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Mini Review

Required Elements for Next-generation Prognostic Index beyond Left Ventricular Ejection Fraction in Heart Failure

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Abstract

Many reports are showing no differences in prognosis between patients with Heart Failure (HF) with preserved and reduced ejection fraction. All-in-one analysis with a multivariable model, including clinical characteristics, blood test, comorbidity, and echocardiographic indices, on clinical outcomes in patients with HF has not been performed rarely in previous studies. We have to accept the need to be more comprehensive in the outcome analysis of patients with HF and consider the intricate interplay of multiple variables in patient outcomes.

More Information

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In a super-aging society, admission for Heart Failure (HF) remarkably increases, especially HF with preserved ejection fraction (HFpEF) [1]. Naturally, medications for HFpEF have drawn many researchers' attention and the diversity of this clinical entity widely affects the treatment means [2,3]. Left Ventricular (LV) Ejection Fraction (LVEF) is an undeniably important index as a prognostic factor [4], but many reports are showing no differences in prognosis between patients with HFpEF and HF with reduced ejection fraction (HFrEF) [5,6]. The differences in basal disease composition between these patients lead to a significant difference in pharmacological effects [7,8], thus resulting in the evaluation of pharmacological clinical effects according to their LVEF in general. Recently, sodium-glucose cotransporter 2 inhibitors (SGLT2-i) have been drawing a lot of attention because of their pharmacological effects on clinical outcomes in patients with HF, irrespective of LVEF level [9-11]. In other words, LVEF is not the only functional prognostic factor in patients with HF, and other key factors that are essential to determine the prognosis in these patients may be missed so far. It is natural that pharmacological agents, even in SGLT2-i, cannot be clinically effective in all patients with HF. In this sense, treatment means in each phenotype has been advocated [2,12,13]. Although it is important to reveal prognostic factors beyond LVEF, how do we approach defining clinically significant prognostic factors? Each patient is one individual and has many variables to be analyzed. In the previous studies regarding this issue, analytical variables were one, including clinical characteristics, blood tests, and comorbidity, or the other, including echocardiographic indices, but all one analysis has not been performed rarely. In particular, both echocardiographic findings and natriuretic peptide level are not analyzed together [14]. We have to accept the need to be more comprehensive in the prognostic analysis of patients with HFpEF. When the patients are divided into some phenotypes, their variables for the prognostic values may be different.

We recently proposed vascular resistance-integrated diastolic index, diastolic elastance (Ed)/arterial elastance (Ea), Ed/Ea=(E/e')/(0.9×systolic blood pressure), as a prognostic factor in terms of hospital readmission for HF and/or all-cause mortality in old Japanese patients with HFpEF, one of the increasing phenotypes in a super-aging society, when adjusted for all types of variables such as age, sex, laboratory data including natriuretic peptide levels, comorbidities, and echocardiographic data [15]. Ed/Ea is an LV diastolic pressure index, but not the slope of LV pressure during the diastolic phase, showing a relative ratio of LV filling pressure (filling pressure from left atrium) to LV end-systolic pressure [16]. However, there are many modulators such as sex, follow-up time, and clinical endpoint for Ed/Ea as a prognostic factor [17]. Most echocardiographic indices such as longitudinal strain, chamber volume, and intra-cardiac pressure index may fluctuate every moment according to changes in the

pathophysiological state. The levels of hemodynamic-related indices such as Ed/Ea and natriuretic peptide level would change at that time, associated with changes in medications for HF treatment. A variable that may not be easily changed or can easily be examined in daily clinical practice is desirable as a prognostic index. Determination of significant factors for the prognosis of a certain phenotype in HF patients will be helpful as a marker index to perform a specific therapy, thus leading to tailored medicine in each patient shortly. The solution may lie in leveraging Artificial Intelligence (AI) to develop more precise models that consider the intricate interplay of multiple variables in patient outcomes. AI could be a good example of how to combine the elements to achieve the value of the proposition, but the logical structure remains to be provided for developing the AI model.

Conclusion

We have to accept the need to be more comprehensive in the prognostic analysis of patients with HF and consider the intricate interplay of multiple variables beyond LVEF in patient outcomes. Can we receive a far greater gift by using an innovative AI model to cry for the moon?

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