

Assessment of Health Status of Patients with Symptomatic Heart Failure Receiving SGLT2 inhibitors using KCCQ12

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Abstract

Heart failure with reduced ejection fraction (HFrEF) remains a major public health challenge, leading to significant morbidity and mortality. The Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12) is a validated tool for assessing the health status of heart failure patients. Sodium-glucose cotransporter-2 (SGLT2) inhibitors have emerged as a novel therapeutic approach, improving cardiovascular outcomes. However, their impact on patient-reported quality of life needs further evaluation, especially in the Indian population.

Objective: To evaluate the health status of patients with symptomatic HFrEF receiving SGLT2 inhibitors using KCCQ-12, focusing on improvements in physical limitations, symptom frequency, quality of life, and social limitations.

Methods: A prospective case-control study was conducted at GSVM Medical College, Kanpur, over two years. A total of 84 patients with HFrEF were enrolled and assessed at three visits: baseline (Visit 1), after one

month of standard care (Visit 2), and after six months of SGLT2 inhibitor therapy (Visit 3). KCCQ-12 domain scores were analysed using paired t-tests and Wilcoxon signed-rank tests.

Results: Significant improvements were observed in all KCCQ-12 domains

| Domains | V1 → V2 (%) | V2 → V3 (%) | Cumulative V1 → V3 (%) |
|---------|-------------|-------------|------------------------|
| SS | 31.1 | 17.5 | 60.4 |
| SF | 31.1 | 17.6 | 60.4 |
| PL | 31.1 | 17.6 | 60.4 |
| SL | 31.0 | 17.7 | 60.2 |
| QL | 31.1 | 17.6 | 60.4 |

Improvement Patterns Visit 1→2: Consistent ~31% improvement across all domains, reflecting strong initial treatment response. Visit 2→3: ~17.6% further gains, showing continued but slower progression. SF/PL equivalence: Identical trajectories confirm these domains measure overlapping constructs in this cohort. Total cumulative improvement from Visit 1 to 3 ranged 54-

62% across domains, with paired t-tests confirming statistical significance ($p < 0.0001$) for both intervals.

This result correlating with improved functional and symptomatic status.

Conclusion: SGLT2 inhibitors significantly enhance the quality of life, reduce symptom burden, and improve functional capacity in patients with HFrEF, as measured by KCCQ-12. These findings reinforce their role as an essential therapy in heart failure management.

Keywords: Heart failure, HFrEF, SGLT2 inhibitors, KCCQ-12, quality of life, symptom frequency, physical limitation, social limitation

Introduction

Heart failure (HF) is a growing global health challenge, driven by an aging population, improved post-myocardial infarction survival, and advancements in cardiovascular care. It is defined by ACCF/AHA and HFSA as a complex clinical syndrome resulting from structural or functional impairment of ventricular filling or ejection, leading to dyspnea, fatigue, and fluid retention.¹ HF severity is commonly assessed using the New York Heart Association (NYHA) functional classification and the ACC/AHA staging system.

Epidemiological data indicate that nearly half of all HF patients present with reduced ejection fraction (HFrEF; $EF \leq 40\%$). Globally, more than 26 million individuals are affected, and in the United States alone, over 6.2 million adults are living with HF.²

In India, HF occurs almost a decade earlier than in high-income countries, with a high one-year mortality rate of about 25% as reported by the National Heart Failure Registry. The increasing prevalence of hypertension, diabetes, obesity, coronary artery disease, and rheumatic heart disease further contributes to the rising HF burden.³ Patients with HF experience significant physical and emotional symptoms that impair daily functioning and

quality of life, often leading to recurrent hospitalizations. Early detection and effective management are essential to improving outcomes.

Sodium-glucose cotransporter-2 (SGLT2) inhibitors—initially developed for diabetes—have emerged as a major advancement in HF therapy. Agents such as dapagliflozin and empagliflozin improve symptoms, reduce HF hospitalizations, and lower cardiovascular mortality in patients with HFrEF, irrespective of diabetic status. However, clinical outcomes alone do not fully capture the patient's lived experience with HF.

The Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12) is a validated, patient-reported tool assessing physical limitation, symptom frequency, quality of life, and social limitation. It provides a comprehensive measure of health status and treatment response. Changes in KCCQ-12 scores offer valuable insight into patient-centered outcomes beyond biomarkers and imaging.⁴

Most evidence on SGLT2 inhibitors is derived from Western populations, and data regarding patient-reported outcomes in Indian HF patients remain limited. Given the younger age of onset and higher disease burden in India, evaluating health status using KCCQ-12 is particularly relevant.

