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Reply to Letter to the Editor: "Comment On: Evaluation of Left Ventricular Systolic Functions of Patients with Exaggerated High Blood Pressure Response to Treadmill Exercise Test with Two-Dimensional Longitudinal Strain Imaging"

LETTER TO THE EDITOR
REPLY

To the Editor,

First and foremost, the authors would like to express their gratitude to their colleagues[1] who have shown interest in the article titled "Evaluation of the Left Ventricular Systolic Functions of Patients with an Exaggerated Hypertensive Response to Treadmill Exercise Test Using Two-Dimensional Longitudinal Strain Imaging"[2] and shared their valuable comments. Feedback of this nature, aimed at enhancing this study's contribution to clinical practice, serves as a guiding force for future research.

1. **Exaggerated Hypertensive Response and Endothelial Dysfunction**

   As the colleagues have emphasized, the pathophysiology underlying exaggerated hypertensive response (EHR) remains incompletely understood. Endothelium-dependent vasodilation in response to increased systolic wall stress during exercise has been proposed as a potential mechanism for this phenomenon. In this study, the average age of the EHR group was 49.86 ± 10.97 years, indicating a relatively young population. However, given the individual differences and multifactorial risk factors (e.g., sedentary lifestyle, unhealthy eating habits, genetic predisposition, and exposure to environmental toxins) that affect vascular health, the possibility of endothelial dysfunction in young adults is well-documented in the literature and cannot be entirely ruled out.[3-5] The primary objective of this study was to investigate the presence of subclinical cardiac dysfunction by comparing echocardiographic parameters between individuals who exhibit an exaggerated blood pressure response to exercise and those with a normal response. In future studies aimed at more comprehensively elucidating the mechanisms underlying EHR, additional assessments of endothelial function, such as flow-mediated dilatation (FMD), may prove beneficial.

2. **Left Atrial Volume Index and Body Surface Area**

   Although the average left atrial (LA) volumes and BSA are similar between the groups, the statistically significant differences observed in the LA volume index (left atrial volume index [LAVI] = LA volume/body surface area [BSA]) may initially appear paradoxical. This finding indicates that despite comparable group means, there are differences in the intra-group distributions and particularly in the variability of LAV and BSA. Even if LA volume and BSA satisfy normal distribution assumptions, slight variations and outlier effects during the ratio calculation can distort the distribution of LAVI. Furthermore, the relationship between LA volume and BSA is not necessarily linear, which may lead to differences in medians or overall distribution profiles. Consequently, factors such as measurement errors and variance differences can result in statistically significant discrepancies in LAVI, despite similar central tendencies between the 2 groups.

Muhammet Geneş

Department of Cardiology, Sincan Training and Research Hospital, Ankara, Türkiye

Corresponding author:
Muhammet Geneş
✉ muhammedgenes7@gmail.com

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3. **Subendocardial Ischemia and Left ventricular (LV) Strain Values**
   We support the theoretical premise that EHR, driven by increased myocardial oxygen demand under elevated pressure stress and a mismatch with coronary circulation, may lead to global subendocardial ischemia. In this study, although global longitudinal strain (GLS) values remained within normal limits in both groups, the relative decrease observed in the EHR group—along with alterations in diastolic dysfunction parameters—further reinforces the evidence suggesting subclinical myocardial dysfunction. This finding aligns with previous research indicating that GLS can detect early left ventricular dysfunction more sensitively than ejection fraction (EF), even when GLS values are within the normal range, as demonstrated in clinical conditions such as gestational diabetes and systemic lupus erythematosus (SLE).[6,7] Nevertheless, despite the high sensitivity of strain analysis, factors such as sample size and patient characteristics may influence the results. Consequently, to minimize the influence of chance and obtain more robust evidence, future studies with larger populations and preferably multicenter data are warranted.
4. **Future Perspective and Conclusion**
   In accordance with the colleagues' recommendations, future studies would benefit from incorporating endothelial function assessments (e.g., FMD), conducting more detailed BSA analyses, and investigating larger patient cohorts to enhance the understanding of EHR pathophysiology. Furthermore, in light of these new data, evaluating left ventricular strain parameters across various subgroups may provide valuable insights for detecting subclinical ischemia or dysfunction.

The authors would like to express their gratitude once again for the interest in this study, which contributes to the advancement of research and the existing literature.

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