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ABOUT COVER

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LETTER TO THE EDITOR

Advancing cardiovascular outcomes with dapagliflozin and sacubitril in post-acute myocardial infarction heart failure and type 2 diabetes mellitus

Dong-Hua Liu, Xiao-Ming Dong, Wen-Jie Long

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Abstract

Coronary heart disease and type 2 diabetes mellitus (T2DM) often co-occur, presenting substantial health risks, particularly following acute myocardial infarction (AMI). While percutaneous coronary intervention (PCI) is a prevalent treatment, complications such as microvascular dysfunction may lead to heart failure, necessitating additional therapies. This editorial examines the emerging roles of sacubitril/valsartan and sodium-glucose co-transporter 2 inhibitors in managing post-PCI. Recent research investigates the combined effects of dapagliflozin and telmisartan on myocardial microperfusion in post-AMI heart failure patients with T2DM. The findings suggest that this combination enhances myocardial microcirculation, improves cardiac function, and achieves better glycemic control, with a reduced incidence of major adverse cardiovascular events. Despite ongoing challenges, the integration of dapagliflozin and sacubitril/valsartan represents a significant advancement in post-AMI care. Further investigation in larger cohorts and more diverse patient populations is required to confirm its long-term clinical outcomes.

Key Words: Heart failure; Type 2 diabetes mellitus; Dapagliflozin; Sacubitril; Cardiovascular outcomes

Core Tip: This study highlights the combined use of dapagliflozin and sacubitril in patients with post-acute myocardial infarction heart failure and type 2 diabetes. The observed improvements in myocardial microcirculation, cardiac function, and glycemic control were significant, alongside a reduced incidence of major adverse cardiovascular events. The findings underscore the potential synergistic benefits of this therapeutic combination; however, long-term outcomes require further investigation. The results support the need for personalized treatment strategies to enhance cardiovascular care in this high-risk patient group.

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TO THE EDITOR

Coronary heart disease and type 2 diabetes mellitus (T2DM) represent interrelated health challenges, which are often exacerbated by acute myocardial infarction (AMI). AMI necessitates urgent interventions such as percutaneous coronary intervention (PCI). Despite successful revascularisation, complications like microvascular dysfunction frequently lead to heart failure, highlighting the need for adjunctive therapies beyond standard treatments.

In this context, sacubitril/valsartan and sodium-glucose co-transporter 2 (SGLT2) inhibitors have emerged as pivotal therapeutic agents. Sacubitril/valsartan, known for its dual antihypertensive and cardioprotective properties, has established its role in post-PCI management. SGLT2 inhibitors, recommended in international guidelines for improving cardiovascular outcomes in high-risk patients with T2DM, chronic kidney disease, and heart failure with either reduced or preserved ejection fraction[1,2], have demonstrated efficacy in managing heart failure. Mechanistically, dapagliflozin improves myocardial energy efficiency and reduces inflammation[3], while sacubitril/valsartan promotes natriuresis and reduces vascular stiffness, enhancing cardiac output and myocardial perfusion[4]. When combined, these pathways may synergistically improve cardiac function and outcomes in post-AMI heart failure patients with T2DM. However, the clinical benefits of SGLT2 inhibitors in patients with heart failure following AMI remain unclear.

SYNERGISTIC EFFECTS OF DAPAGLIFLOZIN AND SACUBITRIL IN IMPROVING CARDIOVASCULAR OUTCOMES

The DECLARE-TIMI 58 study of 2019[5] provided initial evidence of potential benefits in AMI patients treated with SGLT2 inhibitors. This study demonstrated a 16% relative risk reduction and a 2.6% absolute risk reduction in cardiovascular events among T2DM patients with prior AMI receiving dapagliflozin compared to controls (HR 0.84, 95%CI: 0.72-0.99, $P = 0.039$), with no such effect observed in patients without prior AMI.

The study by Lv and Luo[6] investigated the combined effects of dapagliflozin and telmisartan on myocardial microperfusion in patients with post-AMI heart failure and T2DM. Employing a prospective, randomized, controlled trial design, the researchers enrolled 98 patients, adhering to ethical guidelines and employing robust statistical methodologies. Key findings from this study highlighted significant improvements in myocardial microcirculation parameters, cardiac function indicators, and glycemic control metrics in the group receiving both dapagliflozin and telmisartan compared to the control group receiving telmisartan alone. These results underscore the potential synergistic benefits of combining dapagliflozin and telmisartan in optimizing therapeutic outcomes for this vulnerable patient population. Notably, the lower incidence of major adverse cardiovascular events in the observation group highlights the clinical significance of these findings. Safety profiles between the groups were comparable, emphasizing the favorable risk-benefit ratio of adjunctive dapagliflozin therapy.

However, concerns regarding the long-term use of these agents persist, particularly with respect to electrolyte imbalances, hypoglycemia, and volume depletion in older adults or those with chronic kidney disease[7]. Further long-term studies are essential to fully assess the safety of these agents in diverse clinical settings. Ongoing monitoring will provide a more comprehensive understanding of the risk-benefit profile of these therapies in real-world clinical practice.

CHALLENGES AND FUTURE DIRECTIONS FOR COMBINING DAPAGLIFLOZIN AND SACUBITRIL

It is notable that the study did not assess long-term clinical outcomes, particularly improvements in cardiovascular death or heart failure hospitalization rates. The first international multicenter study evaluating the effects of SGLT2 inhibitors in AMI patients, the EMMY trial[8], also did not evaluate long-term clinical outcomes. The smaller-scale DAPA-MI trial investigated SGLT2 inhibitor treatment in post-AMI patients with left ventricular dysfunction or Q-wave myocardial infarction, demonstrating significant improvements in cardiovascular metabolic outcomes (soft endpoints) but no improvement in cardiovascular death or heart failure hospitalization rates, which were the primary endpoints of the trial

[9]. Similarly, the EMPACT-MI study published in 2024 similarly did not show a reduction in heart failure hospitalization or all-cause mortality composite event rates with empagliflozin in patients following AMI, nor was there a substantial difference in the occurrence of secondary endpoint events[10]. However, unlike previous studies on SGLT2 inhibitors, the EMPACT-MI study did not include T2DM as an inclusion criterion, with approximately 30% of patients in both groups having a history of diabetes. Future research should prioritize evaluating these long-term clinical outcomes to establish the role of dapagliflozin and sacubitril in standard post-AMI management.

To generalize the findings to broader populations, it is crucial to evaluate the effects of dapagliflozin and sacubitril across diverse demographic groups, including varying ethnic backgrounds, gender, and age[11]. For instance, elderly patients or those with chronic kidney disease may exhibit altered pharmacodynamics, requiring tailored approaches. Additionally, while the safety profiles of dapagliflozin and sacubitril/valsartan are generally favorable, close monitoring of renal function and electrolytes is recommended, particularly in patients with severe heart failure or advanced kidney disease. Larger trials encompassing diverse demographic groups are needed to validate the global applicability of this therapeutic combination.

CONCLUSION

Despite challenges, the integration of dapagliflozin and sacubitril represents a paradigm shift in post-AMI care, warranting further investigation in larger cohorts and diverse patient demographics. As treatment landscapes evolve, these findings pave the way for personalized therapies aimed at optimizing outcomes in complex cardiovascular conditions.

FOOTNOTES

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