

Skin autofluorescence but not soluble receptor for advanced glycation endproducts relates to microvascular reactivity in diabetic patients



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AIMS

Advanced glycation endproducts (AGEs) play important role in the pathogenesis of diabetic vascular complications. Their accumulation within the skin evokes elevation of skin autofluorescence (AF). According to novel findings, soluble receptors for AGEs (sRAGE) can reduce the pro-inflammatory effect of AGEs due to decreased activation of RAGE. The aim of this study was to evaluate skin autofluorescence and sRAGE levels in diabetic patients in respect of their microvascular reactivity (MVR) and other metabolic parameters.

SUBJECTS and METHODS

Totally, 43 diabetic patients (25 Type 1 /T1DM/, 18 Type 2 /T2DM/; aged 53 ± 15 years) and 26 healthy controls (aged 45 ± 12 years) participated in this study. Skin AF was measured on forearm of non-dominant upper extremity by AGE-Reader (Diagnostics BV, Groningen, the Netherlands) (Figure 1). Results were expressed as arbitrary units (AU) and compared with age, diabetes duration, sRAGE concentration (determined by ELISA kit), glycated hemoglobin HbA_{1c} (expressed in IFCC units) and fructosamine. Parameters of microvascular reactivity were assessed by laser-Doppler fluxmetry using PeriFlux 4001 (Perimed). Post-occlusive reactive hyperemia (PORH, % change) and thermal hyperemia (TH, % change) were measured by two laser probes on forearm and middle finger of non-dominant upper extremity.

RESULTS

Skin AF and sRAGE levels were lower in both T1DM and T2DM as compared to controls (2.3 ± 0.4 and 2.5 ± 0.5 vs. 2.0 ± 0.5 AU, ANOVA, $p < 0.01$; 1478 ± 616 and 1280 ± 633 vs. 1160 ± 530 ng/l, ANOVA, NS) (Figure 2 and 3).

No difference was observed in HbA_{1c} and fructosamine concentrations in both types of diabetic patients (7.4 ± 2.0 vs. 6.7 ± 1.8 %, NS).

Significantly lower post-occlusive reactive hyperemia (PORH) was observed in T2DM as compared to T1DM and controls (354 ± 116 vs. 480 ± 208 and 483 ± 90 %, $p < 0.03$), while differences in thermal hyperemia between T1DM and T2DM did not reach a significant level (Figure 4 and 5).

No relationship between HbA_{1c} or fructosamine and MVR was detected. On the contrary, strong inversed correlation was observed between AF and PORH in T1DM ($r = -0.60$, $p < 0.002$) (Figure 6) and between AF and thermal hyperemia (TH) in both T1DM and T2DM ($r = -0.55$, $p < 0.006$; $r = -0.52$, $p < 0.03$) (Figure 7). There was no relationship between parameters of MVR and sRAGE levels in both types of diabetic patients.