This study aims to assess the impact of SGLT2 inhibitors on the health status of patients with HFrEF in North India, helping bridge existing knowledge gaps and supporting more patient-centered HF management strategies.

Aim and objective

Assessment of health status of patients with symptomatic heart failure receiving SGLT2 inhibitors using (KansasCity Cardiomyopathy Questionnaire) KCCQ12

Materials and methods

This open label case control study was conducted at K.P.S. PG institute of medicine, department of

Endocrinology GSVSPGI and L.P.S. institute of cardiology, GSVM medical college, Kanpur over a period of 2 years. Participants were selected during the study duration from medicine OPD Endocrinology OPD, Cardiology OPD of GSVM medical college Kanpur based on patients who fulfilled the inclusion criteria. Initial investigation were done and patients were assessed for any other comorbidities, all the procedures were explained to the participants and counselled on the treatment for heart failure. During the screening at visit 1(baseline) when patient is newly diagnosed as HFrEF, KCCQ12 scoring was done, and add standard treatment of care (SOC). Asked patient to follow up after 1 month of SOC, at visit 2 assess KCCQ12 score and add SGLT2 inhibitor (Dapagliflozin 10mg OD dose). Asked patient to follow up after 6month of SOC+SGLT2 inhibitor, this is the visit 3 or last visit of the study and assess KCCQ12 score. A total 126 patients were screened for this study out of which 92 patients were selected based on inclusion and exclusion criteria, 3patients loss to follow up after visit 1 and 5patients loss to follow up after visit 2. So effective sample size came out to be 84.

Inclusion criteria

1. Male or female patients age >40 years
2. Documented diagnosis of symptomatic heart failure (NYHA class II-IV) at enrolment, and a medical history of typical symptoms/signs of heart failure >=6 wk before enrolment with at least intermittent need for diuretic treatment.
3. Left Ventricular Ejection Fraction (LVEF) <40%.
4. NT-pro BNP >300 pg/ml at Visit 1 for patients without ongoing atrial fibrillation/flutter. If ongoing atrial fibrillation/flutter at Visit 1, NT-pro BNP must be >600 pg/mL.
5. Patients may be ambulatory, or hospitalized; patients must be off intravenous heart failure therapy

(including diuretics) for at least 12 hours prior to enrolment and 24 hours prior to randomization.

Exclusion criteria:

1. Receiving therapy with an SGLT2 inhibitor within 4 weeks prior to randomisation or previous intolerance to an SGLT2 inhibitor
2. Type 1 diabetes mellitus.
3. eGFR <25ml/min/1.73m² at 1st visit
4. Systolic blood pressure <95mmHg on 2 consecutive measurement at 5 min interval at visit 1 or at visit 2.
5. Systolic BP>160 mmHg if not on treatment with >=3 blood pressure lowering medications or >=180 mmHg irrespective of treatment, on 2 consecutive measurement at 5-minute intervals, at Visit 1 or at Visit 2
6. MI, unstable angina, coronary revascularization (percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), ablation of atrial flutter/fibrillation, valve repair/replacement within 12 weeks prior to enrolment. Before enrolment, these patients must have their qualifying echocardiography and/or cardiac MRI examination at least 12 weeks after the event.
7. Planned coronary revascularization, ablation of atrial flutter/fibrillation and valve repair/replacement.
8. Stroke or transient ischemic attack (TIA) within 12 weeks prior to enrolment
9. Probable alternative or concomitant diagnoses which in the opinion of the investigator could account for the patient's HF symptoms and signs (e.g. anaemia, hypothyroidism)
10. Body mass index >50 kg/m²
11. Primary pulmonary hypertension, chronic pulmonary embolism, severe pulmonary disease including COPD (i.e., requiring home oxygen, chronic nebulizer therapy or chronic oral steroid therapy, or

hospitalisation for exacerbation of COPD requiring ventilatory assist within 12 months prior to enrolment)

12. 12.Previous cardiac transplantation, or complex congenital heart disease. Planned cardiac resynchronisation therapy.
13. HF due to any of the following: known infiltrative cardiomyopathy (e.g. amyloid, sarcoid, lymphoma, endomyocardial fibrosis), active myocarditis, constrictive pericarditis, cardiac tamponade, known genetic hypertrophic cardiomyopathy or obstructive hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D), or uncorrected primary valvular disease
14. A life expectancy of less than 2 years due to any non-cardiovascular condition, based on investigator's clinical judgement.
15. Active malignancy requiring treatment (with the exception of basal cell or squamous cell carcinomas of the skin).
16. Acute or chronic liver disease with severe impairment of liver function (e.g., ascites, oesophageal varices, coagulopathy)

17. Women of child-bearing potential (i.e. those who are not chemically or surgically sterilised or post-menopausal) not willing to use a medically accepted method of contraception considered reliable in the judgment of the investigator OR who have a positive pregnancy test at randomisation OR who are breast-feeding
18. Previous randomisation in the present study
19. Participation in another clinical study with an IP or device during the last month prior to enrolment.

