COMMENT ON NORDWALL ET AL.

Impact of HbA_{1c}, Followed From Onset of Type 1 Diabetes, on the Development of Severe Retinopathy and Nephropathy: The VISS Study (Vascular Diabetic Complications in Southeast Sweden). Diabetes Care 2015;38:308–315

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I read with great interest a recent article by Nordwall et al. (1) that investigated the association of long-term glycemic control with microvascular complications in patients with type 1 diabetes. They obtained data of HbA_{1c} measured during the whole follow-up period of 20–24 years and calculated weighted mean HbA_{1c} ($wHbA_{1c}$) as a marker of long-term glycemic control.

However, their analysis was at risk for misevaluation of glycemic control. In their analysis, $wHbA_{1c}$ was derived from HbA_{1c} values until the last follow-up time in patients free from microvascular events, whereas in those who experienced the events, it was from HbA_{1c} values until the onset. Take two cases, for example. Both cases had 9% of mean HbA_{1c} levels for the first 10 years and 6% of mean HbA_{1c} levels for the next 10 years. One case developed a microvascular complication at 10 years. The other case completed the 20-year follow-up without any microvascular event. According to their analysis, the former case had 9% of $wHbA_{1c}$, whereas the latter had 7.5% of $wHbA_{1c}$. The fact that the latter case had 9% of $wHbA_{1c}$ for the first 10 years similar to the former case was completely neglected, simply because the latter case was "by chance" free from any microvascular event at 10 years. Thus, in their analysis, an outcome measure (i.e., microvascular events) substantially influenced its explanatory variable (i.e., $wHbA_{1c}$ as a marker of long-term glycemic control), which would not be favorable to assessing the influence of glycemic control on microvascular events. Their current implications might be therefore based on an inadequate assessment.

I just wonder if their current implications could be validated by a different statistical approach, for example, a Cox hazards analysis with microvascular events treated as a dependent variable and $wHbA_{1c}(t)$ treated as a time-dependent covariate, where $wHbA_{1c}(t)$ indicates the weighted mean HbA_{1c} between time 0 (i.e., onset of diabetes) and arbitrary time t.

A perfect database of HbA_{1c} during the whole follow-up period of decades is still rare and valuable in this field; therefore, I look forward to such a validation with the use of their database.

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References

1. Nordwall M, Abrahamsson M, Dhir M, Fredrikson M, Ludvigsson J, Arnqvist HJ. Impact of HbA_{1c}, followed from onset of type 1 diabetes, on the development of severe retinopathy and nephropathy: the VISS Study (Vascular Diabetic Complications in Southeast Sweden). Diabetes Care 2015;38:308–315

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