



COMMENT ON OHKUMA ET AL.

# Cardiac Stress and Inflammatory Markers as Predictors of Heart Failure in Patients With Type 2 Diabetes: The ADVANCE Trial. *Diabetes Care* 2017;40:1203–1209

Tomoyuki Kawada

*Diabetes Care* 2018;41:e38 | <https://doi.org/10.2337/dc17-2319>

Ohkuma et al. (1) examined biomarkers for the prediction of heart failure in patients with type 2 diabetes. They conducted a nested case-cohort study and presented adjusted hazard ratios for heart failure with 95% CIs based on N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitivity cardiac troponin T (hs-cTnT), interleukin-6, and high-sensitivity C-reactive protein. I have some concerns about their study.

First, the authors clarified that only the addition of NT-proBNP to the model of conventional risk factors presented improvement of 5-year prediction of heart failure in patients with type 2 diabetes. Although these four biomarkers have no direct benefit for predicting heart failure, they may serve as indicators of cardiac pathogenesis. To avoid adverse clinical outcomes, there is an advantage to using different biomarkers for early detection of heart failure in patients with type 2 diabetes.

Second, the combination of hs-cTnT and NT-proBNP increased predictive ability for cardiovascular events and death in patients with type 2 diabetes (2). Moreover, a report states that hs-cTnT is a more useful biomarker than NT-proBNP for vascular risk prediction (3).

As these reports did not include heart failure as one of the cardiovascular events, caution should be exercised in monitoring the progression of heart failure to cardiovascular events.

Third, Nambi et al. (4) reported an advantage in combining hs-cTnT and NT-proBNP to predict the risk of heart failure, with a mean follow-up of 10.4 years. The percentage of patients with diabetes was 15.6%, and the contribution of type 2 diabetes to the subsequent heart failure incident was unknown. When the standard intervention and intensive glucose-lowering intervention were compared in patients with type 2 diabetes, the intensive glucose-lowering intervention showed significant reduction of risk of cardiovascular events, including new or worsening congestive heart failure (5). Glycemic control affects subsequent heart failure in patients with type 2 diabetes.

Finally, the authors handled electrocardiogram findings as independent variables, and the combination of electrocardiogram findings with biomarkers should also be considered in the analysis. In addition, the adjustment of medication for type 2 diabetes, such as dipeptidyl peptidase 4 inhibitors, should be considered in the analysis because of

its possible association with heart failure in previous literature.

**Duality of Interest.** No potential conflicts of interest relevant to this article were reported.

## References

1. Ohkuma T, Jun M, Woodward M, et al.; ADVANCE Collaborative Group. Cardiac stress and inflammatory markers as predictors of heart failure in patients with type 2 diabetes: the ADVANCE trial. *Diabetes Care* 2017;40:1203–1209
2. Hillis GS, Welsh P, Chalmers J, et al. The relative and combined ability of high-sensitivity cardiac troponin T and N-terminal pro-B-type natriuretic peptide to predict cardiovascular events and death in patients with type 2 diabetes [published correction appears in *Diabetes Care* 2015;38:1393]. *Diabetes Care* 2014;37:295–303
3. Price AH, Weir CJ, Welsh P, et al. Comparison of non-traditional biomarkers, and combinations of biomarkers, for vascular risk prediction in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study. *Atherosclerosis* 2017;264:67–73
4. Nambi V, Liu X, Chambless LE, et al. Troponin T and N-terminal pro-B-type natriuretic peptide: a biomarker approach to predict heart failure risk—the Atherosclerosis Risk in Communities study. *Clin Chem* 2013;59:1802–1810
5. Hayward RA, Reaven PD, Wiitala WL, et al.; VADT Investigators. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2015;372:2197–2206

Department of Hygiene and Public Health, Nippon Medical School, Tokyo, Japan

Corresponding author: Tomoyuki Kawada, [kawada@nms.ac.jp](mailto:kawada@nms.ac.jp).

© 2018 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <http://www.diabetesjournals.org/content/license>.