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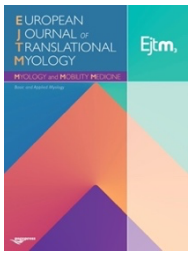

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Analysis of the effects of dapagliflozin on cardiac myocyte injury markers and left ventricular diastolic function in heart failure patients with preserved ejection fraction after percutaneous coronary intervention

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Abstract

The objective of this study was to analyze the effects of Dapagliflozin on cardiac myocyte injury markers and left ventricular diastolic function in patients with Heart Failure with Preserved Ejection Fraction (HF-PEF) after Percutaneous Coronary Intervention (PCI). The study included 120 HF-PEF patients post-PCI treated at our hospital between May 2021 and May 2024. Patients were divided into two groups: conventional therapy (n=49) and Dapagliflozin plus conventional therapy (n=71). Serum Cardiac Troponin I (cTnI) and Serum Amyloid A (SAA) were measured. Left ventricular function was assessed by Ejection Fraction (EF) and the E/e' ratio. The incidence of Major Adverse Cardiovascular Events (MACE) was also recorded. After treatment, the Dapagliflozin group showed significantly lower cTnI and SAA levels compared to the conventional group ($p<0.05$). EF was higher and E/e' ratio was lower in the Dapagliflozin group ($p<0.05$). The incidence of MACE was reduced to 1.41% versus 12.24% in the conventional group ($p<0.05$). In conclusion, Dapagliflozin effectively reduces cardiac myocyte injury markers, improves left ventricular diastolic function, and lowers the incidence of MACE in HF-PEF patients after PCI, demonstrating significant translational benefits for cardiac muscle function.

Key words: dapagliflozin; cardiac myocyte injury; left ventricular diastolic function; HF-PEF; PCI.

Heart Failure with Preserved Ejection Fraction (HF-PEF) is a common cardiac condition that follows Percutaneous Coronary Intervention (PCI), characterised by a normal or near-normal Left Ventricular Ejection Fraction (LVEF) and preserved left ventricular systolic function, but impaired diastolic function. Clinical manifestations include dyspnea, respiratory distress, lower extremity edema, and fatigue.[1-2] The occurrence of HF-PEF significantly increases the incidence of Major Adverse Cardiovascular Events (MACE), posing substantial risks to patient safety.[3] While routine antiplatelet therapy after PCI can improve cardiac function and alleviate symptoms, its overall efficacy remains suboptimal.[4] Dapagliflozin, a sodium-glucose cotransportation system 2 (SGLT2) inhibitor, inhibits myocardial calcium overload and sodium ion influx, thereby improving myocardial fibrosis and preventing ventricular hypertrophy.[5-6] This study investigates the effects of dapagliflozin on cardiac troponin, Serum Amyloid A (SAA), and Left Ventricular End-Diastolic Volume (LVEDV) in post-PICF patients.

Materials and Methods

General information

This study enrolled 120 post-PPCI HF-PEF patients treated at our hospital from May 2021 to May 2024, divided into two groups based on treatment methods: the Conventional Group (n=49) and the Daglirenet Group (n=71). The Daglirenet group included 38 males and 33 females, with an average age of 63.55±5.04 years. NYHA classification showed 15 Grade II, 35 Grade III, and 21 Grade IV patients. The number of stents placed ranged from 2 to 3, averaging 2.34±0.57. The Conventional group comprised 28 males and 21 females, aged 53-73 years (average 63.27±5.14), with NYHA classifications of 11 Grade II, 24 Grade III, and 14 Grade IV patients. Stent placement averaged 2.36±0.51, ranging from 1 to 3. Both groups were comparable ($p>0.05$). Inclusion criteria: i) met the diagnostic criteria for "HF-PEF" as defined in the Chinese Expert Consensus on Diagnosis and Treatment of Heart Failure with Preserved Ejection Fraction;[7] ii) age ≥18 years with no gender restrictions; iii) First-time PCI patients; iv) no abnormalities in major organ functions such as kidney or liver; v) good cooperation with auditory, visual, and communication abilities. Exclusion criteria: i) patients with heart failure caused by ventricular aneurysm formation or papillary muscle dysfunction; ii) participants in other studies during the same period; iii) patients with immune deficiency diseases or coagulation disorders; iv) patients with concurrent malignancies; v) patients

with severe infectious diseases; vi) patients with hemodynamic instability. The hospital's ethics committee has approved these criteria.

Methodology

This was a prospective observational study. Both groups received basic postoperative care, including continuous low-flow oxygen therapy, electrocardiographic monitoring, and bed rest after PCI, tailored to individual patient conditions. The conventional group continued standard antiplatelet therapy: Aspirin Enteric-coated Tablets (100mg orally, once daily), Clopidogrel (75mg orally, once daily) or Ticagrelor (75mg twice daily), along with Metoprolol Succinate Extended-release Tablets (11.875-47.5mg once daily). This regimen was maintained for 3 months. The Dapagliflozin Group received an additional 3-month treatment with Dapagliflozin: Dapagliflozin Tablets (10mg orally, once daily).

Observation indicators

Serum cardiac troponin I (cTnI) and SAA: Collect 5mL of fasting venous blood from patients before and after treatment. Centrifuge at 3000r/min for 10 minutes with a 10cm radius. The supernatant was separated and stored at-80°°C. C-troponin T (cTnT) was detected using rapid solid-phase immunocapillary chromatography, while SAA was analyzed via enzyme-linked immunosorbent assay (ELISA). (2) Left ventricular function indicators: Using a color Doppler ultrasound system (model: ACUSON SC2000; manufacturer: Siemens), measurements were taken to determine left ventricular ejection fraction (EF) and the E/e' ratio, calculated as the ratio of early diastolic mitral blood flow peak velocity to mitral annulus motion velocity.

