Diabetes therapy and cardiac risk

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TO THE EDITOR: Recently, Drs. Zimmerman and Pantalone[1] cited the Diabetes Control and Complications Trial (DCCT)[2] and the United Kingdom Prospective Diabetes Study (UKPDS)[3] as evidence that glycemic control lowers cardiac risk in type 2 diabetes. And in a related counterpoint article, Drs. Menon and Aggarwal[4] also discussed the UKPDS.

These studies should not be cited in this context, since the DCCT is a study of type 1 and not type 2 diabetic patients, and the UKPDS was performed in an era when statins were not available. The UKPDS was launched in 1977 and completed in 1997, and statins were not available until 1987. Indeed, the UKPDS showed that the strongest risk factor for myocardial infarction was an elevated level of low-density lipoprotein cholesterol, followed by a low level of high-density lipoprotein cholesterol.[5] It is therefore not surprising that in the initial UKPDS report the incidence of myocardial infarction was not increased in the group with a 0.9% higher hemoglobin A_{1c}, but that in the 10-year follow-up, when statins were probably used by most patients, myocardial infarction was reduced by a significant 15% ($P = .01$).[3,6] As would be expected in the more modern studies, ie, the Action to Control Cardiovascular Risk (ACCORD),[7] the Action in Diabetes and Vascular Disease (ADVANCE),[8] and the Veteran Affairs Diabetes Trial (VADT),[9] cardiovascular events were not reduced with improved glycemic control.

While the UKPDS clearly demonstrated a decrease in microvascular disease due to improved glycemic control, it should not be used as evidence that improved glycemic control in type 2 diabetes decreases cardiac events.[3,6]

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IN REPLY: We appreciate Dr. Bell's interest in and comments regarding our recent article. Dr. Bell contends that the DCCT[1] and UKPDS[2] studies should not be cited since the DCCT is a study of type 1 and not type 2 diabetic patients, and the UKPDS was performed in an era when statins were not available.

While we can appreciate his point of view, we disagree with his interpretation of the available data. These studies, and their respective observational follow-up reports,[3,4] provide evidence that early intervention may reduce cardiovascular risk, and that our approach to examining cardiovascular risk reduction in high-risk cardiovascular patients, as in ACCORD,[5] ADVANCE,[6] and VADT,[7] may be shortsighted. There is an important difference

between reducing long-term cardiovascular risk by treating younger and healthier patients with diabetes (type 1 or type 2) early in the disease course, before the development of complications (including cardiovascular disease), as was the case in DCCT and UKPDS, vs treating older patients with diabetes who have established cardiovascular disease or who have numerous risk factors substantially increasing their cardiovascular risk, as in ACCORD, ADVANCE, and VADT.

To his second point, that the UKPDS did not demonstrate cardiovascular risk reduction until after the 10-year follow-up when statins were probably utilized by the vast majority of patients, there would not have been a difference in cardiac events between treatment and control groups during this observational period if the statins were the cause of the reduced rate of cardiac events. The control and treatment groups would have had the same reduction in events. That was not the case. The finding of a lower risk of myocardial infarction at the completion of the follow-up period, despite ubiquitous statin use by both the treatment and control groups during this 10-year period, suggests another variable—ie, that the early differences in glycemic control achieved between the treatment and control groups during the UKPDS was responsible for the observed reduction in the risk of myocardial infarction.

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