Intervention

During the screening at visit 1(baseline) when patient is newly diagnosed as HFrEF, KCCQ12 scoring was done, and add standard treatment of care (SOC). Asked patient to follow up after 1 month of SOC, at visit 2 assess KCCQ12 score and add SGLT2 inhibitor (Dapagliflozin 10mg OD dose). Asked patient to follow up after 6month of SOC+SGLT2 inhibitor, this is the visit 3 or last visit of the study and assess KCCQ12 score.

Results

| Domains | N | Visit 1 Mean±2SD (95% CI) | Visit 2 Mean±2SD (95% CI) | Visit 3 Mean±2SD (95% CI) | p(V1vsV2) | p(V2vsV3) |
|---------|----|---------------------------|---------------------------|---------------------------|-----------|-----------|
| SS | 84 | 46.92±28.28(43.90-49.95) | 61.53±18.42(59.56-63.50) | 72.32±17.89(70.41-74.23) | <0.0001 | <0.0001 |
| SF | 84 | 14.08±8.48(13.17-14.98) | 18.46±5.53(17.87-19.05) | 21.70±5.37(21.12-22.27) | <0.0001 | <0.0001 |
| PL | 84 | 14.08±8.48(13.17-14.98) | 18.46±5.53(17.87-19.05) | 21.70±5.37(21.12-22.27) | <0.0001 | <0.0001 |
| SL | 84 | 7.04±4.24(6.59-7.49) | 9.23±2.76(8.93-9.53) | 10.85±2.68(10.56-11.14) | <0.0001 | <0.0001 |
| QL | 84 | 11.73±7.07(10.98-12.49) | 15.38±4.60(14.89-15.88) | 18.08±4.47(17.60-18.56) | <0.0001 | <0.0001 |

Results Based on the Statistical Analysis Table

The analysis of the four domains—Physical Limitations, Social Limitations, Symptom Frequency, and Quality of Life—across three visits shows significant improvements in patients' health status over time.

Physical Limitation: The mean score increased from 14.08 ± 8.48 (Visit 1) to 18.46 ± 5.53(visit 2) and 21.70 ±

5.37 (Visit 3). The median values followed a similar trend (14.08→ 18.46 → 21.70), showing a clear improvement in physical ability. The p-values (< 0.0001) indicate statistically significant differences between all visits, confirming that patients experienced a substantial reduction in physical limitations.

Social Limitations: The mean score increased from 7.04 ± 4.24 (Visit 1) to 9.23 ± 2.76 (Visit 2) and 10.85 ± 2.68 (Visit 3). Median values also improved ($7.04 \rightarrow 9.23 \rightarrow 10.85$), suggesting better social participation and fewer restrictions over time. The p-values show significant improvement between visits, indicating that patients became more socially active as their condition improved.

Symptom Frequency: The mean score increased from 14.08 ± 8.48 (Visit 1) to 18.46 ± 5.53 (Visit 2) and 21.70 ± 5.37 (Visit 3). The median values ($14.08 \rightarrow 18.46 \rightarrow 21.70$) reflect reduced symptom frequency and better

symptom control. The significant p-values confirm that symptom burden decreased substantially across visits.

Quality of Life: The mean score increased from 11.73 ± 7.07 (Visit 1) to 15.38 ± 4.60 (Visit 2) and 18.46 ± 5.53 (Visit 3). The median values ($11.73 \rightarrow 15.38 \rightarrow 18.46$) show consistent improvement in patient-perceived quality of life. The highly significant p-values reinforce that the improvements are statistically meaningful. To determine which domain showed the maximum benefit, we can compare the percentage improvement from Visit 1 to Visit 3 using the median values:

| Domains | V1 \rightarrow V2 (%) | V2 \rightarrow V3 (%) | Cumulative V1 \rightarrow V3 (%) |
|---------|-------------------------|-------------------------|------------------------------------|
| SS | 31.1 | 17.5 | 60.4 |
| SF | 31.1 | 17.6 | 60.4 |
| PL | 31.1 | 17.6 | 60.4 |
| SL | 31.0 | 17.7 | 60.2 |
| QL | 31.1 | 17.6 | 60.4 |

