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A prospective study to evaluate changes in 2D Echocardiographic parameter and 6-minitues walk test (6MWT) in patients with Heart Failure on Dapagliflozine.

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Abstract

Background: Left ventricular ejection fraction measures resting systolic function, while six-minute walk distance reflects functional capacity. Measuring both during heart failure treatment allows assessment of whether changes in cardiac function correspond to changes in walking ability. Aim: To evaluate changes in LVEF and six-minute walk distance over three months after initiation of dapagliflozin and to assess the correlation between the two changes. ***Materials and methods***: This single-centre prospective observational study included 250 adults with heart failure who started dapagliflozin 10 mg once daily. LVEF was measured by two-dimensional echocardiography, and walking distance was assessed using the 6MWT at baseline, one month and three months. Paired t tests assessed baseline-to-three-month changes. Linear mixed-effects models compared outcomes across visits, and Pearson's correlation assessed the association between individual changes. ***Results***: Mean LVEF increased from 32.60 ± 4.80% at baseline to 33.59 ± 4.85% at one month and 36.08 ± 4.84% at three months. The mean paired three-month increase was 3.48 percentage points (95% CI 3.31–3.65, $p < 0.001$). Among 180 patients who completed the 6MWT at both baseline and three months, mean walking distance increased from 252.46 ± 54.60 m to 304.47 ± 57.91 m, a gain of 52.02 m (95% CI 50.31–53.72, $p < 0.001$). The correlation between changes in LVEF and walking distance was close to zero ($r = 0.022$, 95% CI -0.124 to 0.168, $p = 0.766$). ***Conclusion***: LVEF and six-minute walk distance increased over three months in this cohort. The weak association between individual changes supports assessing cardiac function and walking capacity separately during follow-up.

Keywords: Dapagliflozin, heart failure with reduced ejection fraction, six-minute walk test.

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INTRODUCTION

For a patient with heart failure, the ability to walk farther without stopping is a meaningful outcome alongside the risk of hospitalisation. McMurray et al. (2019) [1] reported that dapagliflozin reduced the risk of worsening heart failure or cardiovascular death in patients with left ventricular ejection fraction (LVEF) of 40% or less, including those without diabetes. Solomon et al. (2022) [2] demonstrated a reduction in the same composite outcome among patients with LVEF above 40%. Whether these clinical benefits are accompanied by measurable changes in cardiac structure and walking capacity is a separate question. In DAPA-MODA, Pascual-Figal et al. (2023) [3] observed reductions in left atrial and left ventricular volumes over six months in patients receiving dapagliflozin. Evidence for improvement in walking capacity has varied. In PRESERVED-HF, Nassif et al. (2021) [4] found that patients with preserved ejection fraction assigned to dapagliflozin walked an average of 20.1 m farther than those assigned to placebo at 12 weeks (95% CI 5.6–34.7 m). In contrast, McMurray et al. (2024) [5] found no significant improvement in six-minute walk distance with dapagliflozin in either of the DETERMINE trials. Serial measurement of LVEF and walking distance in the same patients offered an

opportunity to examine whether changes in systolic function tracked with changes in everyday exercise capacity during the first three months of treatment.

AIM

To evaluate changes in LVEF and six-minute walk distance over three months in patients with heart failure who started dapagliflozin.

OBJECTIVES

1. To compare LVEF measured by two-dimensional echocardiography at baseline, one month and three months.
2. To compare six-minute walk distance at baseline, one month and three months.
3. To assess the correlation between within-patient changes in LVEF and walking distance from baseline to three months.

MATERIALS AND METHODS

Study design, location and source of data

The protocol described a single-centre, prospective observational study in the Cardiology Outpatient Department of the Superspeciality Hospital, SVNGMCH, Yavatmal, Maharashtra. Adults with heart failure who had newly been prescribed dapagliflozin as part of routine care constituted the source population. Each patient served as their own baseline comparator. The study proforma captured clinical assessments, echocardiographic LVEF and six-minute walk test (6MWT) observations.

Study duration

The protocol specified an overall duration of 15 months. The recruitment section described seven months of data collection, whereas the project timeline allocated ten months to data collection. In the supplied workbook, baseline visits were dated 1–15 January 2026, one-month visits 31 January–14 February 2026 and three-month visits 1–15 April 2026. These dates describe the available visit records.

