Relationship of oxidative stress to urinary angiotensin converting enzyme 2 in type 2 diabetes patients

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INTRODUCTION AND OBJECTIVES

Angiotensin converting enzyme 2 (ACE2) is highly expressed in the kidney and cleaves angiotensin II to Angiotensin-(1–7), annihilating the deleterious effects of angiotensin II which is known to be a strong activator of oxidative stress (1, 2, 3).

We aimed to evaluate the relationship of oxidative stress to urinary ACE2 (uACE2) in type 2 diabetes mellitus (T2DM) patients.

METHODS

We included consecutive normo or microalbuminuric T2DM patients in an observational transversal study.

In addition to the routine laboratory investigations we also performed:

- uACE2 (ELISA method)
- serum malondyaldehyde (MDA, fluorimetric thiobarbituric method) as a marker of prooxidant capacity
- superoxide dismutase (SOD, cytochrome reduction method) and catalase (CAT) activity (in erythrocyte lysate by the modification of absorbance at 240nm) as two measures of serum antioxidant capacity

RESULTS

- 53 T2DP were (64.2% male, mean age 64.98±10.62 years) were included in the study (table 1).
- **Evaluation of the main determinants of the oxidative stress:**
  - MDA showed a negative correlation with SOD (r=-0.44, p=0.001, CAT (r=-0.37, p=0.006), urinary ACE2 (r=-0.33, p=0.016) (Fig. 1) and systolic blood pressure (SBP) (r=-0.28, p=0.039) and a positive correlation with HbA1c (r=0.49, p<0.001).
  - CAT was positively correlated to urinary ACE2 (r=0.29, p=0.037) (Fig. 2).
  - SOD was negatively correlated with glycemia (r=-0.71, p<0.001), HbA1c (r=-0.53, p<0.001) and positively correlated with SBP (r=0.29, p=0.038).

Patients with lower MDA (when divided according to median value of 3.88 nmol/ml had higher uACE2 57.15 (40.3-71.2) pg/ml compared to 38.5 (31.8-45.95)pg/ml in patients with higher MDA(p<0.001) (Figure 3).

In multivariate logistic regression uACE2 was the only predictor for MDA above or below it's median (OR=0.94, 95%CI[0.90-0.98], p=0.002).

Parameters	Patients (n=53)
Diabetes duration (years)	8.00 (6.00-15.00)
BMI (kg/m2)	32.07±5.96
Total cholesterol (mg/dl)	189.68±45.83
HDL cholesterol (mg/dl)	44.55±12.53
Triglycerides (mg/dl)	140.00 (103.00-215.50)
CRP (mg/dl)	0.32 (0.18-0.48)
Serum glucose (mg/dl)	142.62 (126.19-173.15)
HbA1C (%)	7.45 (6.63-8.98)
uACR (mg/g)	15.36 (4.35-36.02)
eGFR (mL/min)	89.30 (67.86-99.50)
MDA (nmol/ml)	4.00±1.59
SOD (U/mg)	619.30±139.92
CAT (U/mg)	3.13 (2.60-3.46)
uACE2 (pg/ml)	43.50 (35.15-63.65)

Table 1. Descriptive clinical and biological characteristics of the studied subjects