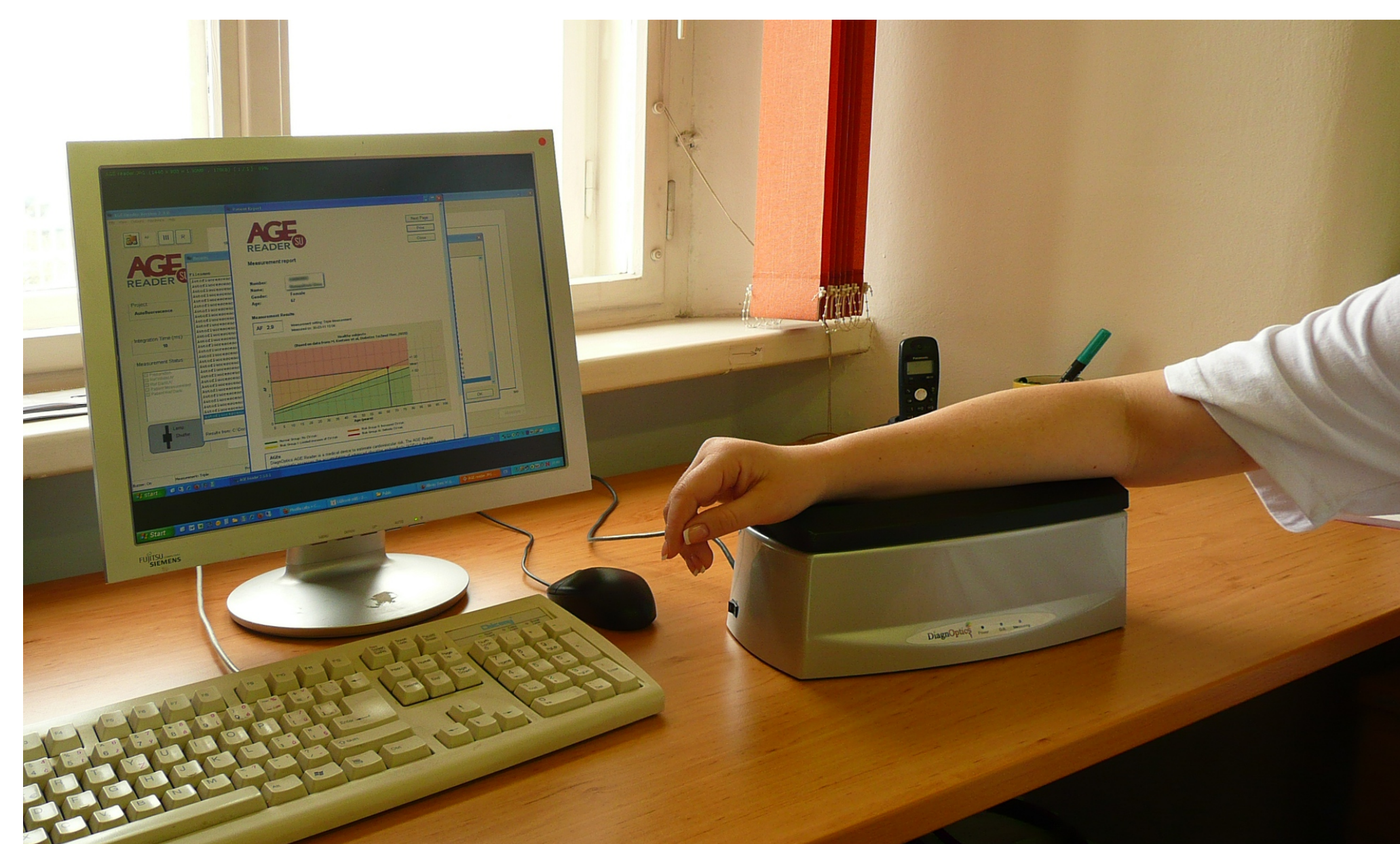


Figure 1: Skin AF measurement by AGE-Reader.