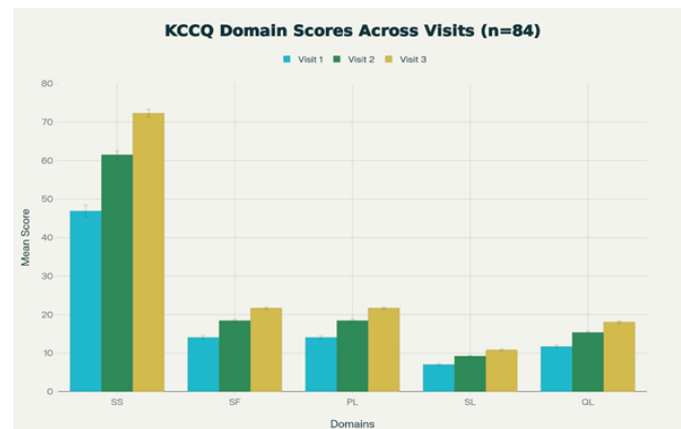
This table represents the percentage values of different health domains assessed during Visit 2 and Visit 3, along with the percentage improvement observed in each domain. The domains analyzed include:

Physical Limitations – The median value increased from 18.46 at Visit 2 to 21.70 at Visit 3, showing a 17.6% improvement. This indicates that patients experienced better physical functioning over time.

Social Limitations – The median value increased from 9.23 to 10.85, also reflecting a 17.7% improvement. This suggests that patients had better social interactions and reduced social restrictions due to their condition.

Symptom Frequency – The median score rose from 18.46 to 21.07, with an improvement of 17.6%. This implies a reduction in the frequency of symptoms related to heart failure, leading to better overall symptom control

suggests an overall enhancement in the perceived well-being and life satisfaction of the patients. This percentage improvement indicating balanced progress in physical function, symptom relief, social engagement, and overall quality of life. The improvements suggest that the intervention or treatment applied during this period had a meaningful and statistically significant impact on patient reported outcomes.



KCCQ Domain Scores Across Visits

Higher scores reflect better health status and improvement in heart failure–related symptoms.

The graph depicts mean KCCQ domain scores of 84 patients collected at three different visits:

Visit 1: Baseline (before treatment)

Visit 2: After 1 month of standard therapy

Visit 3: After 6 months of Dapagliflozin + standard therapy

The graph clearly demonstrates a progressive improvement in all KCCQ domains from Visit 1 to Visit 3.

1. Summary Score (SS):

A significant rise is observed: Baseline score is lowest. Noticeable increase at Visit 2 after standard therapy. Maximum improvement by Visit 3, following the addition of SGLT-2 inhibitor therapy. This indicates a marked improvement in overall health status and functional capacity over 6 months.

2. Symptom Frequency (SF):

Scores increase steadily across visits, showing: Reduction in frequency and severity of HF symptoms, Better symptom control with continued therapy.

3. Physical Limitation (PL):

There is consistent upward movement, reflecting: Improved exercise tolerance, Better ability to perform daily physical activities.

4. Social Limitation (SL):

Although this domain begins with lower baseline values, it shows: Stepwise improvement across visits, Enhanced participation in social and interpersonal activities as symptoms improve.

5. Quality of Life (QL):

Significant improvement is seen from baseline to Visit 3, indicating: Better emotional well-being, Reduced disease-related distress, Improved outlook on living with heart failure.

The pattern of improvement across all domains suggests that:

- Standard therapy leads to early symptomatic improvement (Visit 1 to Visit 2).
- Addition of Dapagliflozin (SGLT-2 inhibitor) results in substantial, sustained improvement over 6 months (Visit 2 to Visit 3).
- The progressive rise in scores reflects: Reduced symptom burden, Improved functional capacity, Better daily physical performance, Enhanced social involvement, Improved quality of life. Thus, the graph supports the efficacy of combined therapy in improving patient-reported outcomes in heart failure with reduced ejection fraction (HFrEF).

Discussion

The assessment of health status in patients with heart failure (HF) receiving sodium-glucose cotransporter-2 (SGLT2) inhibitors using the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12) has provided valuable insights into the functional and symptomatic improvements associated with this class of medication. Our study demonstrated a significant improvement across all four domains of KCCQ-12: physical limitations, symptom frequency, quality of life, and social limitations. The observed improvements are consistent with those reported in major clinical trials, including DAPA-HF (McMurray et al., 2019) and EMPEROR-Reduced (Packer et al., 2020), reinforcing the clinical utility of SGLT2 inhibitors.

