# Editorial

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# Association of Blood Pressure and Prognosis of Heart Failure With Systolic Dysfunction: A Myth That Should Be Solved

# Junho Hyun 💿, MD, MSc

Division of Cardiology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

 See the article "The Association Between On-treatment Ambulatory Central Blood Pressure and Left Ventricular Reverse Remodeling in Heart Failure With Reduced Ejection Fraction" in volume 5 on page 150.

Management of heart failure with reduced ejection fraction (HFrEF) has evolved into the paradigm of quadruple combination therapy.<sup>1)</sup> Accordingly, the introduction of a sophisticated combination of multiple drug classes has contributed to improved outcomes.<sup>2)</sup> However, as the number of available medications has increased substantially, it is now unclear what criteria should be used to titrate guideline-directed medical therapy (GDMT). In particular, the effect of the blood pressure (BP) lowering properties of heart failure (HF) medications remains uncertain; should this effect be regarded as detrimental unless evidence of hypoperfusion exists? Obviously, previous studies consistently reported an association between low BP and a poor prognosis, highlighting the negative implications.<sup>3,4)</sup> In contrast, the recent STRONG-HF randomized trial reported a significant reduction in adverse HF events with intensified up-titration of medical therapy if patients had a systolic BP of 95 mmHg or higher.<sup>5)</sup>

Hypotension is not uncommon during the implementation of GDMT, posing a challenging problem in clinical practice. However, there is a significant lack of evidence available to clinicians to guide the balance between efficacy and the safety threshold during optimal GDMT titration. Most of the large-scale randomized trials excluded patients with low BP.<sup>2)</sup> In this issue of the International Journal of Heart Failure, Ha et al.<sup>6</sup> retrospectively analyzed 93 patients with HFrEF who performed ambulatory blood pressure monitoring (ABPM) to investigate the clinical implications of ambulatory central and brachial BP compared to office BP. Although both ambulatory central and brachial BP measurements did not demonstrate an improved prognostication ability compared to office BP measurements, patients who achieved left ventricular reverse remodeling (LVRR) exhibited a higher BP, in line with previous findings.<sup>3,4)</sup> Besides, the results of the current study suggest that patients exhibiting low systolic BP of 100-109 mmHg on ambulatory systolic brachial BP have a significantly reduced chance of LVRR compared to those with 120-129 mmHg, which was not found for the office BP measurements. While the current study did not show the overall efficacy of ABPM usage, these findings derived from a limited number of patients suggest a potential need for further research on the utility of ABPM for HF patients because there is considerable ambiguity about appropriate BP levels or defining tolerability during GDMT titration. Another implication of this study is that ABPM results may reveal a high-risk subset of HFrEF patients who may benefit from close monitoring, following the patient frequently and optimizing the HF therapy earlier. Accordingly, the current study's results raise questions about whether

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## Correspondence to

#### Junho Hyun, MD, MSc

Division of Cardiology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43gil, Songpa-gu, Seoul 05505, Korea. Email: jhhyun0609@gmail.com

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This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https:// creativecommons.org/licenses/by-nc/4.0) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited. intensified monitoring and therapy based on ABPM results could lead to improved outcomes.

There are several issues that require interpreting this study's results with caution. First, the results do not suggest that HF management targeting a lower BP level is associated with a poor prognosis. The nature of its retrospective design limits drawing any conclusion about this issue. Moreover, patients exhibiting low BP may be representative of a frail subset with a greater comorbidity burden and a more advanced stage of HF.<sup>7</sup> Although the results of the STRONG-HF trial suggested an acceptable level of systolic BP ( $\geq$ 95 mmHg), this is one of the various clinical criteria, and it does not provide definitive evidence of an adequate BP level for HF. Second, ABPM measurements of HF patients can provide an opportunity to find masked cases of hypertension (reported incidence of up to 6% among patients with HFrEF), which can be a reason for up-titrating GDMT.<sup>8)</sup> Lastly, further research on the utility of ABPM for HF with left ventricular ejection fraction (LVEF) over 40%, which was not covered in the current study, is worth anticipating, as sacubitril/valsartan and sodium-glucose cotransporter 2 inhibitors that have BP-lowering potential have evidence for benefit in HF and LVEF over 40%.9

## ORCID iDs Junho Hyun 🕩

https://orcid.org/0000-0003-4211-3081

## **Conflict of Interest**

The author has no financial conflicts of interest.

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