



COMMENT ON SJÖHOLM ET AL.

## Association of Bariatric Surgery With Cancer Incidence in Patients With Obesity and Diabetes: Long-term Results From the Swedish Obese Subjects Study. *Diabetes Care* 2022;45:444–450

*Diabetes Care* 2022;45:e72 | <https://doi.org/10.2337/dc21-2477>

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We were interested by the recent article in *Diabetes Care* by Sjöholm et al. (1), who reported that the incidence of cancer was reduced 21.3 years after bariatric surgery in patients with diabetes who participated in the Swedish Obese Subjects (SOS) cohort, with an especially promising 60% reduction for the 102 subjects whose diabetes remitted for 10 years, mainly ( $N = 91$ ) after the intervention. In their discussion, the authors hypothesized that the most plausible mechanism to explain this remarkable result was the reduction of hyperinsulinism; however, the relation between initial serum insulin levels and later cancers was not significant.

We suggest that another mechanism contributes to the reduced incidence of cancer after the remission of diabetes: as shown by the reduction of microvascular complications (2), well-controlled glycemia during decades of diabetes remission probably reduced the generation and tissular accumulation of advanced glycation end products (AGEs). Biological studies have shown that these molecules not only are involved in diabetic vascular complications but also can favor the development of cancer (3). We recently reported that the skin autofluorescence (SAF) of AGEs was a predictor of later cancer in 413 subjects with type 2 diabetes (4). The article by

Sjöholm et al. (1) prompted us to test whether this was also true for our patients with BMI higher than 35 kg/m<sup>2</sup>, the usual threshold to discuss bariatric surgery for subjects with type 2 diabetes.

One hundred twenty-seven subjects with type 2 diabetes (aged 61 ± 8 years, duration of diabetes 15 ± 10 years, HbA<sub>1c</sub> 9.0 ± 1.7%) and BMI at 39.6 ± 4.3 kg/m<sup>2</sup> were followed during 5.2 ± 2.3 years, and 15 of them developed a cancer. These subjects did not differ from others for age, BMI, duration of diabetes, or HbA<sub>1c</sub>. More were men (73.3% vs. 42.9% without new cancer,  $P = 0.03$ ), and their SAF, measured with an AGE-Reader (Diagnoptics, Groningen, the Netherlands), was higher: 3.02 ± 0.50 vs. 2.68 ± 0.63 arbitrary units,  $P = 0.04$ . Most of the cancer cases (13/15) occurred in subjects with SAF above the median at 2.7 arbitrary units (log rank  $P = 0.02$ ). New cancers were related to the SAF by Cox regression analysis adjusted for age and sex: hazard ratio 2.40, 95% CI 1.11–5.19.

Weight loss interventions reduce serum AGE concentrations, but their effects on concentrations of the soluble receptor for AGE are less clear (5). We are not aware of any study on SAF before/after bariatric surgery. As their long-term exposure to hyperglycemia

was presumably less improved than that for 10-year diabetes remitters, it would be interesting to know whether the 168 subjects whose diabetes remitted for only 2 years had an intermediate risk of later cancer in the SOS study.

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

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