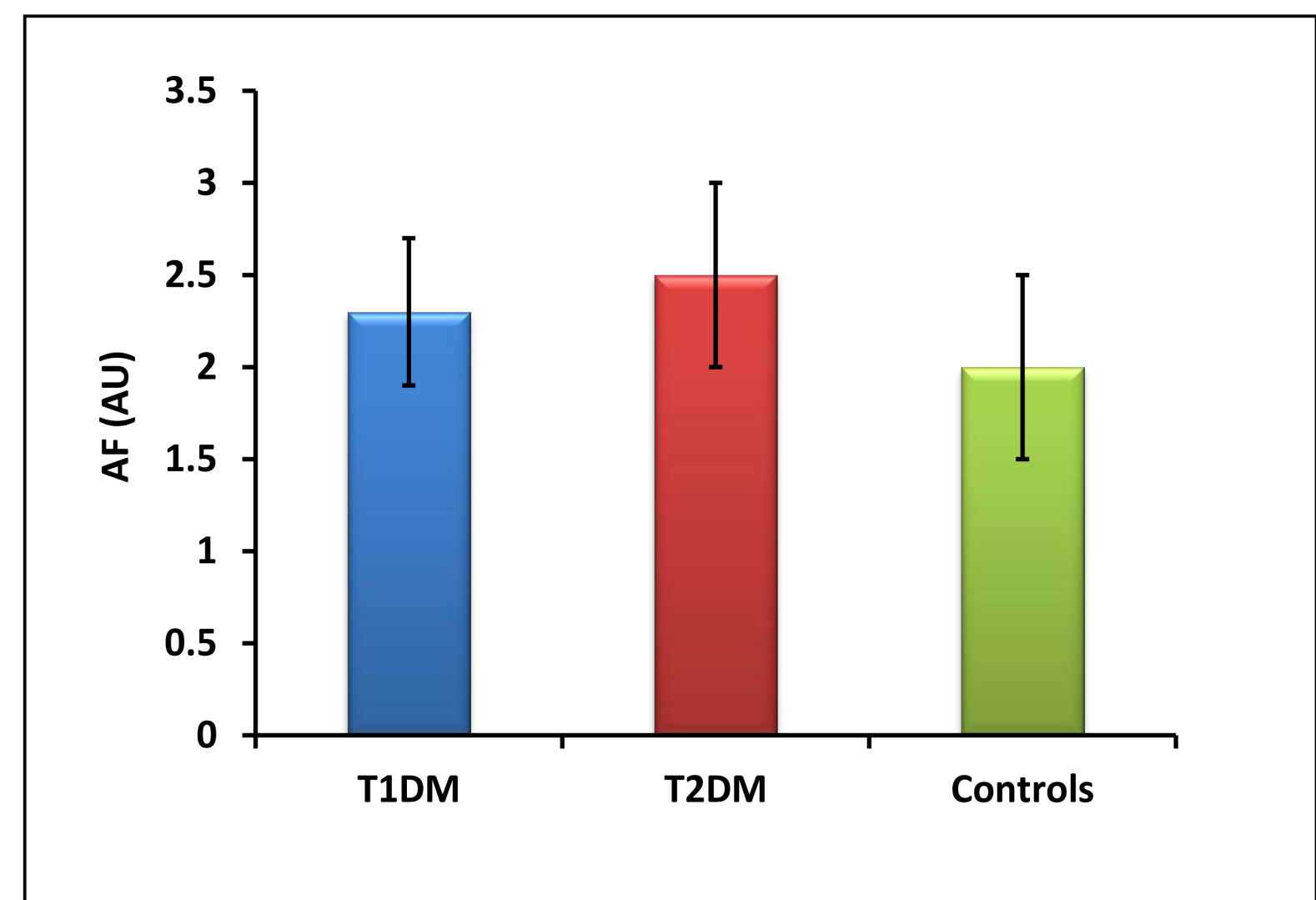


Figure 2: Skin autofluorescence (AF) in T1DM, T2DM and controls; ANOVA, $p < 0.01$.

