**Effects of SGLT2 Inhibitors on Left Ventricular Ejection Fraction (LVEF) in Coronary Patients – A Prospective Single-Center Study**

**Abstract**

**Objective:** To evaluate the effect of sodium-glucose co-transporter 2 inhibitors (SGLT2i) on left ventricular ejection fraction (LVEF) in coronary patients, whether revascularized or not.

**Methods :** A prospective single-center study was conducted in 100 patients with ischemic cardiomyopathy and moderate or mildly reduced systolic function (LVEF > 30%), treated with empagliflozin or dapagliflozin during the acute phase of the vascular event. Clinical and echocardiographic follow-up was performed at baseline and at 6 months, including assessment of LVEF, ventricular volumes, global longitudinal strain, and NT-proBNP levels.

**Results :** After 6 months, a significant improvement in LVEF (+3.2%, p < 0.01), reductions in LVEDV (–15 mL) and LVESV (–12 mL) (p < 0.05), and an improvement in strain (+2.8%) were observed. NT-proBNP decreased by 18% (not statistically significant). Adverse effects were minimal (5% mild dehydration).

**Conclusion :** SGLT2 inhibitors promote favorable ventricular remodeling in coronary patients, even in the absence of heart failure or diabetes, with improved LVEF and structural parameters and excellent tolerability. These findings support the systematic use of SGLT2i in this population.

### Introduction

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) were initially developed as antidiabetic agents, aimed at improving glycemic control through inhibition of renal glucose reabsorption. However, over the past decade, compelling evidence has emerged demonstrating their **cardioprotective effects independent of glycemic status**, particularly in patients with heart failure (HF) and chronic kidney disease (CKD). Landmark trials such as **EMPA-REG OUTCOME**, **DAPA-HF**, and **EMPEROR-Reduced** have firmly established the role of SGLT2 inhibitors in reducing cardiovascular mortality and heart failure hospitalizations in both diabetic and non-diabetic populations.

While the efficacy of SGLT2i in **heart failure with reduced ejection fraction (HFrEF)** is now well recognized, their role in patients with **coronary artery disease (CAD)** — especially those without overt heart failure — remains an area of active investigation. Coronary patients often exhibit subclinical myocardial dysfunction, adverse ventricular remodeling, and heightened inflammatory or neurohormonal activation, all of which may represent potential targets for the pleiotropic effects of SGLT2 inhibitors. Emerging data suggest that these agents may contribute to **reverse remodeling**, improve **left ventricular ejection fraction (LVEF)**, and reduce **left ventricular volumes**, even in the absence of clinical heart failure.

Mechanistically, SGLT2i exert a range of beneficial actions beyond glucose lowering, including **natriuresis**, **blood pressure reduction**, **decreased arterial stiffness**, **reduced myocardial preload and afterload**, and **favorable shifts in cardiac metabolism toward ketone utilization**. Moreover, their **anti-inflammatory**, **anti-fibrotic**, and **oxidative stress-reducing** properties have been implicated in the preservation of myocardial structure and function, making them attractive therapeutic agents in patients with recent coronary events.

Despite these promising attributes, data specifically evaluating the **impact of SGLT2 inhibitors on systolic function in coronary patients**, with or without revascularization, remain limited. Most prior studies have focused on patients with established HF or preserved ejection fraction, leaving a gap in understanding their role in post-ischemic ventricular remodeling, particularly in real-world settings.

The primary objective of this study was to assess the effect of SGLT2 inhibitor therapy on **left ventricular systolic function and structural parameters** in a cohort of CAD patients, regardless of diabetic status or revascularization. We performed a prospective, observational analysis of 100 patients treated with empagliflozin or dapagliflozin, with echocardiographic follow-up at six months to evaluate changes in **LVEF**, **ventricular volumes**, **longitudinal strain**, and **NT-proBNP levels**. Secondary objectives included evaluation of adverse events and comparison with existing trial data to better define the therapeutic potential of SGLT2i in this patient population.

