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Editorial

The use of sacubitril/valsartan in different forms of heart failure

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To the editor,

Chen et al. present an interesting study that provides new insights into the impact of sacubitril/valsartan on ventricular remodeling in patients with heart failure with reduced ejection fraction (HFrEF) following valvular surgery. This editorial offers a concise review of the relevant literature and a critical analysis of the study's findings.

In the countries represented by the European Society of Cardiology (ESC), approximately 15 million patients have been diagnosed with heart failure (HF) [1]. Globally, around 26 million patients are living with HF [2]. In the PARADIGM-HF trial treating patients with HFrEF, sacubitril/valsartan demonstrated superiority over enalapril in reducing the risk of death and hospitalization due to HF [3]. Of note, the beneficial effects of sacubitril/valsartan were observed regardless of the underlying etiology in these patients [4].

Chen et al. analyzed 420 patients, among whom 34 developed HFrEF following valvular surgery. Of these, 30 patients were divided into two groups: a sacubitril/valsartan-treated group (n = 15) and a non-sacubitril/valsartan-treated group (n = 15). Repeated F-test analysis demonstrated significantly greater improvement in left ventricular ejection fraction (LVEF) in the sacubitril/valsartan-treated group. In addition, preoperative left ventricular end-diastolic diameter (LVEDD) was identified as an independent predictor of HFrEF development following valve surgery. Consistent with these data in our systematic analysis of 240 patients with chronic HFrEF with ischemic (ICMP) or non-ischemic cardiomyopathy (NICMP) followed over 24 months, we demonstrated sustained improvements in echocardiographic parameters, including LVEF, systolic pulmonary artery pressure (PAPsys), and valvular insufficiency [5]. Additionally, sacubitril/valsartan was associated with reduced left ventricular enlargement and greater improvement in filling pressures. It was reported that structural and functional changes are predicting cardiovascular (CV) mortality and HF events in patients following acute myocardial infarction (MI) [6].

Of note, although the data reported by Chen et al. are optimistic, caution is warranted taking into consideration the small sample size of the study. Additionally, in this context, the pathomechanism of post-operative HFrEF and the factors contributing to acute worsening may differ. For example, the rapid impairment of myocardial function caused by transient ischemia during surgery should be considered. Following the restoration of blood flow, myocardial function typically recovers over a period of days to weeks. This phenomenon, characterized by prolonged post-ischemic ventricular dysfunction, is known as myocardial stunning [7]. Therefore, left ventricular dysfunction and worsening following valvular surgery could represent a transient phenomenon, similar to the acute phase of Takotsubo syndrome (TTS), where left ventricular function may recover within a short period of time [8,9].

Of note, Chen et al. did not evaluate the role of biomarkers, particularly inflammatory markers, in their study. A systemic inflammatory response has also been reported following cardiac surgery [10]. Weather these inflammatory markers could predict the worsening of post-operative HF hat not yet been studied. Sacubitril/valsartan has been shown to reduce inflammatory responses, myocardial edema, and fibrosis through inhibition of the TLR4/NF-κB signaling pathway in animal models [11]. In the non-sacubitril/valsartan-treated group, Chen et al. reported that LVEF improved from 32.93 %±9.48 % at baseline to 48.87 %±9.58 % at 6 months, supporting our hypothesis that transient ischemia and myocardial stunning contribute to post-surgical left ventricular dysfunction. However, in the sacubitril/valsartan-treated group, LVEF showed even greater improvement, increasing from 34.67 % ±7.23 % at baseline to 55.73 %±5.63 % at 6 months, accounting for intra- and inter-observer variability in LVEF measurement. This greater improvement may reflect the additional anti-inflammatory and anti-fibrotic effects of sacubitril/valsartan in patients following valvular

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surgery.

In addition, Chen et al. reported a lower rate of beta-blocker use (33.3 %) in the sacubitril/valsartan-treated group compared to 26.7 % in the non-sacubitril/valsartan-treated group, with no statistically significant difference between the groups. This rate is lower than what we reported in our previously published data [12,13]. However, the benefits of sacubitril/valsartan were consistent regardless of background therapy and independent of prior coronary revascularization or beta-blocker dose [14].

For another example, despite the negative results of the PARAGON-HF trial, treatment with sacubitril/valsartan in patients with heart failure with preserved ejection fraction (HFpEF) was shown to improve left ventricular remodeling and diastolic function, likely due to its anti-inflammatory and antifibrotic properties [15]. In patients with HFpEF, sacubitril/valsartan may not only enhance ejection fraction but also help prevent its progressive decline over time.

Sacubitril/valsartan could be an effective therapy for improving outcomes in patients with postoperative HF following discharge from cardiac surgery; however, further data are needed, including larger patient cohorts and randomized clinical trials. In addition, the potential additive benefits of other HF therapies, such as beta-blockers, SGLT2 inhibitors, and aldosterone antagonists, should also be considered.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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