Total incidence of major adverse cardiovascular events (MACE): the total incidence of MACE including malignant arrhythmia, recurrent angina pectoris, recurrent myocardial infarction, revascularization, and cardiogenic death was calculated.

Statistical methods

SPSS26.0 software was used for statistical analysis. For the measurement data （$\bar{x}\pm s$）, t-test was adopted, and for the counting data [n/(%)], $\chi 2$ test was adopted. $p<0.05$, and the comparison showed differences.

Results

Comparison of serum cTnI and SAA between the two groups

Before treatment, serum cTnI and SAA levels in dapagliflozin group and conventional group were compared ($p>0.05$). After treatment, serum cTnI and SAA levels in both groups decreased compared with that before treatment ($p<0.05$), and serum cTnI and SAA levels in dapagliflozin group were lower than those in conventional group ($p<0.05$), as shown in Table 1.

Comparison of left ventricular function indexes between the two groups

Before treatment, no EF or E/e' ratio differences were found between the dapagliflozin and control groups ($p>0.05$). After treatment, EF levels increased in both groups compared to baseline, while E/e' ratio decreased in daglilizumab group ($p<0.05$). Conversely, EF level rose and E/e' ratio decreased in daglilizumab group compared to the conventional group ($p<0.05$), as shown in Table 2.

Comparison of total MACE incidence between the two groups

The overall incidence of MACE in the dapagliflozin group (1.41%) was lower than that in the conventional group (12.24%) ($p<0.05$), as shown in Table 3.

Discussion and Conclusions

Post-PPCI myocardial ischemia-reperfusion injury can lead to myocardial cell death, resulting in massive release of cardiac troponin. This triggers increased left ventricular wall tension and left atrial volume, significantly increasing the risk of ventricular remodeling and substantially elevating the incidence of HF-PEF.[8,9] Although patients with HF-PEF maintain relatively normal LVEF, their prognosis remains comparable to those with HFrEF patients. This condition severely compromises quality of life and imposes substantial burdens on both families and society, making it a clinically significant concern.[10,11] Therefore, developing effective therapeutic strategies to improve cardiac function in post-PPCI HF-PEF patients has become a critical focus in modern clinical practice. This study demonstrated that the dapagliflozin group showed lower serum cTnI and SAA levels post-treatment compared to the conventional group, indicating its effectiveness in suppressing

myocardial protein and SAA release in HF-PEF patients after PCI. The reduction in cTnI and SAA observed in this study reflects a direct protective effect of dapagliflozin on cardiac myocytes, suggesting reduced myocardial injury and fibrosis, which is central to preserving cardiac muscle function.

Furthermore, the dapagliflozin group showed increased LVEF and decreased E/e′ ratio ($p<0.05$), suggesting its efficacy in restoring left ventricular function after PCI. These findings bridge basic pathophysiological mechanisms, such as inhibition of myocardial fibrosis and improved diastolic relaxation, with meaningful clinical outcomes, including improved EF and reduced MACE, highlighting the translational impact of dapagliflozin. The underlying mechanisms may involve multiple pathways. Dapagliflozin helps control blood glucose levels while exerting mild diuretic effects and enhancing function of vascular endothelium.[12] Its benefits can be attributed to improved myocardial microcirculation, inhibition of ventricular remodeling, and prevention of fibrosis.[13,14] Potential mechanisms include attenuation of oxidative stress, improved coronary microcirculation, inhibition of fibroblast activity, and reduction of extracellular matrix deposition, all of which protect myocardial tissue integrity[15]. Similar findings from previous studies[16] confirm that dapagliflozin effectively improves cardiac function and reduces adverse events in HF-PEF patients, consistent with our results.

Given emerging evidence that SGLT2 inhibitors also modulate skeletal muscle metabolism and exercise tolerance, future studies should explore parallel benefits in both cardiac and skeletal muscle physiology. This will be particularly relevant to translational myology, linking cardiac and skeletal muscle protection within the same therapeutic framework.

Clinically, dapagliflozin may serve as an adjunct therapy post-PCI to reduce hospital readmissions and long-term healthcare burden in HF-PEF patients. These translational implications highlight its potential role as a muscle-protective therapeutic strategy in cardiovascular medicine.

This study has a few shortcomings, such as its single-center design, relatively short duration, and lack of additional inflammatory or imaging biomarkers. Future multicenter trials with longer follow-up should incorporate advanced imaging markers and skeletal muscle function assessments to validate and extend these findings.

List of abbreviations

HF-PEF, Heart failure with preserved ejection fraction

PCI, Percutaneous coronary intervention

cTnI, Cardiac troponin I

cTnT, Cardiac troponin T

SAA, Serum amyloid A

LVEDV, Left ventricular end-diastolic volume

LVEF (EF), Left ventricular ejection fraction

E/e', Ratio of early mitral inflow velocity to mitral annular early diastolic velocity

MACE, Major adverse cardiovascular events

NYHA, New York Heart Association

ELISA, Enzyme-linked immunosorbent assay

SGLT2, Sodium–glucose cotransporter 2

HF, Heart failure

PPCI, Post-percutaneous coronary intervention

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Conflict of interest

The authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval

The Ethics Committee of The Second Affiliated Hospital of South Anhui Medical Colle approved this study (Ethical approval number: WYEFYLS2025120). The study is conformed with the The Second Affiliated Hospital of South Anhui Medical College of 18 November 2025, concerning human and animal rights.

Informed consent

All patients participating in this study signed a written informed consent form for participating in this study.

Patient consent for publication

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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