risk bias among included studies and their findings, as shown in Figure 9.

Change in LVEF

Among the 13 included studies, 6 studies discussed the changes in LVEF for varying follow up (max. 18 months and min. 30 days) after empagliflozin in comparison to placebo (28, 34, 37, 38).There was slight difference in LVEF among empagliflozin and placebo groups (Mean difference= 0.41; -0.81 to 1.64 Cl: 95%, p<0.00001), and heterogeneity was found (df = 2; I2 = 99%), as shown in figure 10. The symmetrical distribution of studies on funnel plot showed low risk bias as shown in Figure 11.

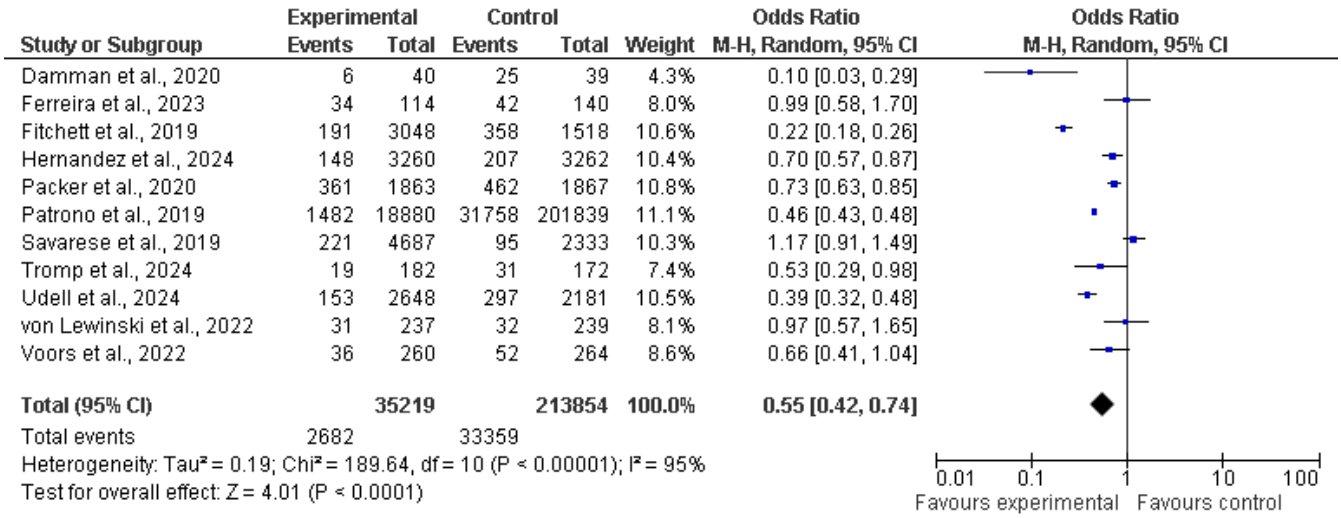

Figure 6. Forest plot of Total HF hospitalization after empagliflozin as compared to placebo.

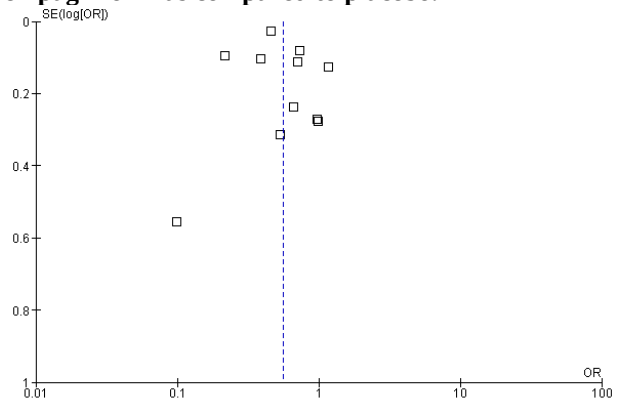

Figure 7. Funnel plot of Total HF hospitalization after empagliflozin as compared to placebo.