Sample size and calculation

The protocol recruitment target was 245 participants. The workbook contained 250 distinct patient IDs, each represented at all three visits. The protocol cited planning means of 37%, 45% and 38% and standard deviations of 10, 11 and 12 percentage points, respectively, with 80% power, a two-sided 5% significance level and a 10% allowance for attrition. It reported 32 participants per group and referred to eight groups, although the design followed one cohort over three visits. These inputs do not reproduce the stated target of 245.

For planning a paired baseline-to-three-month comparison of LVEF, the normal-approximation equation was:

$n_{paired} = \lceil (1.96 + 0.842)^2 \times \sigma^2_d / \Delta^2 \rceil$ and $n_{recruitment} = \lceil n_{paired} / 0.90 \rceil$

Here Δ was the minimum mean change of interest in percentage points, and σ_d was the standard deviation of individual changes. If estimated from visit-specific SDs, $\sigma^2_d = s_0^2 + s_3^2 - 2\rho s_0 s_3$, where ρ was the within-patient correlation. The protocol did not specify σ_d or ρ. The recorded target and cohort count were therefore reported separately from this design-appropriate equation.

Participants and assessments

Inclusion criteria

Eligibility required age ≥18 years, a clinical diagnosis of heart failure, baseline LVEF <50% on two-dimensional echocardiography, a new prescription for dapagliflozin 10 mg once daily and willingness to provide informed consent. Patients with diabetes were eligible. Baseline LVEF in the workbook ranged from 25% to 40%, so all available records were in the reduced-ejection-fraction range.

Exclusion criteria

The protocol excluded patients with serum creatinine >2 mg/dL, end-stage renal disease requiring dialysis, known or suspected pregnancy, chronic obstructive pulmonary disease or another pulmonary disorder considered likely to affect NT-proBNP levels, severe valvular heart disease requiring immediate surgery, previous heart transplantation or ventricular assist device implantation. It also listed incomplete medical records or missing data as exclusions. Early termination of a walk was recorded separately from a missed visit.

Procedure and methodology

The protocol required Institutional Ethics Committee approval before recruitment and written informed consent before participation. The baseline assessment coincided with initiation of dapagliflozin 10 mg once daily as part of routine treatment. Baseline measurements comprised clinical functional class, LVEF and walking distance. Two-dimensional

echocardiography and the 6MWT were scheduled again at one and three months. LVEF was recorded as a percentage. The echocardiographic acquisition and tracing method was unspecified in the source documents.

The protocol specified the American Thoracic Society procedure for the 6MWT. The intended measure was the distance covered in six minutes, in metres. At each visit, the proforma captured oxygen saturation, heart rate and blood pressure before and after the walk, together with symptoms, completion status and the reason for stopping. These fields allowed an investigator to distinguish a rest during the six-minute interval from early termination when the source test record supported that distinction.

Sample processing

The primary and secondary outcomes were derived from echocardiographic and walking-test measurements. The protocol described serum creatinine as an eligibility measure. It specified no serial specimen collection, processing or storage for either outcome.

Data collection and statistical methods

Data collection

The Excel proforma contained separate worksheets for baseline, one month and three months. Patient ID linked the three observations. Registration number, age, sex, visit date, New York Heart Association functional class, LVEF, walking distance and the accompanying walk-test fields were available at each visit. The same 250 IDs appeared in all three worksheets. Completion status was marked "Yes" for 214, 220 and 209 tests, respectively. A total of 180 IDs had a completed test at both baseline and three months.

Statistical methods

The protocol specified descriptive summaries and comparisons across visits. The following analysis plan was developed for the recorded data. Categorical variables were to be summarised as n (%) with explicit denominators, and continuous variables as mean (SD) or median (interquartile range), according to distribution.

For LVEF and walking distance, separate linear mixed-effects models were planned with visit as a categorical fixed effect and patient ID as a random intercept. The main comparison was three months versus baseline. The one-month versus baseline contrast described the early response. Changes were to be expressed in percentage points for LVEF and metres for walking distance, with 95% confidence intervals. Residual distributions were to be checked, with Holm adjustment for multiple visit contrasts within each outcome.

Before modelling walking distance, tests marked incomplete were to be reviewed against the stop reason and test sheet. Distances from valid six-minute observation periods, including permitted rests, were eligible for the main analysis. Distances from prematurely terminated tests were to be described separately. Completion rates and reasons for termination were to be reported by visit because excluding symptomatic patients could overstate functional improvement.