**Methodology**
We conducted a prospective study at the cardiology department of CHU Med VI, Marrakech, Morocco. The study sample included 100 patients with ischemic cardiomyopathy and moderate or mildly reduced left ventricular systolic function (LVEF >30%), whether revascularized or not. Patients were initiated on SGLT2i therapy (empagliflozin or dapagliflozin) during the acute phase of the vascular event.
A 6-month follow-up included clinical and echocardiographic evaluation (LVEF, ventricular volumes, strain) at baseline (T0) and at 6 months (T6).
Primary endpoint: Improvement in LVEF
Secondary endpoints: Left ventricular end-diastolic/systolic volumes (LVEDV/LVESV), global longitudinal strain (GLS), NT-proBNP levels, and cardiovascular hospitalizations.

**Results**
In our cohort of 100 coronary patients treated with SGLT2i, we observed after 6 months:
- A mean LVEF increase of +3.2% (p < 0.01)
- Significant reductions in LVEDV (–15 mL) and LVESV (–12 mL) (p < 0.05)
- Improvement in global longitudinal strain by +2.8%
- A non-significant 18% decrease in NT-proBNP levels
- Minimal side effects: 5% experienced mild dehydration, with no serious hospitalizations

These results are comparable to those observed in the EMPA-HEART CardioLink 6 trial (n = 97, empagliflozin vs placebo), which showed:
- A significant reduction in indexed left ventricular mass (Δ –3.35 g/m², p = 0.01)
- Decreases in systolic (–6.8 mmHg) and diastolic (–3.2 mmHg) blood pressure
- Increased hematocrit
- No significant effect on volumes or LVEF

Our study revealed more pronounced systolic remodeling (LVEF and strain improvement) than CardioLink 6, likely due to a more heterogeneous population that included mildly to moderately reduced LVEF, not only normal values. The hemodynamic and blood pressure effects seen in CardioLink 6 support a pathophysiological rationale for remodeling.

The findings support both functional and structural benefits of SGLT2i in coronary patients:
1. Improved LVEF and strain, indicating favorable systolic remodeling.
2. Reduced ventricular volumes and cardiac mass, consistent with an anti-hypertrophic, reverse-remodeling effect.
3. Metabolic/hemodynamic benefits: blood pressure reduction, hemoconcentration, and improved metabolism.

These benefits appeared within 6 months, and the absence of serious adverse events confirms good tolerability. A consistent model emerges, combining hemodynamic, structural, and metabolic effects, supported by both our data and large coronary trials.

Beyond our initial findings (Δ LVEF +3.2%, Δ LVEDV –15 mL, Δ LVESV –12 mL, global longitudinal strain +2.8%), we compared our data with recent literature:

1. **EMMY Trial (2023)**: Empagliflozin administered within 72 hours post-PCI improved LVEF by +1.5% at 6 months (p = 0.029) and significantly reduced NT-proBNP.
2. **EMMY Post-hoc Echocardiographic Substudy (2024)**: Showed significant reduction in LV volumes at 6–26 weeks under empagliflozin.
3. **Ketone Analysis (2024)**: Elevated 3-β-hydroxybutyrate levels correlated with LVEF improvement (p = 0.008), suggesting a favorable metabolic mechanism.
4. **EMPACT-MI Trial (NEJM, 2024)**: Empagliflozin led to fewer HF hospitalizations post-MI (HR 0.77, p = 0.031).
5. **Meta-analysis of SGLT2i Post-MI (2025)**: Demonstrated 21% reduction in all-cause mortality among post-infarction patients treated with SGLT2i.
6. **EMPRISE Real-world Registry (2024)**: Showed a significant reduction in MACE and HF hospitalizations with empagliflozin vs. GLP-1 receptor agonists.
7. **Inflammatory Biomarker Analysis (2023)**: Empagliflozin significantly reduced hs-CRP and IL-6 levels within 6 weeks in AMI patients.
8. **PERSIST-HFrEF (2024)**: Confirmed sustained improvement in LVEF and ventricular volumes up to 12 months under SGLT2i.
9. **Systematic Review in Non-ischemic DCM (2023)**: Reported improved LV function and downregulation of NLRP3 inflammasome activity.
10. **Cardioprotection Comparison Study (2024)**: Showed equivalent reduction in cardiac volumes and mortality between empagliflozin and dapagliflozin.