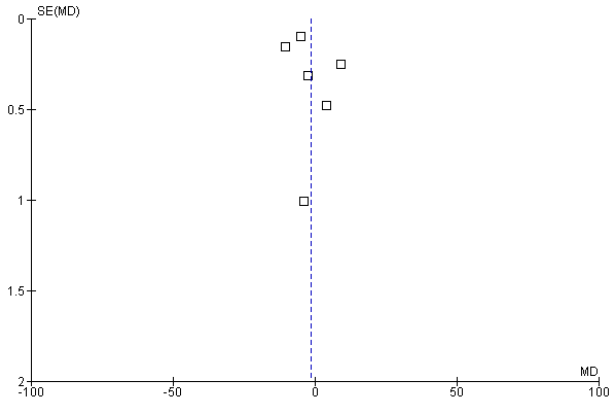

Figure 9: Funnel plot of mean difference of NT-proBNP among empagliflozin and placebo groups.

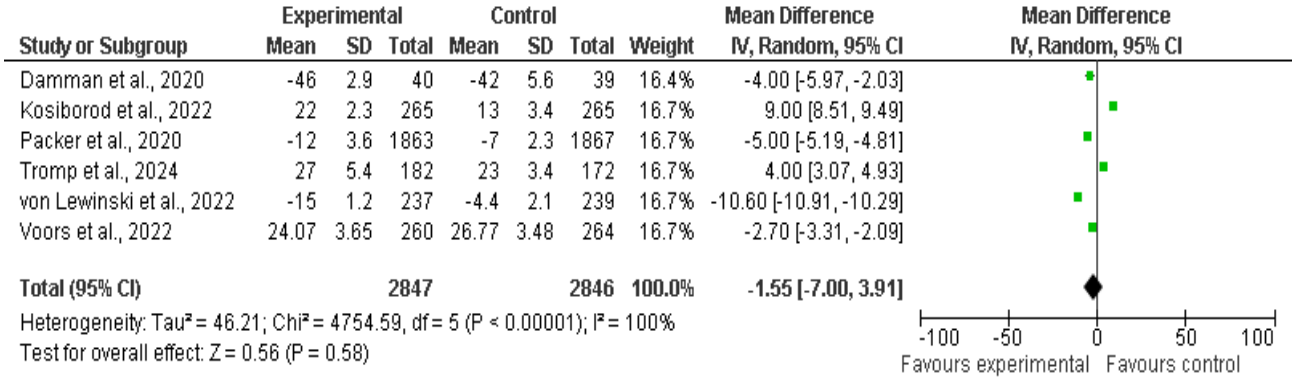

Figure 8: Forest plot of mean difference of NT-proBNP among empagliflozin and placebo groups

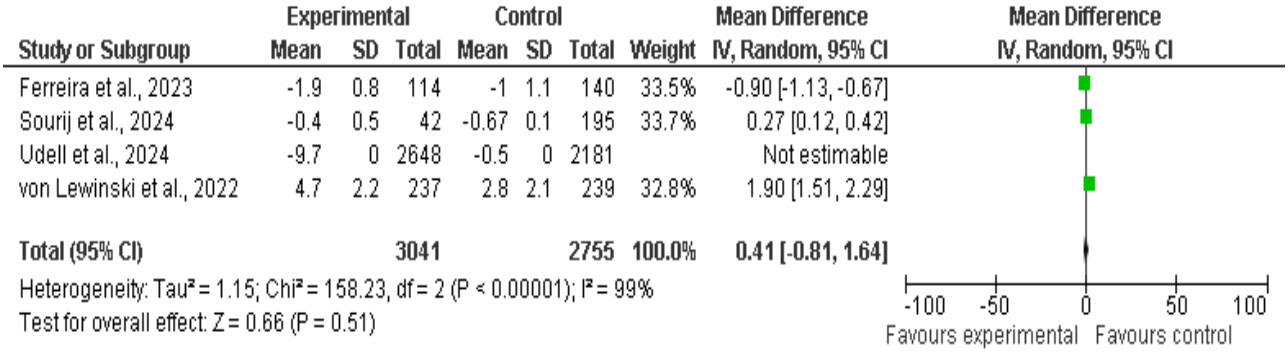

Figure 10. Forest plot of mean difference of LVEF among empagliflozin and placebo groups.

