COMMENT ON IPP AND KUMAR

A Clinical Conundrum: Intensifying Glucose Control in the Presence of Advanced Diabetic Retinopathy. Diabetes Care 2021;44:2192–2193

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Diabetes Care 2022;45:e39| https://doi.org/10.2337/dc21-2071

We were interested by the recent article from Ipp and Kumar (1), who questioned whether we should slow down glycemic normalization in subjects with type 2 diabetes and advanced retinopathy due to the recent report from the Veterans Affairs Diabetes Trial (VADT) (2). Diabetic retinopathy is a strong predictor of other complications, such as cardiovascular events (3) and lower extremity arterial disease (4), and we wondered whether a quick decline of HbA_{1c} relates to their occurrence.

Three hundred and eighty-nine subjects (age 62 ± 9 years; duration of diabetes 14 ± 9 years; 56.9% men) were admitted in our Diabetology ward from 2009 to 2017 for uncontrolled (HbA_{1c} 8.5 ± 1.7%) and/or complicated type 2 diabetes (macroangiopathy 35.8%, diabetic kidney disease 42.8%, and history of foot ulcer 22.0%). During 54 ± 26 months of follow-up, 29 new or worsening retinopathies, 47 cardiovascular events, and 36 foot ulcers occurred.

Ninety-six subjects (24.6%) had diabetic retinopathy at admission. By Cox regression analysis adjusted for age and sex, retinopathy at admission was related to later worsening retinopathy (hazard ratio [HR] 3.49, 95% CI 1.58–7.71), cardiovascular events (HR 1.877, 95% CI 1.01–3.45), and foot ulcers (HR 3.38, 95% CI 1.72–6.64).

Sixty-six subjects (17%) had experienced a dramatic decline of their HbA_{1c} of more than −1.5% during the 4 months before their admission, as defined by Shurter et al. (5); their reduction was −3.0 ± 1.5%. They were similarly distributed among subjects with (16.7%) and without (17.1%) retinopathy. We observed a significant interaction between dramatic decline of HbA_{1c} and retinopathy for their relationships to each later complication (all $P < 0.01$). For these 66 "dramatic decliners," baseline retinopathy was related to higher risks of later worsening retinopathy (HR 38.74, 95% CI 3.79–395.59), cardiovascular events (HR 3.34, 95% CI 1.01–11.14), and foot ulcers (HR 7.03, 95% CI 1.74–28.43). For the other 323 subjects with overall stable HbA_{1c}, retinopathy was associated with later foot ulcers (HR 3.08, 95% CI 1.38–6.89) but not worsening retinopathy (HR 1.64, 95% CI 0.58–4.65) or cardiovascular events (HR 1.70, 95% CI 0.82–3.52).

Diabetic retinopathy can progress when glucose control improves quickly, and aggressive treatment with intraocular VEGF inhibitors may prevent this worsening, as proposed by Ipp and Kumar (1). However, it is a marker of more generalized vascular lesions, which can also worsen with hurried glucose control. Our study may be biased by its observational design, but it suggests that glucose lowering should be slow and cautious for subjects with retinopathy and uncontrolled type 2 diabetes.

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

References

1. Ipp E, Kumar M. A clinical conundrum: intensifying glucose control in the presence of advanced diabetic retinopathy. Diabetes Care 2021;44:2192–2193
2. Azad N, Agrawal L, Bahn G, et al.; VADT Study Group. Eye outcome in Veterans Affairs Diabetes Trial after 17 years. Diabetes Care 2021;44:2397–2402
3. Kramer CK, Rodrigues TC, Canani LH, Gross JL, Azevedo MJ. Diabetic retinopathy predicts all-cause mortality and cardiovascular events in both type 1 and 2 diabetes: meta-analysis of observational studies. Diabetes Care 2011;34:1238–1244
4. Foussard N, Saulnier PJ, Potier L, et al.; SURDIAGENE Study Group. Relationship between diabetic retinopathy stages and risk of lower-extremity arterial disease in patients with type 2 diabetes. Diabetes Care 2020;43:2751–2759
5. Shurter A, Genter P, Ouyang D, Ipp E. Euglycemic progression: worsening of diabetic retinopathy in poorly controlled type 2 diabetes in minorities. Diabetes Res Clin Pract 2013;100:362–367

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Received 6 October 2021 and accepted 8 October 2021