For the exploratory objective, the three-month minus baseline change in LVEF was to be correlated with the corresponding change in walking distance among patients with valid paired measurements of both outcomes. Pearson's r was planned for an approximately linear relationship without influential outliers, and Spearman's ρ otherwise. The analysis was to report the paired sample size, coefficient, 95% confidence interval and two-sided p value. Statistical significance was set at $p < 0.05$. Changes over time were interpreted as within-cohort associations during treatment.

RESULTS

Table 1: Paired changes in LVEF and six-minute walk distance from baseline to three months

Outcome	Paired n	Baseline, mean (SD)	Three months, mean (SD)	Mean paired change (95% CI)	Paired *t* (df)	*p* value
LVEF (%)	250	32.60 (4.80)	36.08 (4.84)	+3.48 (+3.31 to +3.65) percentage points	41.00 (249)	<0.001
Six-minute walk distance (m)	180	252.46 (54.60)	304.47 (57.91)	+52.02 (+50.31 to +53.72) m	60.21 (179)	<0.001

Among 250 patients with paired echocardiographic measurements, mean left ventricular ejection fraction (LVEF) increased from 32.60 ± 4.80% at baseline to 36.08 ± 4.84% at three months. The mean within-patient increase was 3.48 percentage points (95% CI 3.31 to 3.65, paired $t = 41.00$, $p < 0.001$). Among the 180 patients who completed the six-minute walk test at both visits, mean walking distance increased from 252.46 ± 54.60 m to 304.47 ± 57.91 m, a mean gain of 52.02 m (95% CI 50.31 to 53.72, paired $t = 60.21$, $p < 0.001$).

Table 2: Comparison of LVEF measured by two-dimensional echocardiography across three visits

Visit	n	LVEF (%), mean (SD)	Comparison	Estimated change, percentage points (95% CI)	*z*	Adjusted *p*
Baseline	250	32.60 (4.80)	Reference			

One month	250	33.59 (4.85)	One month - baseline	+0.99 (+0.85 to +1.13)	14.17	<0.001
Three months	250	36.08 (4.84)	Three months - baseline	+3.48 (+3.34 to +3.62)	49.72	<0.001
			Three months - one month	+2.49 (+2.35 to +2.63)	35.55	<0.001

LVEF across three visits. Among all 250 patients, mean LVEF increased from 32.60 ± 4.80% at baseline to 33.59 ± 4.85% at one month and 36.08 ± 4.84% at three months. The mixed-effects model showed a significant change across visits (Wald $\chi^2(2) = 2624.41$, $p < 0.001$). LVEF increased by 0.99 percentage points during the first month (95% CI 0.85 to 1.13) and by a further 2.49 percentage points between months one and three (95% CI 2.35 to 2.63). The estimated increase over three months was 3.48 percentage points (95% CI 3.34 to 3.62). All three pairwise comparisons had Holm-adjusted $p < 0.001$.

Table 3: Comparison of six-minute walk distance across three visits

Visit	Completed test, n (%) of 250	Distance (m), mean (SD)	Comparison	Estimated change, m (95% CI)	*z*	Adjusted *p*
Baseline	214 (85.6)	248.90 (55.81)	Reference			
One month	220 (88.0)	267.99 (56.10)	One month - baseline	+20.64 (+19.32 to +21.96)	30.68	<0.001
Three months	209 (83.6)	304.10 (57.67)	Three months - baseline	+52.13 (+50.79 to +53.46)	76.45	<0.001
			Three months - one month	+31.48 (+30.15 to +32.81)	46.35	<0.001

Six-minute walk distance across three visits. Of the 250 patients, 214 (85.6%) completed the walk test at baseline, 220 (88.0%) at one month and 209 (83.6%) at three months. Among those who completed the test at each visit, mean walking distance was 248.90 ± 55.81 m, 267.99 ± 56.10 m and 304.10 ± 57.67 m, respectively. The mixed-effects model showed a significant change across visits (Wald $\chi^2(2) = 5916.09$, $p < 0.001$). The estimated gain was 20.64 m from baseline to one month (95% CI 19.32 to 21.96) and a further 31.48 m from one to three months (95% CI 30.15 to 32.81). The estimated three-month gain was 52.13 m (95% CI 50.79 to 53.46). All three pairwise comparisons had Holm-adjusted $p < 0.001$.