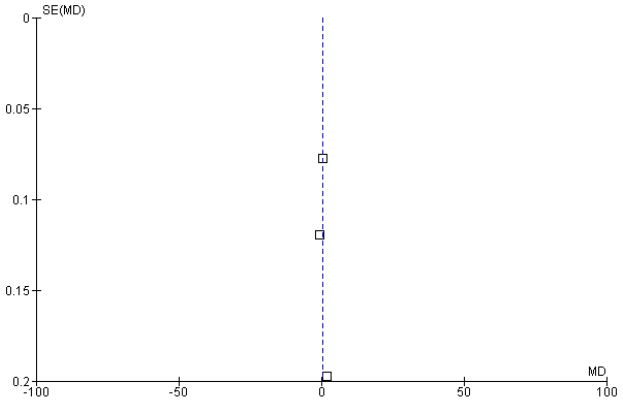

Figure 11: Funnel plot of mean difference of LVEF among empagliflozin and placebo groups.

Adverse Events

Among the 13 included studies, 10 studies discussed the adverse events (e.g., severe hypoglycaemic events, number of genital infections, number of ketoacidosis events, and acute liver or renal injury) as outcomes during varying follow up (max. 18 months and min. 30 days) after empagliflozin in comparison to placebo.[27-31, 33-36, 39] The pooled analysis favored the experimental group as drug has controlled over total adverse events among heart failure patients as (Odds Ratio=0.59; 0.40 to 0.88 Cl: 95%, p=0.009) and heterogeneity was found (df = 10; I2 = 82%), as shown in Figure 12. The symmetrical distribution of studies on funnel plot showed low risk bias as shown in Figure 13.

