



COMMENT ON LACY ET AL.

## Long-term Glycemic Control and Dementia Risk in Type 1 Diabetes.

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We read with great interest the recent article by Lacy et al. (1), who investigated the association of long-term glycemic control with dementia in older individuals with type 1 diabetes. They reported that those with majority exposure to HbA<sub>1c</sub> 8–8.9% and ≥9% had increased dementia risk (1). We agree that intensive diabetes therapy, aimed at achieving glycemic control as close to the nondiabetic range as safely as possible, decreases the risk for developing multiple micro- and macrovascular complications.

However, tight glycemic control can expose the patient to hypoglycemia. Multiple studies have found an association between hypoglycemia and reduced cognition, as well as greater risk for developing dementia. In a study conducted by Whitmer et al. (2), the attributable risk of dementia between individuals with and without a history of hypoglycemia was 2.39% per year (95% CI 1.72–3.01). The Korea National Diabetes Program (KNDP) cohort study (3) also found an increased risk of dementia in subjects with hypoglycemia (HR 2.689 [95% CI 1.080–6.694]), as did the study by Lin and Sheu (4), which reported a rate ratio of 2.76 (95% CI 2.06–3.70,  $P \leq 0.001$ ) in subjects with hypoglycemia

vs. 1.60 (95% CI 1.19–2.14,  $P = 0.002$ ) in subjects without.

It is particularly interesting that the mean age of dementia onset was 64.6 years (median 63.3 years), especially considering dementia diagnoses as early as 56.1 years of age. Dementia in younger patients presents a particular challenge. Young-onset dementia includes patients with onset before 65 years of age; the differential diagnosis is often broad but of great interest because many of the young-onset dementias are treatable. A diagnosis of dementia tends to attract therapeutic nihilism and, although treatment is only symptomatic for many patients, there are other nondegenerative diseases that can present with cognitive impairment and can be successfully treated, necessitating further investigation (5).

Therefore, we are not convinced that the authors' conclusion that those with majority exposure to HbA<sub>1c</sub> ≥8% had increased dementia risk is definitive. We think that it is crucial to point out that hypoglycemia is an important contributing factor that was undermined in this study by only taking into account severe episodes of hypoglycemia. Finally, we strongly agree this is a topic that should be examined in greater detail in future

studies. These results suggest adults with type 1 diabetes are at increased risk of developing dementia and may have increased risk at younger ages than the general population. Most are of employable age and many might be the main income earner, suggesting the socioeconomic burden would be of great relevance.

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

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