Table 4: Correlation between within-patient changes in LVEF and six-minute walk distance

Patients with paired measurements, n	Change in LVEF, percentage points, mean (SD)	Change in walking distance, m, mean (SD)	Pearson's *r* (95% CI)	*t* (df)	*p* value
180	+3.50 (1.35)	+52.02 (11.59)	0.022 (-0.124 to 0.168)	0.30 (178)	

Correlation between changes in LVEF and walking distance. Among the 180 patients with paired measurements for both outcomes, the mean three-month increase was 3.50 ± 1.35 percentage points in LVEF and 52.02 ± 11.59 m in walking distance. The correlation between individual changes was close to zero (Pearson's r = 0.022, 95% CI -0.124 to 0.168, p = 0.766).

DISCUSSION

Table 1. Paired changes in LVEF and six-minute walk distance

During three months of dapagliflozin treatment, mean left ventricular ejection fraction (LVEF) increased from 32.60% to 36.08% in 250 patients, a gain of 3.48 percentage points (95% CI 3.31–3.65). Among the 180 patients who completed the six-minute walk test at both visits, mean walking distance increased from 252.46 to 304.47 m, a gain of 52.02 m (95% CI 50.31–53.72). The closest comparison is the DAPA-VO_2 trial by Palau et al. (2022) [1], which studied patients with reduced ejection fraction at the same one- and three-month intervals. Dapagliflozin improved peak oxygen consumption relative to placebo, but the investigators found no significant between-group difference in either LVEF or six-minute walk distance. This distinction matters because the present study measured change from each patient's baseline. Its confidence intervals describe the precision of that observed change, while the contribution of dapagliflozin relative to concurrent treatment and clinical recovery remains uncertain.

The findings can also be placed alongside trials that measured outcomes important to patients. McMurray et al. (2019) [2] reported a lower risk of worsening heart failure or cardiovascular death with dapagliflozin in DAPA-HF. Berg et al. (2021) [3] found that this benefit was evident by 28 days, and Docherty et al. (2020) [4] found it across a range of background heart failure therapies. In DEFINE-HF, Nassif et al. (2019) [5] reported that more patients receiving dapagliflozin achieved a meaningful improvement in health status or natriuretic peptide concentration at 12 weeks. Kosiborod et al. (2020)[6] also documented improvements in patient-reported symptoms and physical limitations in DAPA-HF. These studies support the

clinical relevance of assessing patients early after treatment initiation. Their outcomes, however, cannot establish how much of the 52-m walking gain in the present cohort was attributable to dapagliflozin.

Table 2. Changes in echocardiographic LVEF across three visits

Mean LVEF increased from 32.60% at baseline to 33.59% at one month and 36.08% at three months. The estimated gain was 0.99 percentage points during the first month and a further 2.49 points over the next two months. All three pairwise comparisons remained significant after Holm adjustment ($p < 0.001$). The larger absolute gain during the second interval should be interpreted in light of its longer duration. Pastore et al. (2024) [7] studied patients with LVEF below 50% and found favourable changes in myocardial deformation with dapagliflozin. In DAPA-MODA, Pascual-Figal et al. (2023) [8] observed reductions in left atrial and ventricular volumes over six months. These findings provide echocardiographic evidence of changes in cardiac structure and function during treatment. The present study adds a three-month LVEF trajectory, although LVEF alone cannot identify whether its rise reflected smaller ventricular volumes, altered loading conditions, or improved contractile function.

Controlled imaging studies have produced mixed findings. Singh et al. (2020) [9] found no significant effect of dapagliflozin on magnetic resonance measures of ventricular remodelling after one year in the REFORM trial. In contrast, Santos-Gallego et al. (2021) [10] reported improvements in ventricular volumes and LVEF with empagliflozin in patients with reduced ejection fraction without diabetes. Lee et al. (2021) [11] also found lower indexed ventricular volumes with empagliflozin in SUGAR-DM-HF, while Verma et al. (2019) [12] found a reduction in left ventricular mass in a different population with diabetes and coronary artery disease. The drug, population, imaging measure and follow-up interval therefore matter when comparing effect sizes. Lang et al. (2015) [13] recommended standardised ventricular volume measurement for echocardiographic LVEF estimation. With a one-month mean change of only 0.99 percentage points, consistency of image acquisition and tracing is particularly important before interpreting a similar change in an individual patient.

