Biomarkers of vascular changes in Type 1 and Type 2 diabetes mellitus related to skin autofluorescence

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AIMS

There is large evidence of advanced glycation endproducts (AGEs) participation in the development of diabetic vascular changes. Since recently, skin autofluorescence (AF), a quick and non-invasive method reflecting AGEs accumulation, has been introduced for risk evaluation of diabetic vascular complications.

The aim of this project was to evaluate skin AF levels in Type 1 and Type 2 diabetic patients in respect of their classical markers of vascular changes.

SUBJECTS and METHODS

Skin AF was measured in 62 Type 1 /T1DM/, 58 Type 2 /T2DM/ diabetic patients (aged 54 ± 16 yrs) and 26 healthy controls (aged 45 ± 12 yrs) on forearm of non-dominant upper extremity by AGE-Reader (Diagnoptics BV, Groningen, the Netherlands) (Figure 1). AGE-Reader illuminates a skin surface of approx. 4 cm^2 with an excitation light source between 300 and 420 nm (peak excitation ~ 370 nm). Emission light and reflected excitation light from the skin were measured with a spectrometer. Results were expressed as arbitrary units (AU) and compared with age, diabetes duration, glycated hemoglobin HbA_{1c} (expressed in IFCC units), fructosamine and biomarkers of vascular changes, such as von Willebrand factor (vWF), P-selectin, E-selectin, ICAM-1 and VCAM-1. Albuminuria was expressed as albumin creatinine ratio (ACR) and logarhitmically transformed before analysis.

RESULTS

The results of biochemical variables are shown in Table 1. Skin autofluorescence was significantly higher in Type 1 and Type 2 diabetic patients as compared to healthy controls (2.35 ± 0.56, 2.63 ± 0.68 vs. 2.04 ± 0.47 AU, p=0.0003). No relationship was observed between AF and HbA_{1c} or fructosamine in both T1DM and T2DM. Interestingly, patients with normal albuminuria (ACR<2.5 g/mol creatinine) had significantly lower AF in comparison to patients with positive (micro)albuminuria (T1DM: 2.25 ± 0.52 vs. 2.75 ± 0.57 AU, p=0.0003; T2DM: 2.45 ± 0.61 vs. 3.01 ± 0.84 AU, p=0.0003) (Figure 2). Significant positive relationship was found between AF and (micro)albuminuria in both T1DM and T2DM (r=0.36, p<0.005 and r=0.42, p<0.003) (Figure 3).

Strong correlation between AF and vWF (r=0.52, p=0.005) (Figure 4), and AF and ICAM-1 (r=0.61, p=0.0007) (Figure 5) was observed in T1DM, but not in T2DM. There was no relationship found between AF and VCAM-1, P-selectine or E-selectine in both T1DM or T2DM.

Figure 1: Skin AF measurement by AGE-Reader.

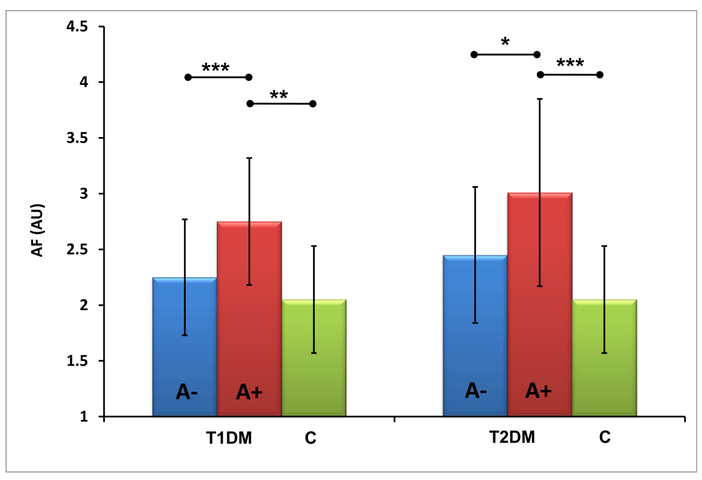

Figure 2: Skin AF in diabetic patients and controls
"A-" ACR < 2.5 mg/mmol creatinine
"A+" ACR > 2.5 mg/mmol creatinine

	HbA_{1c} (%, IFCC)	AF (AU)	vWF (µg/l)	P-selectin (µg/l)	E-selectin (µg/l)	ICAM (µg/l)	VCAM (µg/l)	ACR (g/mol)
T1DM	7.5 ± 1.8^{c}	2.35 ± 0.56^{x}	116 ± 45^{a}	113 ± 36	30 ± 16	270 ± 89^{b}	907 ± 498^{c}	1.2^{c} (0.6 – 1.8)
T2DM	7.0 ± 2.1^{c}	2.63 ± 0.68^{c}	123 ± 48^{b}	101 ± 35^{a}	36 ± 16	266 ± 79^{b}	816 ± 272^{c}	1.9^{c} (1.2 – 2.6)
Controls	3.6 ± 0.3	2.04 ± 0.47	88 ± 32	140 ± 76	40 ± 19	206 ± 64	365 ± 70	0.47 (0.2 – 1.1)
ANOVA	0.0001	0.0003	0.004	0.03	ns	0.002	0.0001	0.003

Results are means ± SD or mean with 1 SD range. One-way ANOVA was performed, with p values in the last row of the table. Statistical significance expressed by Bonferroni's multiple comparison test between DM and control persons: $^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$; and between T1DM and T2DM: $^{x}p<0.01$.

