Glucose variability in subjects with type 1 diabetes: the relationships with non-enzymatic glycation, albuminuria and renal function

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Background

- **Recent studies recognized increased glucose variability (GV) as an independent risk factor for chronic kidney disease (CKD) in diabetes. On the other hand, renal function could affect daily glucose fluctuations in patients with diabetes.**
- **The changes of GV patterns at different CKD stages, as well as the mechanisms of deteriorative effect of high GV on the kidney, remain to be clarified.**
- **Non-enzymatic glycation is considered as important contributor to progression of diabetic kidney disease.**

The aim:

to assess the relationships between GV parameters, serum levels of glycation products, albuminuria and renal function in subjects with type 1 diabetes (T1D) at early and advanced stages of CKD.

Materials and methods

- **148 T1D patients, 53 M/95 F, from 18 to 65 years of age, including 95 ones with CKD C1-2 and 53 patients with CKD C3-5 (13 subjects on hemodialysis).**
- **Control group: 20 healthy subjects**

Table 1

Clinical characteristics of patients

Parameter	CKD C1-2 (n=95)	CKD C3-5 (n=53)
Age, yrs	33 (25; 44)	35 (29; 49)
Diabetes duration, yrs	13 (7; 22)	20 (16.5; 28.5)
Daily insulin dose, IU/kg	0.63 (0.53; 0.79)	0.58 (0.46; 0.66)
HbA1c, %	8.3 (7.4; 9.8)	9.2 (7.8; 11)
eGFR, ml/min/1.73 m^2	87 (76; 105)	37 (15.5; 49.5)
UAE, mg/L	7.2 (2.0; 15.9)	400 (101; 643)

The data are shown as medians (25; 75 percentiles).
eGFR, estimated glomerular filtration rate; UAE, urinary albumin excretion.

- **72-h continuous glucose monitoring (CGM) with Time in Range (TIR), Time Above Range (TAR), Time Below Range (TBR) analysis.**
- **CGM-derived GV parameters assessment: Mean Amplitude of Glucose Excursions (MAGE), Lability Index (LI), Low Blood Glucose Index (LBGI), High Blood Glucose Index (HBGI), 2-hour Continuous Overlapping Net Glycemic Action (CONGA), Mean Absolute Glucose (MAG), and M-value.**
- **ELISA for determination of the levels of 1,5-anhydroglucitol (1,5-AG), glycated albumin (GA) and advanced glycation end products (AGEs) in blood serum.**

Results

- **In patients with CKD C1-2 HbA1c correlated positively with mean monitored glucose, TIRs and GV parameters (Table 2). In patients with more advanced CKD these relationships were lost.**

Table 2

The relationships between HbA1c and CGM parameters in T1D patients depending on renal function

Parameter	CKD C1-2	CKD C3-5
Mean glucose	0.55*	0.08
TIR	-0.52*	0.1
TAR	0.53	0.1
TBR	-0.3	-0.1
MAGE	0.47*	-0.24
LI	0.44*	-0.16
CONGA	0.55*	0.09
HBGI	0.6*	-0.10
LBGI	-0.003	-0.25*
MAG	0.38*	0.03
M-value	0.57*	-0.09

The data are shown as Spearmen`s correlation coefficients. *P < 0.001

▪ **Concentrations of GA and AGEs were elevated significantly in subjects with diabetes as compared to control (p=0.004 and p<0.0001, respectively). The levels of 1,5-AG was reduced (p<0.0001), reflecting increase in GV (Fig. 1).**

