Editorial Comment

α-Glucosidase Inhibitors: New Therapeutic Agents for Chronic Heart Failure

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Chronic heart failure is a major health issue in both Western and Asian countries (*1*, *2*). In spite of advances in treatment with angiotensin-converting enzyme (ACE) inhibitors, diuretics and β-blockers, the mortality of patients with heart failure remains high. At the same time, the prevalence of type II diabetes has increased significantly in accordance with worldwide changes in lifestyle (*3*). While the most common cardiac manifestation in diabetic patients is ischemic heart disease, diabetes mellitus has also been related to cardiac dysfunction (*4*, *5*), including both diastolic and systolic heart failure.

Metabolic disorder plays a role in the development of myocardial dysfunction; hyperglycemia, impaired myocardial glucose uptake, and increased turnover of free fatty acids contribute to hyperglycemia-related cardiac dysfunction (*6–8*). Lack of physical activity, hypermetabolic state, intracellular metabolic defects, and low muscle perfusion also affect cardiac performance. Advanced heart failure is related to marked insulin resistance, and insulin resistance contributes to impairment of glucose tolerance and the onset of type 2 diabetes mellitus. As a possible mechanism for these effects, endothelial dysfunction may cause insulin resistance and impaired glucose intolerance in patients with chronic heart failure. Activation of the sympathetic system in chronic heart failure not only increases insulin resistance but also decreases the release of insulin from the pancreatic β cells.

Although the interaction between insulin resistance and heart failure has been widely studied, there have been few reports on the relation between postprandial hyperglycemia and chronic heart failure. Liao *et al*. previously reported that improvement of glycemic control through voglibose therapy inhibited cardiac remodeling by decreasing myocardial oxidative stress in mice with cardiac pressure overload (*9*). In this issue, Kim *et al*. evaluate the prevalence of abnormalities of glucose metabolism in patients with chronic heart failure by measuring fasting glucose levels and by oral glucose tolerance test (OGTT) (*10*). In addition, they examine whether an α-glucosidase inhibitor can improve the severity of chronic heart failure due to dilated cardiomyopathy, whether the abnormalities of glucose metabolism are tightly associated with the severity of chronic heart failure, and whether these abnormalities contribute to the deterioration of chronic heart failure in patients with dilated cardiomyopathy. Their results show that the α-glucosidase inhibitor corrected the abnormalities of glucose metabolism and improved the pathophysiology of chronic heart failure in patients with chronic heart failure due to dilated cardiomyopathy with impaired glucose tolerance. However, the mechanisms by which heart failure causes impaired glucose tolerance and transient glucose spike impairs cardiac function remain unknown. Kim *et al*. (*10*) clearly show the efficacy of an α-glucosidase inhibitor for postprandial hyperglycemia in patients with nonischemic heart failure. The STOP-NIDDM trial suggests that treating impaired glucose tolerance (IGT) patients with acarbose results in a significant reduction in the risk of cardiovascular disease and hypertension (*11*). There are few useful drugs for improving the outcome of patients with chronic heart failure. This paper suggests that α-glucosidase inhibitors may be useful as novel agents for the treatment of chronic heart failure, in addition to such conventional drugs as renin angiotensin system inhibitors, diuretics, and β-blockers. If the mechanism by which post-prandial hyperglycemia impairs cardiac func-

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tion can be clarified, a new aspect of the pathology of chronic heart failure will be elucidated. It remains to be determined whether improved post-prandial hyperglycemia favorably influences the outcome of diabetic heart failure patients, and large clinical studies are needed to address this important question.

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