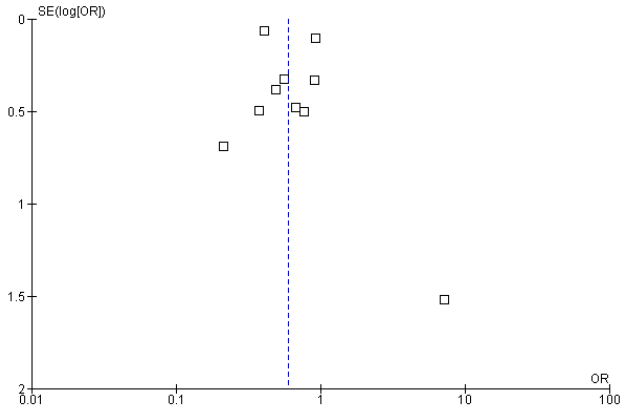

Figure 13: Funnel plot of adverse events among empagliflozin and placebo

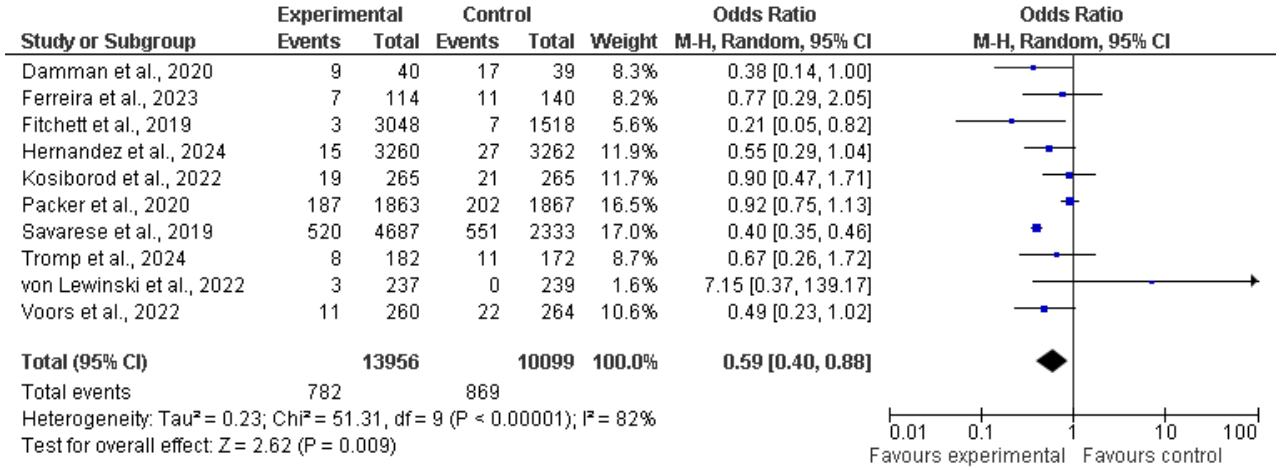

Figure 12. Forest plot of adverse events among empagliflozin and placebo.

Discussion

In recent systematic review and meta-analysis, in total 13 RCT's with 72,871 heart failure (HF) patients were analyzed to compare the effectiveness and safety of empagliflozin with placebo. The primary outcomes of first HF hospitalization, total HF hospitalization, change in NT-proBNP, change in LVEF and adverse events (death) were analyzed in recent study through pooled analysis. The empagliflozin group showed significant reduction in frequency of first HF hospitalization, total HF hospitalization and adverse events while the levels of LVEF and NT-proBNP were also changed in comparison to placebo. The pooled analysis favored the experimental group as drug has controlled over first HF hospitalization among heart failure patients (Odds Ratio= 0.67; 0.52 to 0.876 Cl: 95%, p=0.13), total HF hospitalization among heart failure patients as (Odds Ratio=0.55; 0.42 to 0.74 Cl: 95%, p<0.00001), and total adverse events among heart failure patients as (Odds Ratio=0.59; 0.40 to 0.88 Cl: 95%, p<0.00001). However, the levels of LVEF and NT-proBNP were reduced as reported through mean difference of LVEF (Mean difference= 0.41; -0.81 to 1.64 Cl: 95%, p<0.00001) and NT- proBNP among empagliflozin and placebo groups (Mean difference-1.55; -7.00 to 3.91 Cl: 95%, p<0.00001) [13-24]

Empagliflozin is often used for patients with HF, regardless of LVEF, after being approved by the U.S. Food and Drug Administration (FDA) in February 2022 to lower the risk of cardiovascular death and hospitalization.[40] SGLT2i are found at the early proximal tubule surface or boundary, where they reabsorb almost all of the filtered glucose.[40, 41] The promotion of glucose excretion resulted in a drop in blood glucose levels. In a cohort study, lower blood glucose levels were linked to a decreased death rate from heart failure. Nevertheless, as alternative antidiabetic medications with larger effects did not demonstrate the same coronary beneficial effects, the outcome cannot be fully explained by reduced blood glucose. SGLT2i also inhibits glucose reabsorption in the proximal tubule, which contributes to secondary mechanical effects, which in turn cause natriuretic and diuretic consequences. [42]