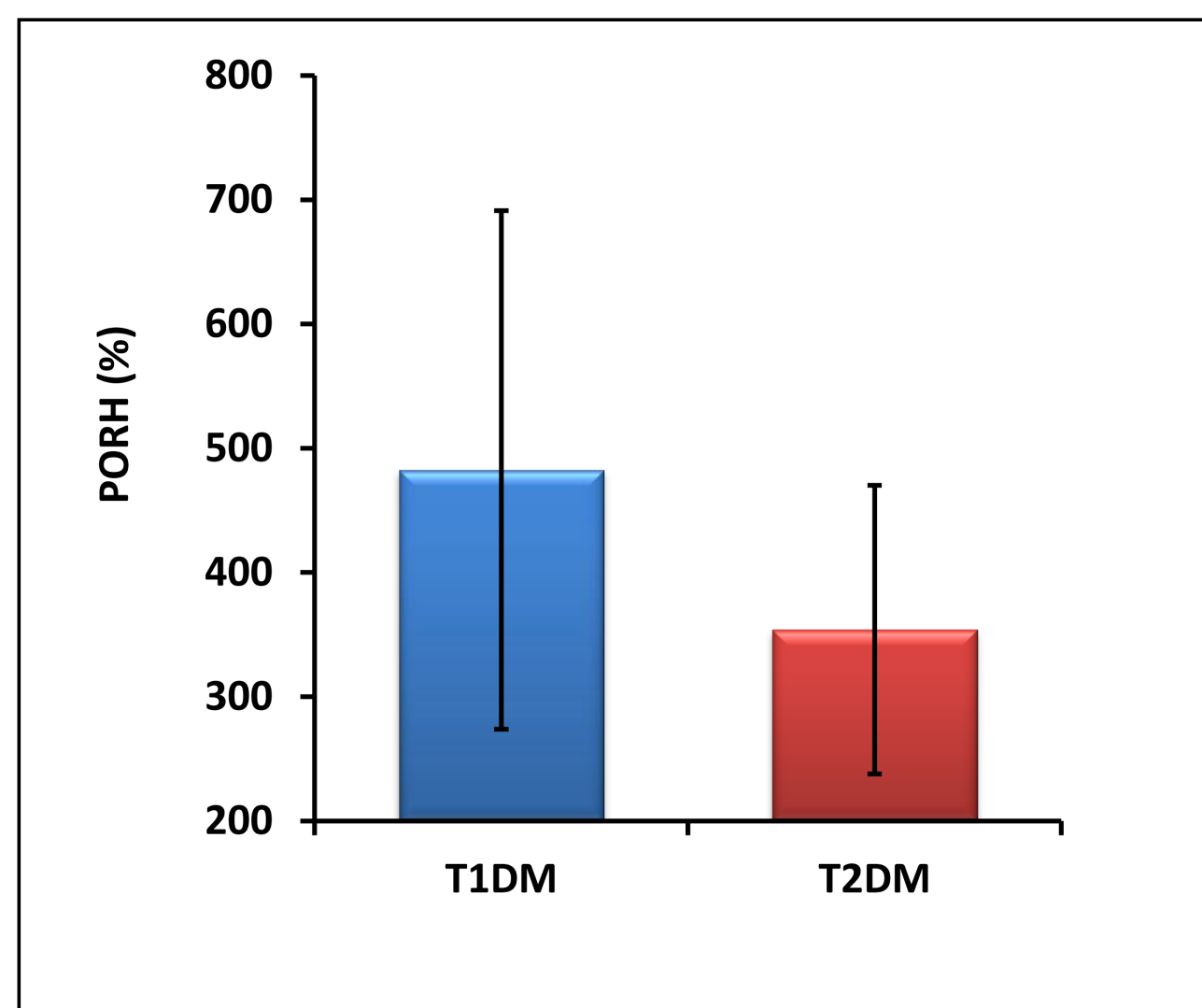


Figure 4: Post-occlusive reactive hyperemia (PORH) in T1DM and T2DM; $p < 0.03$.

