Advanced glycation end products in systemic amyloidosis

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INTRODUCTION

Glycation is a non-enzymatic addition of reducing sugars to amino groups of proteins which results in the formation of advanced glycation end products (AGEs). AGEs are formed under influence of oxidative and glycemic stress on long-lived proteins and have been implicated in several age-related diseases. Post-translation modification of proteins may play a role in amyloidogenesis and oxidative stress is present in amyloid depositions in systemic amyloidosis[1].

OBJECTIVE

To examine whether skin AGE accumulation is increased in systemic amyloidosis and whether AGEs are related to amyloid load and other disease related factors.

PATIENTS AND METHODS

Seventy-two AL patients, 23 ATTR patients and 15 AA patients were included. Skin autofluorescence (SAF), as measure for the accumulation of AGEs, was noninvasively assessed with the AGE-reader (Diagnoptics Technologies BV, Groningen, The Netherlands). Routine laboratory assessments, including creatinine, N-terminal pro-B-type natriuretic peptide (NTproBNP), troponin T, alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT), C -reactive protein and glucose were performed in all patients. Fat aspiration biopsy for semi-quantification of amyloid was also performed. Expected values of SAF were calculated as function of age and smoking status[2].

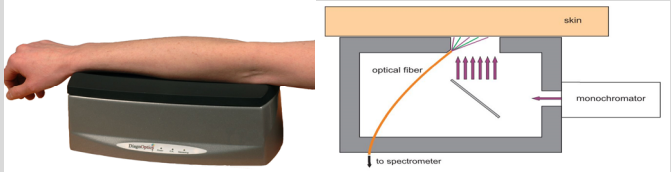

Figure 1. Assesment of AGE accumulation. AGE accumulation was assessed as skin autofluorescence (SAF) on the ventral site of the lower arm with the AGE-Reader. This is a validated and non-invasive technique making use of the autofluorescent properties of AGEs[3]. The AGE-reader consists of a tabletop box containing an excitation light source and a spectometer to measure light emitted from the skin. Skin AF is calculated by dividing the mean value of the emitted light intensity by the mean value of the excitation light intensity, expressed as arbitrary units (AU).

RESULTS

SAF is significantly increased in patients with AA amyloidosis compared to expected values (mean 2.7 AU vs 2.1 AU, p=0.02). AL and ATTR patients exhibited normal SAF values (**figure 2**).
SAF was not related to amyloid load in fat tissue (**figure 3**).
In AL patients SAF was positively related to GGT (r= 0.237, p=0.008).
In ATTR patients SAF was related to creatinine (r=0.4, p=0.02), GGT (r=0.5, p=0.002) and NTproBNP (r=0.4, p=0.04).

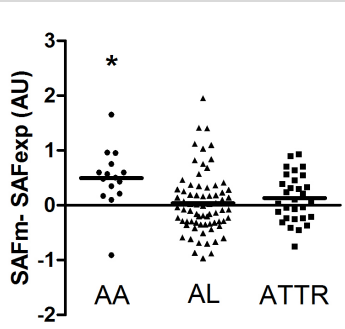

Figure 2. Absolute difference between measured skin autofluorescence (SAFm) and expected skin autofluorescence (SAFexp). The mean is indicated by the horizontal line.
AU: arbitrary units.
* Skin autofluorescence is significantly increased in AA (p=0.02) but not in AL or ATTR amyloïdosis patients.

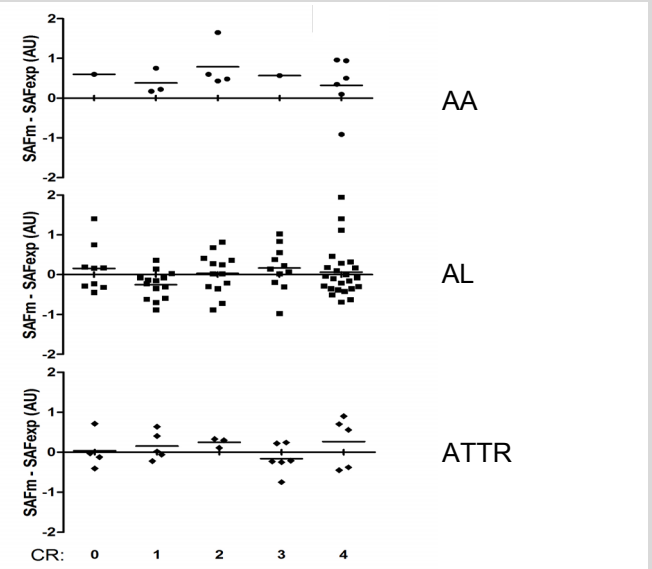

Figure 3. Absolute difference in skin autofluorescence (SAF) (measured minus expected) subdivided by the Congo Red (CR) score of the abdominal fat

CONCLUSIONS

- **Skin AGE accumulation is increased in AA but not in AL and ATTR amyloidosis patients.**
- **AGE accumulation is not related to amyloid load.**
- **AGE accumulation in AA amyloidosis rather seems to be related to organ dysfunction than an etiological factor.**

REFERENCES
1. Ando et al. BBRC 1997; 232: 497-502.
2. Koetsier et al. Diabetes Technol Ther. 2010; 12: 399-403.
3. Mulder et al. Diabetes Technol Ther. 2006; 8: 523-35.

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