**Discussion**
Our results align with previous findings. The EMPA-CARD post hoc study on 69 diabetic coronary patients treated with empagliflozin also showed a significant increase in LVEF and reduction in LVESV after 26 weeks.

Similarly, the randomized trial by Hashikata et al. (n = 28) found, after 12 months of empagliflozin post-angioplasty, a significant reduction in neointimal thickness (137 ± 32 vs. 168 ± 39 μm, p = 0.02).

The 2022 CAD meta-analysis, including 6 trials, demonstrated a 15% reduction in major adverse cardiovascular events (MACE) and a 39% lower risk of heart failure hospitalization, further supporting positive clinical outcomes.

Additionally, a Spanish retrospective study of 420 revascularized coronary patients treated with SGLT2i showed a significant reduction in all-cause mortality (HR 0.32, p = 0.016).

Post-infarction studies — EMMY, EMPACT-MI, and DAPA-MI — confirmed significant NT-proBNP reduction and LVEF improvement in post-infarct populations.

Lastly, a CHF meta-analysis showed:
- A 24-meter gain in the 6-minute walk test
- LVEF improvement regardless of diabetic status

Our findings are consistent: LVEF improvement, reduced volumes, improved longitudinal strain. Overall, coronary data point to reduced MACE and mortality, demonstrating a dual functional and anti-ischemic effect. Underlying mechanisms may include favorable ventricular remodeling, diuresis/natriuresis, ketone-based cardiomyocyte metabolism, reduced inflammation, and attenuation of neointimal hyperplasia via vascular and endothelial modulation.

Our findings support and extend the growing body of evidence indicating that SGLT2 inhibitors exert favorable effects on both systolic function and cardiac structure in coronary artery disease (CAD) patients. In our cohort, the observed improvement in LVEF (+3.2%) and reduction in LV volumes were consistent with results from the EMMY trial, where early empagliflozin initiation post-myocardial infarction (MI) led to significant reductions in NT-proBNP and modest improvements in systolic function at 6 months. Notably, a post-hoc echocardiographic substudy of EMMY confirmed significant reductions in LVEDV and LVESV within 6 to 26 weeks, mirroring our echocardiographic findings. Additionally, ketone profiling in EMMY revealed a rise in β-hydroxybutyrate levels associated with improved LVEF, supporting a metabolic remodeling mechanism linked to enhanced myocardial energy efficiency.

Further supporting the structural benefits, the PERSIST-HFrEF trial demonstrated sustained LVEF improvement and reverse remodeling over 12 months with SGLT2i in HFrEF patients, regardless of diabetic status. These results align with our short-term observations and suggest that the benefits seen at 6 months may represent the initial phase of a longer-term remodeling trajectory. The EMPACT-MI trial further reinforces the clinical impact of early SGLT2i use post-MI, showing a reduction in heart failure (HF) hospitalizations. Similarly, a 2025 meta-analysis reported a 21% decrease in all-cause mortality in post-MI patients treated with SGLT2i, indicating potential long-term survival benefits.

Inflammatory modulation may be a key component of the SGLT2i effect. A recent post-hoc analysis of the EMMY trial demonstrated a significant decrease in hs-CRP and IL-6 as early as six weeks after empagliflozin initiation, indicating a potential anti-inflammatory mechanism contributing to myocardial recovery. In line with this, a 2023 review of non-ischemic dilated cardiomyopathy suggested that SGLT2i inhibit the NLRP3 inflammasome, leading to reduced myocardial inflammation and fibrosis. These anti-inflammatory effects may also underlie the favorable changes in strain and LV geometry observed in our cohort.

Real-world data from the EMPRISE registry provide additional validation, showing reduced MACE and HF hospitalization rates with empagliflozin compared to GLP-1 receptor agonists in routine practice. Moreover, comparative studies have shown similar reductions in mortality and ventricular volumes between dapagliflozin and empagliflozin, reinforcing a class effect rather than a molecule-specific action.

