RESPONSE TO 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

Toshiaki Ohkuma,[1] Mark Woodward,[1,2,3] and John Chalmers,[1] on behalf of the ADVANCE Collaborative Group

Diabetes Care 2018;41:e39 | https://doi.org/10.2337/dci17-0060

We would like to thank Dr. Kawada for the comments (1) on our paper (2).

First, we agree that the use of biomarkers is beneficial for early detection of heart failure and prevention of subsequent other cardiovascular diseases.

Second, we agree with the need for careful monitoring of the incidence of cardiovascular diseases other than heart failure, as heart failure is the second most common initial presentation of cardiovascular disease in patients with type 2 diabetes after peripheral arterial disease (3).

Third, we agree with the possible influence of glycemic control on the incidence of heart failure. As cited by Dr. Kawada, intensive glucose-lowering therapy significantly decreased the risk of a composite of major cardiovascular events including heart failure in the Veterans Affairs Diabetes Trial (VADT) (4). Although a later meta-analysis of randomized controlled trials including the VADT found that the intensive glucose-lowering treatment did not decrease the risk of heart failure (5), we included randomized blood pressure–lowering intervention as well as HbA_{1c} as covariates, given the possible confounding of these factors.

Finally, we agree that electrocardiogram findings were important for the risk prediction of heart failure and thus included them in the model as covariates. However, as the primary objective of our paper was to examine the predictive ability of biomarkers for heart failure, we did not test the prognostic ability of the combination of electrocardiogram findings and biomarkers. We also agree that there is a possible adverse effect for heart failure of medication such as dipeptidyl peptidase 4 inhibitors used to treat type 2 diabetes. However, dipeptidyl peptidase 4 inhibitors were not on the market when the ADVANCE trial started.

Funding. The ADVANCE trial was funded by a grant from the National Health and Medical Research Council of Australia and from Servier. T.O. holds the Japan Society for the Promotion of Science Postdoctoral Fellowship for Research Abroad. M.W. is a National Health and Medical Research Council of Australia Principal Research Fellow (1080206).

Duality of Interest. M.W. reports consultancy fees from Amgen. J.C. reports grants from Servier, administered through the University of Sydney as Co-Principal Investigator for ADVANCE and ADVANCE-ON, and personal fees from Servier. No other potential conflicts of interest relevant to this article were reported.

References

1. Kawada T. 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 (Letter). Diabetes Care 2018;41:e38. https://doi.org/10.2337/dc17-2319
2. 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
3. Shah AD, Langenberg C, Rapsomaniki E, et al. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1.9 million people. Lancet Diabetes Endocrinol 2015;3:105–113
4. 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
5. Ray KK, Seshasai SR, Wijesuriya S, et al. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. Lancet 2009;373:1765–1772

[1]*The George Institute for Global Health, University of Sydney, Sydney, New South Wales, Australia*
[2]*The George Institute for Global Health, University of Oxford, Oxford, U.K.*
[3]*Department of Epidemiology, Johns Hopkins University, Baltimore, MD*

Corresponding author: Toshiaki Ohkuma, tohkuma@georgeinstitute.org.au.