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Associations among Obesity Degree, Glycemic Status, and Risk of Heart Failure in 9,720,220 Korean Adults (*Diabetes Metab J* 2020;44:592-601)

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First of all, we would like to thank Darae Kim for her interest in our article [1]. We are delighted that Kim recognized the impact our study results will have on future research in this field. We found that participants with impaired fasting glucose (IFG) and diabetes showed a significantly increased heart failure (HF) risk compared to normoglycemic participants based on National Health Insurance System (NHIS) data. In addition, this increased risk of HF was most prominent in underweight and class II obese participants versus participants with normal weight, showing a J-shaped relationship. To the best of our knowledge, our study was the first to show a gradual increase in HF risk across glycemic status and obesity grade in three-dimensional analysis.

In our study, participants who had diabetes at baseline were at 1.86-fold increased risk of HF during a median 6.3 years of follow-up compared with normoglycemic participants. However, the more surprising finding was that even participants with IFG showed a small but significant increase in risk of HF (odds ratio, 1.08), suggesting an effect of hyperglycemia on HF development. The presumed mechanisms of HF development with hyperglycemia are myocardial triglyceride accumulation, insulin resistance, cardiomyocyte stiffness and myocardial collagen deposition due to deposition of advanced glycation end products, alterations in myocardial energy metabolism from glucose as the main fuel to fatty acid oxidation, and insulin resistance as an aggravating factor [2-4].

As Kim kindly suggested, there were some differences in HF risk according to age and sex in our study. In subgroup analyses, in those without diabetes, people 65 years or older showed higher HF risk than people younger than 65 years. However, this was exactly the opposite in those with diabetes, in that younger patients showed higher HF risk than older patients. In addition, in analysis according to sex, in those without diabetes, women showed slightly increased HF risk compared with men, while this difference was not significant in those with diabetes. Although we did not further analyze HF risk according to obesity degree in the different sexes as Kim suggested, we could observe that sex has different effects on HF risk [5]. Unfortunately we could not analyze HF risk according to subtype of HF, since there were no echocardiogram data or claim codes for HF subtype in the NHIS data obtained.

We agree with Kim's opinion that the risk of HF associated with obesity or dysglycemia is modifiable. Diastolic dysfunction is often associated with HF with preserved ejection fraction (HFpEF) [6]. Therefore, weight loss could attenuate hemodynamic derangements that can lead to HFpEF, as obesity is one of the pathophysiologic causes of diastolic dysfunction [7]. Recent studies reached a consensus on the positive effects of exercise in the prevention and treatment of HF, probably through weight loss and reduction of cardiac loading [8]. Therefore, we should educate our patients with high HF risk on healthy lifestyle modifications related to diet and exercise. Accordingly, recent guidelines on HF recommended regular exercise as a treatment option for HF [9].

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We would like to thank Darae Kim again for her comprehensive review of the relationship between HF and metabolic risk factors. Furthermore, as she mentioned, we hope that our study will be a starting point for research on the role of lifestyle interventions in HF prevention.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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