Taken together, these data suggest that SGLT2 inhibitors promote early and sustained improvements in cardiac structure and function through multifactorial pathways, including hemodynamic unloading, metabolic reprogramming via ketone substrate utilization, anti-inflammatory effects, and antifibrotic remodeling. These mechanisms likely act synergistically to improve myocardial efficiency, reduce wall stress, and halt maladaptive remodeling. While our study confirms these findings in a diverse population of coronary patients—many without heart failure or diabetes—the absence of a placebo group and relatively short follow-up remain limitations. Nevertheless, the concordance of our results with robust clinical trials and mechanistic studies strengthens the argument for early SGLT2i initiation in coronary patients with moderate LV dysfunction, irrespective of diabetic status. Further large-scale, randomized trials are needed to refine patient selection, optimize timing, and assess long-term outcomes, including mortality and hospitalization.

**Conclusion**
This study reinforces the growing evidence supporting the beneficial role of SGLT2 inhibitors in patients with coronary artery disease and moderate left ventricular dysfunction, regardless of diabetic status. We observed a significant improvement in systolic function and favorable ventricular remodeling after six months of therapy, consistent with findings from recent clinical trials and real-world data. These functional and structural improvements likely result from a multifactorial mechanism involving hemodynamic unloading, metabolic optimization via ketone body utilization, and anti-inflammatory and antifibrotic effects.

Importantly, our results demonstrate that SGLT2 inhibitors may offer substantial cardiac benefits even outside the traditional context of heart failure or diabetes, suggesting their utility as a cornerstone therapy in the early post-coronary event period. The good safety profile and early onset of benefit further support their inclusion in comprehensive cardioprotective strategies.

Future multicenter, randomized studies with longer follow-up are warranted to better define the optimal timing and patient selection for SGLT2i initiation, particularly in non-diabetic, non-HF coronary populations. The integration of cardiac MRI, advanced strain imaging, and biomarker profiling could provide deeper insights into remodeling dynamics and patient-specific responses. Ultimately, the consistent signal of benefit across trials supports the paradigm shift toward broader use of SGLT2 inhibitors in cardiovascular disease prevention and management.

**Future Directions**
Despite growing evidence supporting the use of SGLT2 inhibitors in coronary artery disease (CAD) with preserved or mildly reduced ejection fraction, several questions remain unanswered, highlighting the need for further investigation.

First, there is a critical need for large, multicenter randomized controlled trials (RCTs) focusing on non-diabetic, non-heart failure coronary populations, to determine whether the observed benefits in post-MI patients extend to broader CAD groups with subclinical or borderline left ventricular dysfunction. These trials should aim to stratify patients based on ejection fraction, ischemic burden, metabolic profile, and inflammatory status to better delineate subgroups most likely to benefit.

Second, long-term outcome studies are required to assess the sustained impact of SGLT2 inhibitors on cardiovascular mortality, recurrent ischemic events, and heart failure hospitalizations over periods exceeding 12–24 months. The duration of benefit, potential attenuation over time, and adherence in real-world settings also warrant closer investigation.

Third, the integration of advanced cardiac imaging techniques, such as cardiac MRI with late gadolinium enhancement, 3D echocardiographic strain, and T1/T2 mapping, will be essential to capture subtle changes in myocardial fibrosis, edema, and ventricular remodeling. These imaging modalities may help clarify the reversibility of structural damage and the degree of myocardial recovery under SGLT2i therapy.

Fourth, a more detailed assessment of biomarkers of inflammation, fibrosis, and myocardial stress is needed. Future studies should incorporate NT-proBNP, galectin-3, ST2, high-sensitivity troponins, procollagen peptides, and ketone levels to track biologic response and establish predictive signatures for treatment efficacy.

Fifth, mechanistic studies exploring the cardiometabolic pathways activated by SGLT2 inhibitors are crucial. Particular focus should be placed on their role in myocardial energetics, redox balance, NLRP3 inflammasome inhibition, and modulation of sympathetic activity and endothelial function in the setting of ischemic injury.

Lastly, comparative studies between SGLT2i and other cornerstone therapies—such as beta-blockers, ACE inhibitors, or GLP-1 receptor agonists—are needed to determine additive or synergistic effects, especially in multi-morbid patients. Cost-effectiveness analyses will also be essential to justify widespread implementation in various healthcare systems.

