COMMENT ON ANDERSEN ET AL.

Risk-Factor Trajectories Preceding Diabetic Polyneuropathy: ADDITION-Denmark. Diabetes Care 2018;41: 1955–1962

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We were interested in the article by Andersen et al. (1), who showed that diabetic polyneuropathy (DPN) was related to baseline HbA_{1c} and its increase in 452 participants with type 2 diabetes in the Danish arm of the Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (ADDITION-Denmark) (1). If HbA_{1c} trajectories influence DPN, it could be improved by treatment. In the Kumamoto trial, the vibration perception thresholds (VPT) stabilized in patients on intensive glucose control, whereas they increased from 22 to 37 V in those on conventional treatment (2).

Andersen et al. (1) cautiously mentioned that their results may not apply to people with type 2 diabetes clinically diagnosed later in the disease course, with higher HbA_{1c} that changed more over time. Established DPN has been described as inexorably progressing, with increasing VPT despite improved metabolic markers (3). In addition, a rapid decrease of high HbA_{1c} sometimes leads to "treatment-induced" painful neuropathy (4), which presents an even greater clinical challenge. Whether a long-term frank reduction of HbA_{1c} may alter the VPT has not been reported.

We measured VPT (Horwell Neurothesiometer, U.K.) and HbA_{1c} in subjects admitted for uncontrolled or complicated type 2 diabetes in our Diabetology unit of Bordeaux's University Hospital. We collected retrospectively their HbA_{1c} from previous years, and we measured their skin autofluorescence, a marker of glycemic memory that has been related to DPN (5).

Our 184 participants were mainly men (56%), aged 63 ± 9 years, with 17 ± 10 years duration of diabetes that was poorly controlled (HbA_{1c} 8.5 ± 1.8%) and often complicated: 35.3% had macroangiopathy (history of myocardial infarction, stroke, or revascularization procedures), 46% had diabetic kidney disease, and 26.3% had a sight-threatening retinopathy. We categorized them according to their previous HbA_{1c} trajectories: HbA_{1c} decliners were defined as the lowest quintile of the difference between the latest and the most ancient HbA_{1c}. These 35 decliners underwent a frank long-term decline of HbA_{1c}: 11.6 ± 2.5% (6 years before), 9.1 ± 2.2% (3 years before), 8.6 ± 1.8 (1 year before), and 7.2 ± 1.6% at hospital admission, whereas HbA_{1c} levels were stable for the others: 8.5 ± 1.6%, 8.5 ± 1.8%, 8.8 ± 1.7%, and 8.8 ± 1.7%, respectively, at similar times. HbA_{1c} decliners did not differ from the others in terms of age, sex, diabetes duration, BMI, blood lipids, arterial hypertension, renal function, and albumin excretion rate, but their VPT were higher: 22 ± 17 vs. 16 ± 11 V ($P < 0.05$). By linear regression analysis, the VPT were inversely related to the HbA_{1c} decline over time ($\beta = -0.20$, $P < 0.005$) and this remained significant after adjusting for age, sex, BMI, diabetes duration, blood lipids, and arterial hypertension. In HbA_{1c} decliners, the prevalence of sight-threatening retinopathy (40% vs. 22%) and the skin autofluorescences (3.0 ± 0.3 vs. 2.8 ± 0.5 arbitrary units) were also higher (both $P < 0.05$).

The high VPT and severe retinopathy in our HbA_{1c} decliners may be due to the frank glucose lowering itself, as reported in "treatment-induced" neuropathy (4), or to their hidden previous history of long-term hyperglycemia as suggested by their high skin autofluorescence. Figure 1 from the article by Andersen et al. (1) shows that some of the participants in ADDITION-Denmark also underwent a frank decline in HbA_{1c} over time, and it would be interesting if the authors could analyze whether these decliners had more DPN.

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

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