Table 1: Measured values in diabetic patients and controls

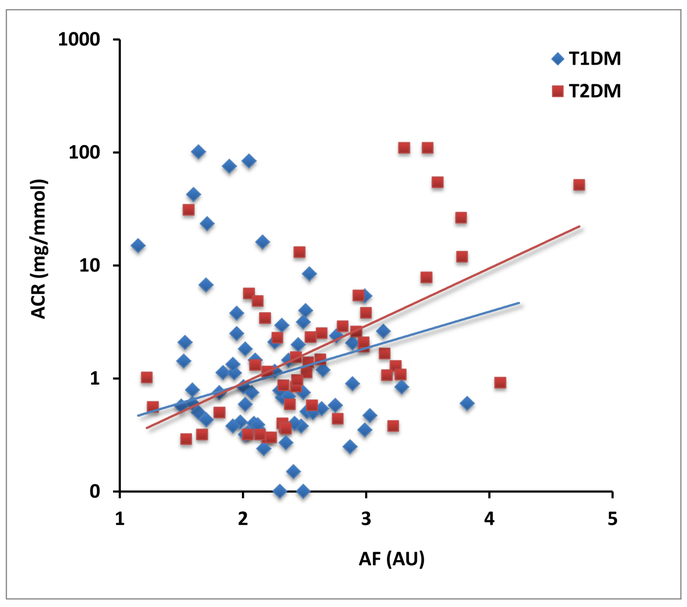

Figure 3: Relationship of skin AF with (micro)albuminuria;
T1DM: r=0.36, T2DM: r=0.42

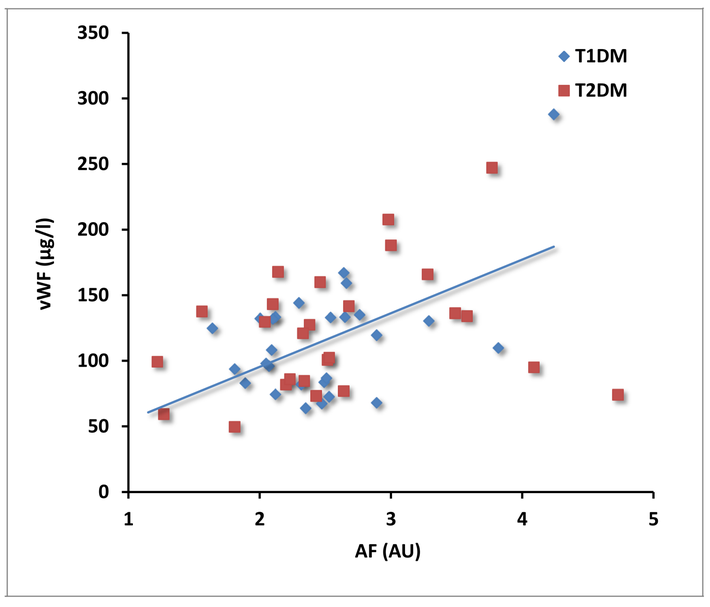

Figure 4: Relationship of skin AF with vWF;
T1DM: r=0.52 (shown), T2DM: r=0.28

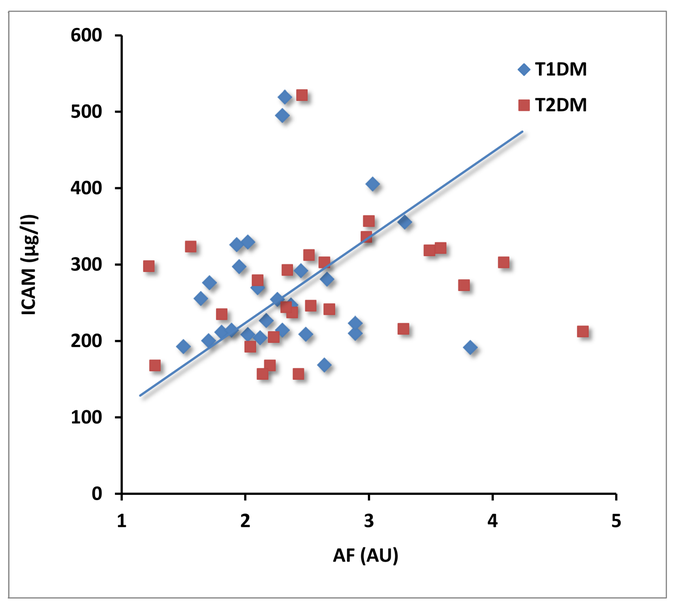

Figure 5: Relationship of skin AF with ICAM-1;
T1DM: r=0.61 (shown), T2DM: r=0.16

CONCLUSIONS

In our study with skin autofluorescence and biochemical markers of endothelial dysfunction, only vWF and ICAM-1 were related to skin autofluorescence, especially in T1DM.

Our results demonstrate that diabetic vascular disease is associated with distinct changes of biomarkers and intensity of skin autofluorescence, too. Thereby, the parameter of skin autofluorescence could serve as an indicator of connective tissue damage induced by long-term hyperglycemia.

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