Table 3. Changes in six-minute walk distance across three visits

The mixed-effects model estimated a gain of 20.64 m at one month and 52.13 m at three months relative to baseline. The three-month estimate closely matched the 52.02-m gain in patients with paired completed tests. The most relevant controlled comparison is DETERMINE-Reduced. McMurray et al. (2024) [14] found that dapagliflozin improved the heart failure symptom score but produced no significant improvement in six-minute walk distance versus placebo at 16 weeks. In PRESERVED-HF, Nassif et al. (2021) [15] reported a placebo-adjusted gain of 20.1 m (95% CI 5.6–34.7) at 12 weeks in patients with preserved ejection fraction. A secondary analysis of that same trial by Lewis et al. (2023) [16] found 66% higher odds of gaining at least 15 m with dapagliflozin. The present cohort's 52-m gain is numerically larger, but it represents a before-and-after comparison in patients with reduced ejection fraction. It should therefore be reported as an observed functional improvement rather than a larger treatment effect.

Test completion also affects interpretation. Of 250 patients, 214 (85.6%) completed the test at baseline, 220 (88.0%) at one month and 209 (83.6%) at three months. Only 180 (72.0%) completed it at both baseline and three months. The close agreement between the paired and model-based estimates is reassuring for the available observations, although both analyses excluded distances from prematurely terminated tests. Patients who stopped because of dyspnoea or fatigue may have had a different functional course. Abraham et al. (2021) [17] found no significant placebo-adjusted improvement in six-minute walk distance in either EMPERIAL trial of empagliflozin. Ferreira et al. (2019) [18] showed in BIOSTAT-CHF that shorter walking distance was associated with older age, more advanced symptoms, orthopnoea and previous stroke, among other factors. Reporting completion rates alongside mean distances therefore gives a fuller account of functional capacity in this cohort.

Table 4. Correlation between changes in LVEF and walking distance

Among the 180 patients with paired measurements for both outcomes, LVEF increased by a mean of 3.50 percentage points and walking distance by 52.02 m. Despite these average gains, the correlation between individual changes was close to zero (Pearson's $r = 0.022$, 95% CI -0.124 to 0.168, $p = 0.766$). Thus, knowing how much a patient's LVEF increased provided little information about how much farther that patient walked. The confidence interval remains compatible with a weak association in either direction. Borlaug et al. (2023) [19] demonstrated in CAMEO-DAPA that dapagliflozin reduced cardiac filling pressures during exercise in patients with preserved ejection fraction. Pandey et al. (2021) [20] described how peripheral oxygen utilisation, vascular function and skeletal muscle performance also contribute to exercise tolerance. These studies offer plausible explanations for the weak correlation, although the present cohort did not measure those mechanisms.

Kitzman et al. (2021) [21] further demonstrated that rehabilitation addressing strength, balance, mobility and endurance improved physical function in older patients after hospitalisation for heart failure. At the level of clinical events, Solomon et al. (2022) [22] showed that dapagliflozin also reduced the risk of worsening heart failure or cardiovascular death in patients with LVEF above 40%. Taken together, the literature and the present findings support measuring both outcomes

during follow-up. Echocardiography documented a modest rise in mean systolic function, whereas the walk test captured a functional change that could not be inferred from an individual patient's change in LVEF.

CONCLUSION

Over three months of follow-up after starting dapagliflozin, mean left ventricular ejection fraction (LVEF) increased by 3.48 percentage points among 250 patients with heart failure and reduced ejection fraction. Among the 180 patients who completed the six-minute walk test (6MWT) at both baseline and three months, walking distance increased by a mean of 52.02 m. Individual changes in LVEF and walking distance showed little correlation (r = 0.022, p = 0.766). Measuring both outcomes therefore provided complementary information: the change in resting LVEF alone was a poor indicator of how much farther an individual patient could walk. The single-cohort design limits attribution of these improvements to dapagliflozin.

LIMITATIONS OF STUDY

1. **Absence of a comparison group.** All patients received dapagliflozin as part of routine care. Concurrent heart failure treatment, changes in fluid status and clinical recovery could also have contributed to the observed improvements.
2. **Incomplete walking tests.** Only 180 of 250 patients (72.0%) completed the 6MWT at both baseline and three months. Excluding patients who stopped early because of symptoms may have overestimated functional improvement and influenced the correlation analysis.
3. **Measurement variability.** The study records did not specify the LVEF tracing method or provide observer-reproducibility estimates. This limits interpretation of small individual changes, particularly given the mean increase of 0.99 percentage points at one month. Familiarity with the repeated walk test could also have influenced walking distance.
4. **Short follow-up.** Three months of observation limited assessment of whether gains were sustained or associated with subsequent heart failure hospitalisation or mortality.
5. **Generalisability.** The cohort came from a single tertiary-care centre, and baseline LVEF ranged from 25% to 40%. The findings therefore apply most directly to patients with reduced ejection fraction.

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