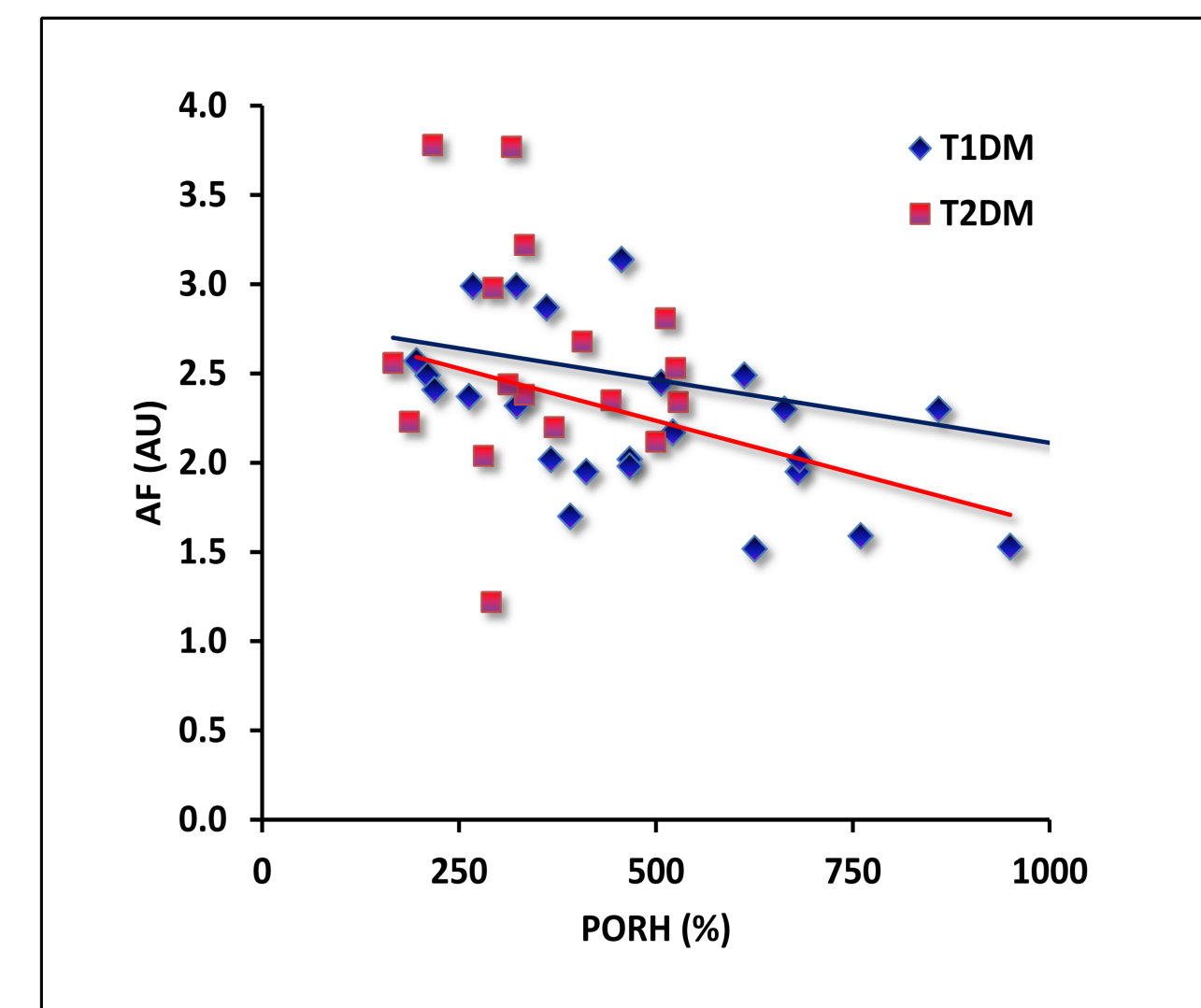


Figure 6: Relationship of skin AF with post-occlusive reactive hyperemia (PORH); T1DM: $r = -0.6$, T2DM: $r = -0.06$