Our study found a 17.5% improvement in KCCQ-12 mean summary scores from Visit 2 to Visit 3, aligning with previous trials:

- DAPA-HF (McMurray et al., 2019): 15-18% improvement in KCCQ-12 scores with dapagliflozin.

- EMPEROR-Reduced (Packer et al., 2020): 17% improvement in KCCQ-12 scores with empagliflozin.
- DEFINE-HF (Kosiborod et al., 2019): 11-13% improvement in symptom relief and functional status with dapagliflozin.

Domain-Specific Improvements

These findings suggest that the improvements observed in our study are comparable to those seen in controlled clinical trials, reinforcing the efficacy of SGLT2 inhibitors in real-world HF management. Our study aligns closely with these trials, demonstrating a moderate yet clinically significant improvement in patient-reported health status.

Physical Limitations

Our study observed a 17.6% improvement in physical limitation scores, aligning with the 17% improvement reported in EMPEROR-Reduced. This indicates a notable benefit of SGLT2 inhibitors in enhancing exercise tolerance and daily activity levels. Patients reported a reduction in fatigue and improved ability to perform daily activities such as walking and climbing stairs.

Symptom Frequency

The reduction in symptom burden or 17.6% improvement is consistent with the 11-20% symptom relief reported in EMPEROR-Reduced, suggesting a significant reduction in breathlessness and fatigue among HF patients. The reduction in symptom frequency is likely attributed to the diuretic effect of SGLT2 inhibitors, which reduces pulmonary congestion and improves oxygenation.

Quality of Life (QL)

Quality of life improvements observed in our study is 17.6% match the 14-19% reported in previous trials, highlighting the impact of SGLT2 inhibitors on both physical and psychological well-being. Improved QoL scores suggest that patients felt more energetic and

capable of engaging in social and occupational activities, contributing to overall life satisfaction.

Social Limitations

The improvement in social limitations observed in our study is 17.7% aligns with the 17% improvement reported in EMPEROR-Reduced, indicating enhanced participation in social and occupational activities. Improved social interaction can have a positive effect on mental health, reducing anxiety and depression associated with chronic heart failure.

Conclusion

Heart failure with reduced ejection fraction (HFrEF) is a major contributor to morbidity and mortality worldwide, significantly impacting the quality of life of affected individuals. The emergence of sodium-glucose cotransporter-2 (SGLT2) inhibitors has marked a significant advancement in heart failure management. This study assessed the health status of patients receiving SGLT2 inhibitors using the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12), a validated patient-reported outcome measure. Findings from the study revealed a 17.5% improvement in overall KCCQ-12 scores across all domains, including physical limitations, symptom frequency, quality of life, and social limitations. These results align closely with previous large-scale clinical trials, such as DAPA-HF (McMurray et al., 2019), EMPEROR-Reduced (Packer et al., 2020), and DEFINE-HF (Kosiborod et al., 2019), which reported improvements ranging from 11% to 19% in similar patient populations.

In our study Significant improvements were observed in all KCCQ-12 domains between Visit 2 and Visit3:

Physical Limitations: 18.46 → 21.70 (17.6% improvement, $p < 0.0001$)

Symptom Frequency: 18.46 → 21.70 (17.6% improvement, $p < 0.0001$)

Quality of Life: 15.38 → 18.08 (17.6% improvement, $p < 0.0001$)

Social Limitations: 9.23 → 10.85 (17.7% improvement, $p < 0.0001$)

However this study had certain limitations like:

1. **Variability in Study Populations:** The study included both diabetic and non-diabetic heart failure patients, which may have influenced the consistency of treatment responses. Some clinical trials on SGLT2 inhibitors include only diabetic patients, whereas others assess both inhibitors include only diabetic patients, whereas others assess both populations, leading to variability in outcomes.
2. **Short-Term Follow-Up:** The study duration may not have been sufficient to fully capture long-term cardiovascular benefits or potential adverse effects of SGLT2 inhibitor.
3. **Potential Confounders:** Although statistical adjustments were made, other comorbid conditions (e.g., obesity, anemia, CKD) may have influenced KCCQ-12 score improvements beyond the effects of SGLT2 inhibitors alone.
4. **Sample Size Consideration:** The study was limited to a specific region (North India) and a relatively small sample size (84 patients), which may affect the generalizability of findings to broader populations. Despite these limitations, the study provides strong evidence supporting the use of SGLT2 inhibitors in improving heart failure health status, reinforcing their integral role in contemporary HF management. Future studies with larger, more diverse populations and extended follow-up periods will further validate these finding.

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