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Letter

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Letter: Effects of 6 Months of Dapagliflozin Treatment on Metabolic Profile and Endothelial Cell Dysfunction for Obese Type 2 Diabetes Mellitus Patients without Atherosclerotic Cardiovascular Disease (J Obes Metab Syndr 2020;29:215–21)

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Hong et al.[1] reported that 6 months of dapagliflozin combined with metformin is beneficial for obese patients with type 2 diabetes mellitus (T2DM) for improvement not only of metabolic parameters, but also of pulse wave velocity (PWV). Based on this finding, they suggested that a decrease in arterial stiffness with dapagliflozin plays a crucial role in explaining its cardiovascular benefit.[1] Considering that the significant improvement of central PWV was observed only in a body fat reduction group and that there was a strong correlation between change of body fat mass and PWV (coefficient in regression, 0.393) in their study,[1] the effect of dapagliflozin on PWV might be caused by reduction of body fat.

Even in subjects without T2DM, reduction of body weight improves PWV in an obese population.[2] In addition, a randomized controlled trial showed that non-pharmacological behavioral weight loss intervention could improve both central and peripheral PWV.[3] Recent meta-analyses confirmed the dose-response relationship between amount of behavioral weight reduction and improvement of PWV.[4,5]

In addition to fat mass, blood pressure and glucose level are independent determining factors for PWV in patients with T2DM;[6,7] blood pressure is the most important.[7] Empagliflozin, another sodium glucose cotransporter 2 (SGLT2) inhibitor, reduces arterial stiffness through glucose lowering, antihypertensive, weight reduction,[8] and improvement of systemic inflammation.[9] SGLT2 inhibitors can also produce acute improvement of systemic endothelial function and arterial stiffness through natriuresis and oxidative stress reduction.[10]

Hong et al.[1] showed a beneficial effect of 6 months of dapagliflozin with metformin on PWV and suggested that fat reduction by dapagliflozin is responsible for that beneficial effect. They did not report the change in blood pressure during the study period. Considering that blood pressure is one of the most important determinants of PWV, this is a major limitation of the study, and the correlation between PWV and fat mass should be investigated with adjustment of blood pressure. Other possible con-

founders such as glucose level, age, sex, and inflammatory markers (if possible) as well as blood pressure should have been incorporated in the analysis on the association between fat mass and PWV.

CONFLICTS OF INTEREST

Bo Kyung Koo has worked as an Associate Editor of the journal since 2019. However, she was not involved in the peer reviewer selection, evaluation, or decision process of this article. Otherwise, no other potential conflicts of interest relevant to this article were reported.

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