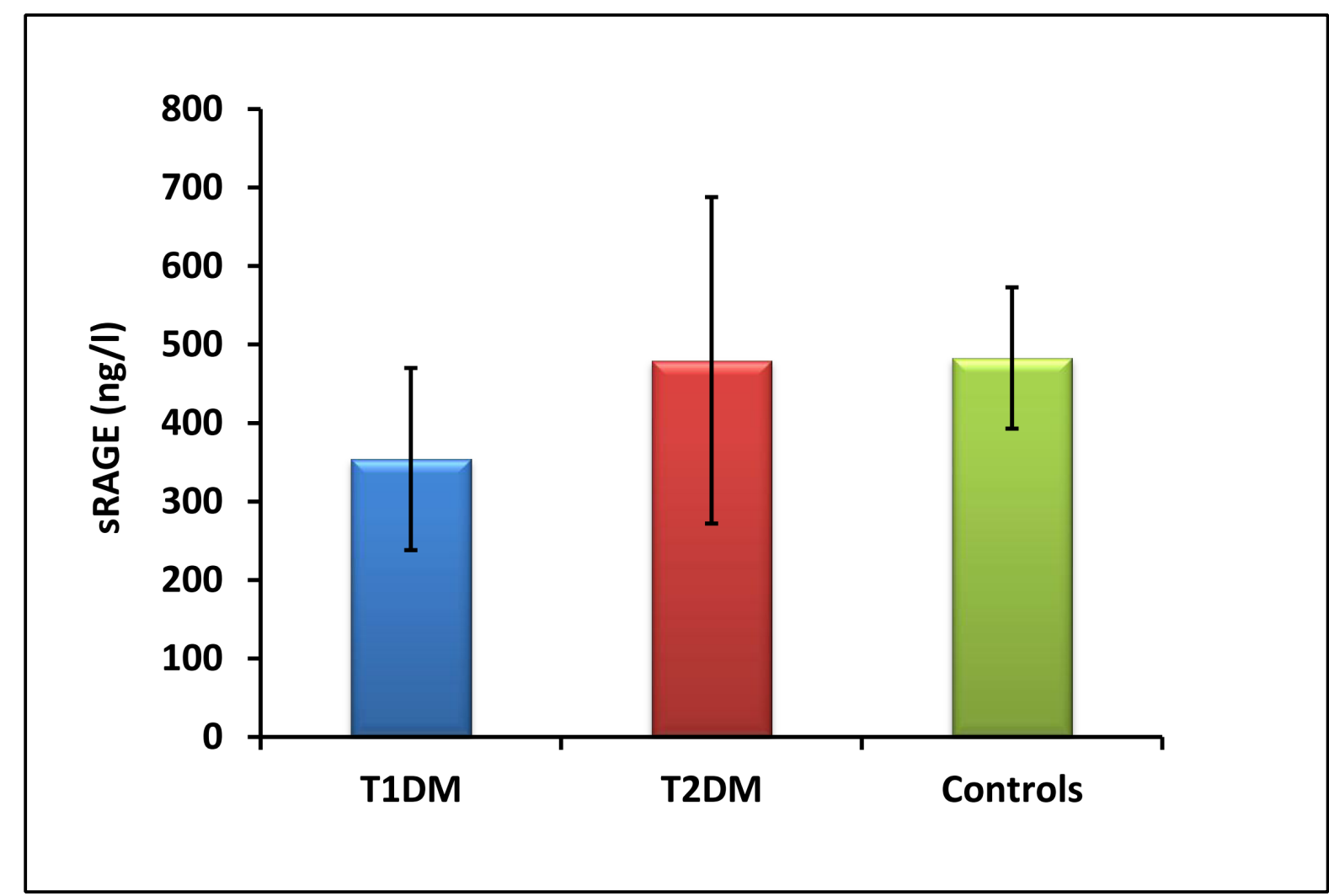


Figure 3: sRAGE concentrations in T1DM, T2DM and controls; ANOVA, NS.