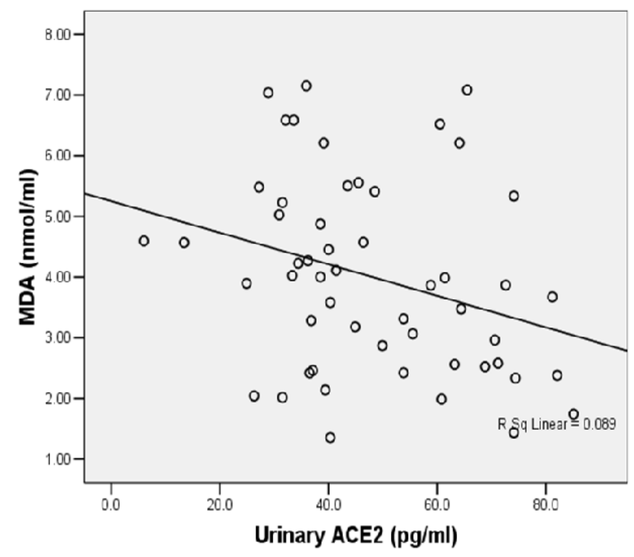

Figure 1. Correlation between uACE2 and MDA in our T2DP

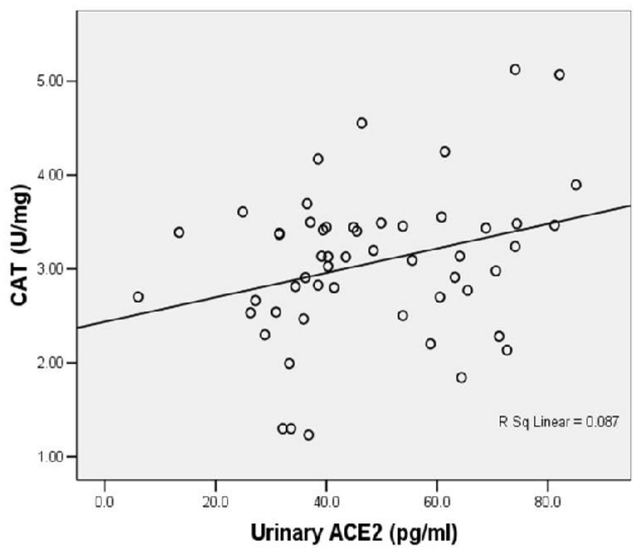

Figure 2. Correlation between uACE2 and MDA in our T2DP

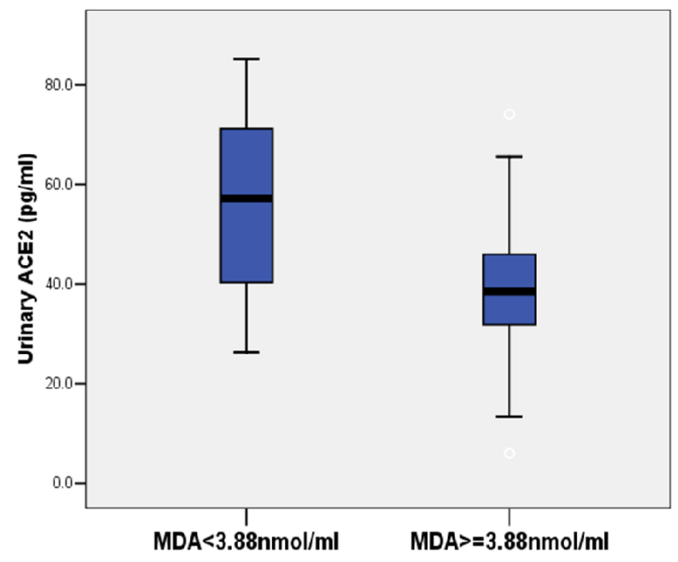

Fig. 3. Urinary ACE2 levels according to MDA median

	MDA<3.90 nmol/ml (n=26)	MDA≥3.90 nmol/ml (n=27)	p
Diabetes duration (years)	8.50 (6.00-12.00)	8.00 (6.00-18.00)	0.810
BMI (kg/m²)	31.22±6.29	32.89±5.63	0.313
Total cholesterol (mg/dl)	180.00 (153.00-219.00)	203.00 (155.00-229.50)	0.520
HDL cholesterol (mg/dl)	45.27±10.44	43.85±14.43	0.685
Triglycerides (mg/dl)	132.50 (94.00-199.00)	142.00 (105.00-223.00)	0.444
CRP (mg/dl)	0.25 (0.17-0.36)	0.37 (0.20-0.61)	0.301
Serum glucose (mg/dl)	136.79 (125.95-180.12)	143.81 (128.63-168.33)	0.896
HbA1C (%)	7.00 (6.50-8.30)	7.82 (7.00-9.80)	**0.030**
eGFR (mL/min/1.73m²)	92.27 (71.57-102.35)	83.11 (52.59-94.84)	0.255
UACR (mg/g)	18.08 (4.06-72.60)	13.09 (4.88-26.39)	0.226
MDA (nmol/ml)	2.67±0.71	5.28±1.06	
SOD (U/g)	654.21±98.12	585.68±165.85	**0.028**
CAT (U/g)	3.39 (2.53-3.49)	2.91 (2.68-3.38)	0.378
uACE2	57.15 (40.30-71.20)	38.50 (31.80-45.95)	**<0.001**

Table 2. Comparison of the patients according to MDA median (3.90 nmol/ml) in the study group

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CONCLUSIONS

Increased prooxidant serum capacity is associated with lower uACE2 levels in T2DP.

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