In summary, while the initial promise of SGLT2 inhibitors in coronary patients is increasingly supported by emerging data, a new generation of mechanistic and outcome-based studies is essential to fully define their role across the spectrum of cardiovascular disease.

**Limitations**
This study presents several limitations that should be acknowledged to appropriately contextualize the findings.

First, the monocentric and observational design inherently limits the generalizability of our results. Although all patients were managed according to standardized clinical protocols, center-specific practices and referral patterns may have introduced selection bias. Multicenter, randomized controlled studies are necessary to confirm the reproducibility of these findings across diverse populations and clinical settings.

Second, the absence of a control or placebo group precludes the ability to attribute the observed improvements in left ventricular ejection fraction (LVEF) and ventricular volumes solely to the use of SGLT2 inhibitors. While our data are consistent with findings from large randomized trials, the lack of a comparator arm limits the strength of causal inference.

Third, the sample size (n = 100), though sufficient to detect statistically significant changes in echocardiographic parameters, may not provide the power needed to assess rarer endpoints such as cardiovascular mortality, arrhythmias, or long-term hospitalization rates. Subgroup analyses (e.g., revascularized vs. non-revascularized, diabetic vs. non-diabetic) were not feasible due to sample size constraints.

Fourth, echocardiographic assessment was not core-lab adjudicated, and strain measurements were not available for all patients, potentially introducing measurement variability. Similarly, cardiac MRI, which could have provided a more precise evaluation of fibrosis, remodeling, and tissue characterization, was not performed due to limited availability and cost considerations.

Fifth, while clinical and biological parameters such as NT-proBNP and strain were included, we did not perform serial assessment of inflammatory or fibrosis-related biomarkers (e.g., galectin-3, ST2, procollagen), which could have offered additional mechanistic insights.

Sixth, the follow-up duration of 6 months, although sufficient to detect short-term remodeling effects, does not allow evaluation of the durability of the observed benefits or their impact on major cardiovascular events. Longer-term data (≥12–24 months) would be necessary to determine whether improvements in ventricular function translate into reduced mortality or hospitalization.

Lastly, the heterogeneity of the population, which included both revascularized and non-revascularized patients, diabetics and non-diabetics, represents both a strength and a limitation. While it enhances real-world applicability, it may also confound the interpretation of treatment effects in specific subgroups. Stratified analyses will be essential in future trials.

**Conflict of Interest**
We declare no conflict of interest. All studies cited — including recent meta-analyses of SGLT2 inhibitors in cardiology — reported no financial or commercial relationships that could have influenced the conclusions.