The first clinical trial related to efficacy of SGLT2 inhibitors was reported by EMPA-REG-OUTCOME and primary endpoints were total heart failure hospitalizations, first HF hospitalization, and all cause mortalities within 1-3 months of first heart failure events.[19] The first retrospective clinical trial to assess the therapeutic advantages of SGLT2 inhibitors across patients with severe heart failure (HF) was the EMPA-RESPONSE-AHF experiment. Eighty patients with acute heart failure, regardless of whether they had type 2 diabetes mellitus, were randomly assigned to either the control group or the 10 mg/day empagliflozin group in this double-blind, randomized, placebo-based, parallel-group study conducted across multiple centers. All medication was given within 24 hours of admission.[15] Remarkably, the advantages were consistent across all groupings, even those with ventricular ejection fractions of 40% or higher and reduced chronic heart failure. The patients were considered to have responded well to the technique and it proved safe. [17]

Pan et al. [23] evaluated the clinical outcomes of empagliflozin in treating patients with acute heart failure (HF) by 2021 through systematic review and meta-analysis. Through 7 RCT's and 5150 heart failure (HF) patients, the clinical outcomes of empagliflozin such as all cause mortalities, Kansas City Cardiomyopathy Questionnaire (KCCQ), total HF hospitalization were evaluated by using pooled analysis. The results imply that empagliflozin was successful in lowering a composite of hospitalization for increasing heart failure or cardiac arrest. Another meta-analysis based study by Mouffokes et al., [43] reported the effects of empagliflozin on cardiac outcomes among patients with acute heart failure (HF) patients and type 2 diabetes mellitus after myocardial infraction. With five RCT's and 571 heart failure patients, the clinical trial evaluated the change in LVEF, left ventricular end-diastolic volume (LVEDV) and NT-proBNP. However, this study ignored the improvements in total HF hospitalization, all cause mortalities and hypoglycemic conditions as clinical outcomes. The findings of study reported that echocardiographic variables may be improved in diabetic patients who have experienced acute MI by starting empagliflozin.[44] However, in this patient population, empagliflozin may not be beneficial for

preventing heart failure or providing optimal glycemic control.

Till the day, recent systematic review and meta-analysis is only study that focused on effectiveness and safety of empagliflozin among heart failure patients by including 13 RCT's. the study reported the major clinical outcomes such as first HF hospitalization, total HF hospitalization, adverse events, change in LVEF and NT-proBNP that were not studied before.[23, 43] As a result, our findings offered more reliable and thorough data to assess empagliflozin's impact on HF. Hospitalizations for heart failure and cardiovascular mortality showed notable declines. Our study, however, demonstrated a larger odd ratio reduction than the previous meta-analysis concerning the two outcomes of a composite of cardiac arrest and hospitalization for worsening heart failure. This finding may suggest that empagliflozin is better in patients with reduced ejection fraction. Thus, there was controversy about the NT-proBNP results. Nevertheless, our results are stronger because the pooled results include fresh, high-standard studies.

There are numerous advantages of recent systematic review and meta-analysis, but few limitations also exist. Firstly, we focused only on RCT's of empagliflozin that were involving only patients with HF, by excluding the RCT's of type 2 diabetes mellitus and renal failure. Secondly, the study follow up were not uniform among all included studies that can disrupt the clinical outcomes of intervention. Thirdly, the number of RCT's were not enough to evaluate or analyze the Kansas City Cardiomyopathy Questionnaire (KCCQ), MWT and New York Heart Association (NYHA) functional class, so we ignored these clinical outcomes of drug. Fourthly, the reported findings were presented in different formats in each trial, and the conversion to a standard format might have added some error. However, we adjusted the results based on pertinent articles to reduce errors as much as feasible.

Conclusion

The findings of recent study reported that empagliflozin, in comparison to placebo, reduced the frequency of first HF hospitalization, total HF hospitalization, and cardiovascular deaths or other adverse events among patients. The levels of LVEF and NT-proBNP were also reduced slightly among group receiving empagliflozin as compared to placebo. However, there is need t compare empagliflozin with other SGLT2 inhibitors-based drugs through subgroup analysis to get more beneficial results. Furthermore large-scale RCTs are needed to assess the long-term efficacy and safety of empagliflozin in patients with HF.

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