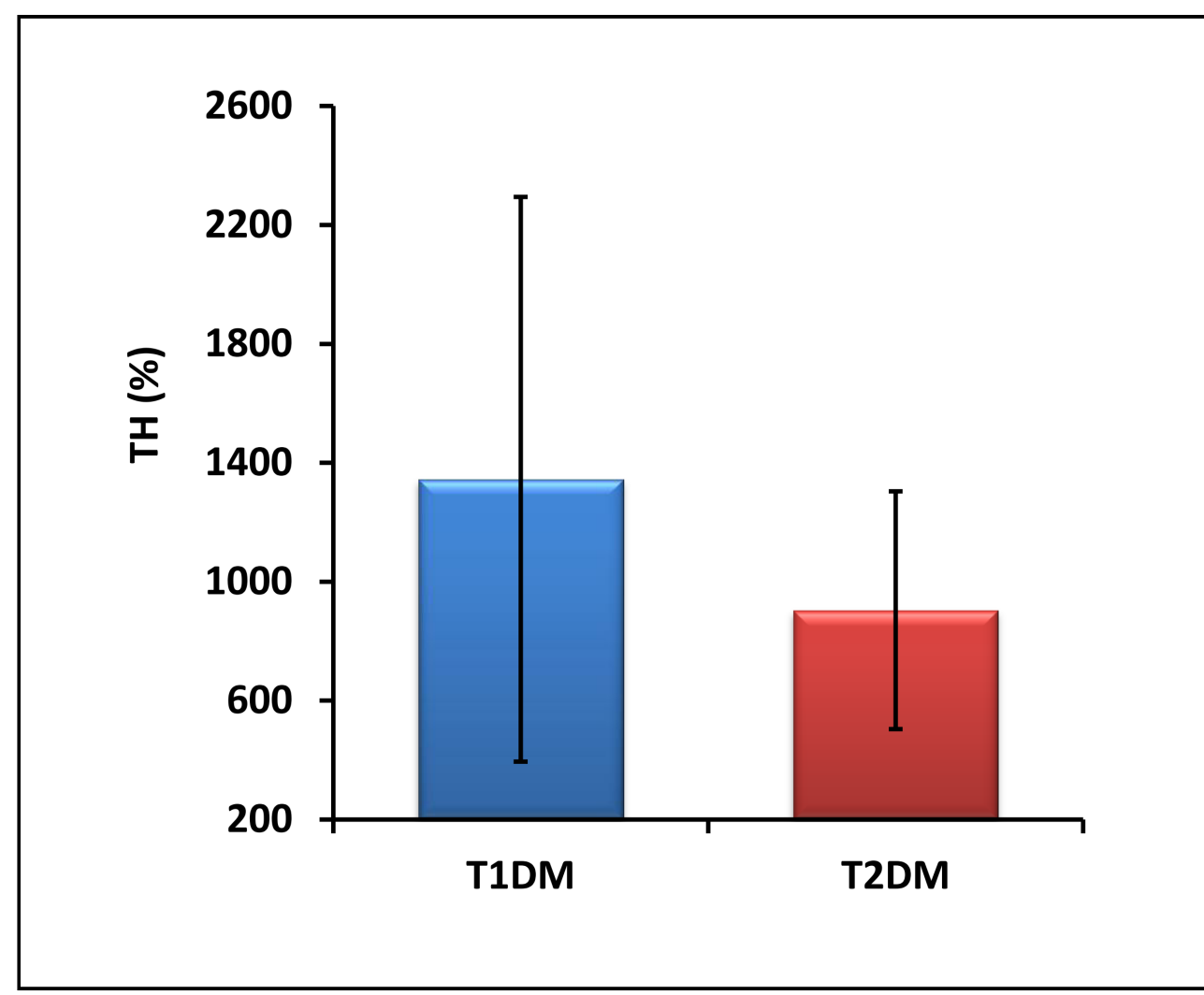


Figure 5: Thermal hyperemia (TH) in T1DM and T2DM; NS.