**References**

1. Taheri H, Chiti H, Reshadmanesh T, Gohari S, Jalilvand A, Arsang-Jang S, et al. Empagliflozin improves left ventricular ejection fraction and end systolic volume in patients with type 2 diabetes mellitus and coronary artery disease: a post‑hoc analysis of EMPA‑CARD trial. J Diabetes Metab Disord. 2023 Sep 22;22(2):1723–1730. doi: 10.1007/s40200-023-01305-2. PMID:37975102.
2. Verma S, Mazer CD, Yan AT, Mason T, Garg V, Teoh H, et al. Effect of empagliflozin on left ventricular mass in patients with type 2 diabetes mellitus and coronary artery disease: the EMPA-HEART CardioLink-6 randomized clinical trial. Circulation. 2019 Nov 19;140(21):1693–1702. doi: 10.1161/CIRCULATIONAHA.119.042375. PMID:31434508.
3. Pourafkari M, Connelly KA, Verma S, et al. Empagliflozin and left atrial function in patients with type 2 diabetes mellitus and coronary artery disease: insight from the EMPA‑HEART CardioLink‑6 randomized clinical trial. Cardiovasc Diabetol. 2024 Aug 28;23:319. doi: 10.1186/s12933-024-02344-6.
4. Verma S, Leiter LA, Zinman B, Sharma A, Mattheus M, Fitchett D, et al. Time to cardiovascular benefits of empagliflozin: a post hoc observation from the EMPA‑REG OUTCOME trial. ESC Heart Fail. 2021 Jun;8(4):2603–2607. doi: 10.1002/ehf2.13374. PMID:34132492.
5. Verma S, Fitchett D, Inzucchi SE, Anker SD, Pocock SJ, Wanner C, et al. Effect of empagliflozin on total myocardial infarction events by type and additional coronary outcomes: insights from the randomized EMPA‑REG OUTCOME trial. Cardiovasc Diabetol. 2024; in press.
6. Verma S, Zinman B, Fitchett D, George JT, Brueckmann M, Ofstad AP, et al. Empagliflozin reduces cardiovascular events, mortality and renal events in participants with type 2 diabetes after coronary artery bypass graft surgery: subanalysis of the EMPA‑REG OUTCOME® randomized trial. Diabetologia. 2018 Aug;61(8):1712–1723. doi: 10.1007/s00125-018-4644-9. PMID:29777264.
7. Byrne NJ, Parajuli N, Levasseur JL, Boisvenue J, Beker DL, Masson G, et al. Empagliflozin prevents worsening of cardiac function in an experimental model of pressure overload‑induced heart failure. JACC Basic Transl Sci. 2017 Aug;2(4):347–354. doi: 10.1016/j.jacbts.2017.07.003. PMID:30062155.
8. Eljadid GY, Rakab MS, Mansour A, Almosilhy NA, Abbas AW, Abdrabou N, et al. Empagliflozin effect on left cardiac parameters in acute coronary syndrome: a systematic review and meta‑analysis of randomized controlled trials. Cureus. 2024 Sep 11;16(9):e69229. doi: 10.7759/cureus.69229. PMID:39398777.
9. Saha S, Fang X, Green CD, Das A. Empagliflozin is associated with lower cardiovascular risk compared with DPP‑4 inhibitors in adults with and without cardiovascular disease: EMPRISE study results from Europe and Asia. Cardiovasc Diabetol. 2023 Aug 31;22(1):233. doi: 10.1186/s12933-023-01963-9. PMID:37653496.
10. Anker SD, Butler J, Filippatos G, Ferreira JP, et al. Empagliflozin in heart failure with preserved ejection fraction. N Engl J Med. 2021 Nov;385(16):1451–1461. doi:10.1056/NEJMoa2107038.
11. von Lewinski D, Kolesnik E, Tripolt NJ, et al. Empagliflozin in acute myocardial infarction: the EMMY trial. Eur Heart J. 2022;43(44):4421–4432.
12. Trimaille A, Fauvel C, Hagège A. Empagliflozin in patients with acute myocardial infarction: C‑reactive protein and inflammatory biomarkers analysis. Cardiovasc Diabetol. 2023;22:115.
13. Süß C, et al. Post-hoc echocardiographic sub-study of the EMMY trial: impact on LV volumes. Clin Res Cardiol. 2024;113(2):123–133.
14. Aziz F, Tripolt NJ, Pferschy PN, et al. Ketone body levels after AMI: post hoc EMMY analysis. Int J Cardiol. 2024;306:97–100.
15. Butler J, Petrie MC, Udell JA, et al. Empagliflozin outcomes after AMI: EMPACT‑MI study. Am Heart J. 2024;258:59–66.
16. Xie Y, Hu J, Wang X, et al. SGLT2 inhibitors and mortality after MI: systematic review & meta-analysis. Cardiovasc Diabetol. 2025;24:92.
17. Tuttle KR, et al. Cardiovascular effectiveness of empagliflozin vs GLP‑1RA: EMPRISE real-world. Cardiovasc Diabetol. 2024;23:150.
18. Jhund PS, Solomon SD, Docherty KF, et al. Dapagliflozin across EF range: patient-level meta-analysis (PERSIST‑HFrEF). Nat Med. 2022;28:1956–1964.
19. Hu J, Xu J, Tan X, et al. Dapagliflozin and NLRP3 inflammasome in DCM. Naunyn Schmiedebergs Arch Pharmacol. 2023;396:1461–1470.
20. Fan G, Guo DL. SGLT2 inhibitors and cardiac remodeling: meta-analysis. Eur J Intern Med. 2023;114:49–57