

Skin collagen glycation, glycoxidation, and crosslinking are lower in subjects with long-term intensive versus conventional therapy of type 1 diabetes: relevance of glycated collagen products versus HbA1c as markers of diabetic complications. DCCT Skin Collagen Ancillary Study Group. Diabetes Control and Complications Trial.

- [Monnier VM](#),
- [Bautista O](#),
- [Kenny D](#),
- [Sell DR](#),
- [Fogarty J](#),
- [Dahms W](#),
- [Cleary PA](#),
- [Lachin J](#),
- [Genuth S](#).

Institute of Pathology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA. vmm3@po.cwru.edu

The relationships between long-term intensive control of glycemia and indicators of skin collagen glycation (furosine), glycoxidation (pentosidine and N(epsilon)-[carboxymethyl]-lysine [CML]), and crosslinking (acid and pepsin solubility) were examined in 216 patients with type 1 diabetes from the primary prevention and secondary intervention cohorts of the Diabetes Control and Complications Trial. By comparison with conventional treatment, 5 years of intensive treatment was associated with 30-32% lower furosine, 9% lower pentosidine, 9-13% lower CML, 24% higher acid-soluble collagen, and 50% higher pepsin-soluble collagen. All of these differences were statistically significant in the subjects of the primary prevention cohort ($P < 0.006$ - 0.001) and also of the secondary intervention cohort ($P < 0.015$ - 0.001) with the exception of CML and acid-soluble collagen. Age- and duration-adjusted collagen variables were significantly associated with the HbA1c value nearest the biopsy and with cumulative prior HbA1c values. Multiple logistic regression analyses with six nonredundant collagen parameters as independent variables and various expressions of retinopathy, nephropathy, and neuropathy outcomes as dependent variables showed that the complications were significantly associated with the full set of collagen variables. Surprisingly, the percentage of total variance (R^2) in complications explained by the collagen variables ranged from 19 to 36% with the intensive treatment and from 14 to 51% with conventional treatment. These associations generally remained significant even after adjustment for HbA1c, and, most unexpectedly, in conventionally treated subjects, glycated collagen was the parameter most consistently associated with diabetic complications. Continued monitoring of these subjects may determine whether glycation products in the skin, and especially the early Amadori product (furosine), have the potential to be predictors of the future risk of developing complications, and perhaps be even better predictors than glycated hemoglobin (HbA1c).

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