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# Skin Advanced Glycation End Product Accumulation Is Poorly Reflected by Glycemic Control in Type 2 Diabetic Patients (ZODIAC-9)

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## Abstract

### Background:

Glycemic memory can be reflected by tissue accumulation of advanced glycation end products (AGEs). In type 1 diabetes mellitus (T1DM) patients, hemoglobin A1c (HbA1c) levels over various time periods poorly predicted the accumulation of different AGEs in skin biopsies. Our aim was to investigate whether HbA1c assessments can predict the change in skin AGEs during time in type 2 diabetes mellitus (T2DM).

### Methods:

We included 452 T2DM patients participating in a shared-care setting, who are screened annually for HbA1c and diabetic complications. Baseline and follow-up levels of skin AGEs were assessed with a validated noninvasive autofluorescence (AF) method, which is based on the fluorescence characteristics of certain AGEs.

#### Results:

Our study population had a mean age of 65 years and 54% were female. After a mean follow-up duration of 3.3 years, linear regression analyses showed weak relationships among different assessments of HbA1c (baseline, maximum, mean, and variance of HbA1c) and skin AF at follow-up. Baseline skin AF and age were predictors of skin AF at follow-up, but diabetes duration, smoking, and creatinine were of less or no predictive value for skin AF at follow-up.

#### Conclusions:

In our T2DM population, integrated HbA1c assessments over years poorly predict the change in skin AGE level measured by skin AF. These findings agree with results in patients with T1DM. This suggests either the need for longer exposure to glucose disturbances to change tissue AGEs or other mechanisms, such as oxidative stress, leading to AGE accumulation.

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**Abbreviations:** (ACR) albumin-to-creatinine ratio, (AF) autofluorescence, (AGE) advanced glycation end product, (AFR) autofluorescence reader, (AU) arbitrary units, (DCCT) Diabetes Control and Complications Trial, (EDIC) Epidemiology of Diabetes Interventions and Complications, (HbA1c) hemoglobin A1c, (T1DM) type 1 diabetes mellitus, (T2DM) type 2 diabetes mellitus, (ZODIAC) Zwolle Outpatient Diabetes project Integrating Available Care

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