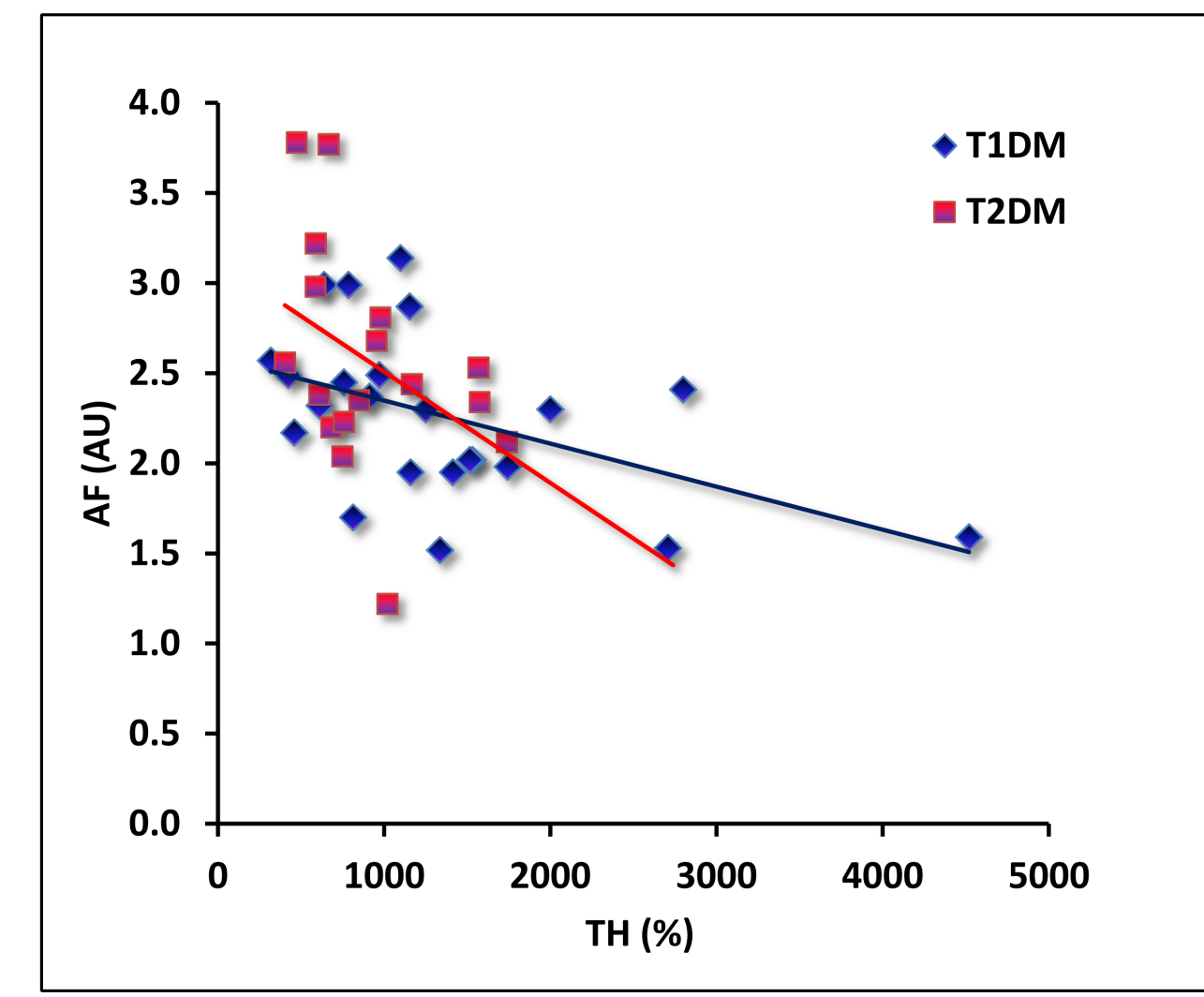


Figure 7: Relationship of skin AF and thermal hyperemia (TH); T1DM: $r = -0.55$, T2DM: $r = -0.52$

CONCLUSIONS

Diabetic vascular damage is associated with changes in microvascular reactivity, AGEs accumulation and higher skin autofluorescence. Moreover, distinct differences in sRAGE concentrations are present.

While significant inversed correlation between microvascular reactivity and skin autofluorescence was observed in this study, there was no relationship of MVR parameters and sRAGE.

The exact role of sRAGE in the whole process of chronic diabetic complications will need further investigation.