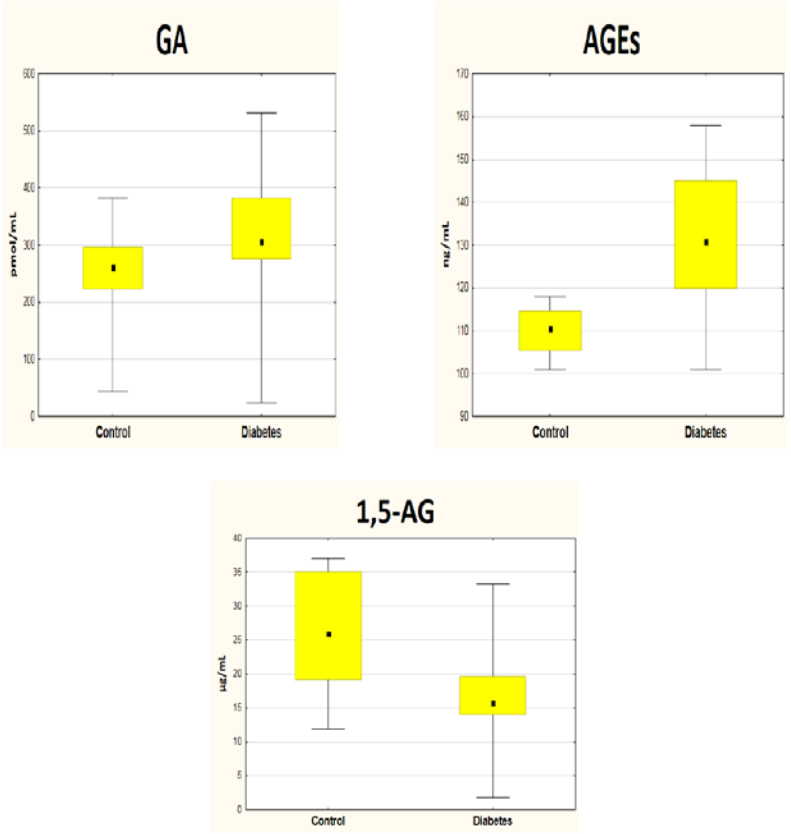

Fig. 1. The levels of 1,5-AG, GA and AGEs in T1D patients and control subjects

▪ **The concentrations of 1,5-AG correlated negatively with GA (r=-0.54, p<0.001), but not with HbA1c or AGEs levels. There was a weak positive correlation between AG and AGEs (r=-0.25, p=0.05). The AGEs correlated with LBGI (r=0.28, p=0.03) and the number of episodes of hypoglycemia (r=-0.32, p=0.01).**

Table 3

The correlations between eGFR and CGM parameters in T1D patients depending on renal function

Parameter	CKD C1-2	CKD C3-5
Mean glucose	0.55*	0.08
TIR	-0.52*	0.1
TAR	0.53	0.1
TBR	-0.3	-0.1
MAGE	0.47*	-0.24
LI	0.44*	-0.16
CONGA	0.55*	0.09
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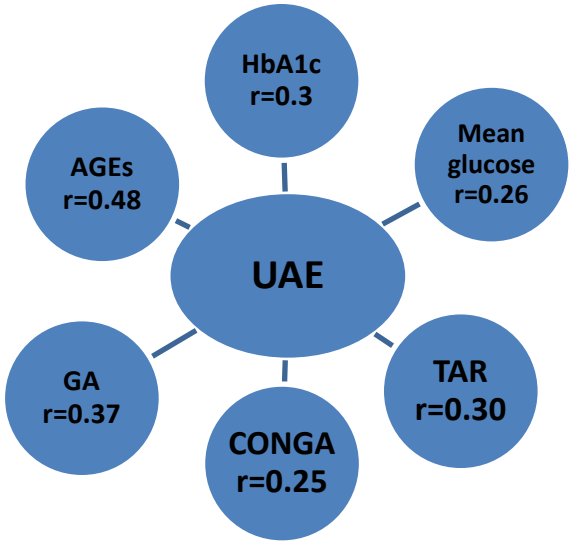

FIG. 2. CORRELATIONS BETWEEN UAE, GV AND GLYCATION PARAMETERS IN T1D PATIENTS WITH EGFR ≥60 ML/MIN/1.73M^2

Conclusions:

- **The results demonstrate different patterns of relationships between eGFR and GV parameters in patients with T1D at early and advanced CKD stages.**
- **In these patients, the enhanced GV may contribute to abuminuria through acceleration of non-enzymatic glycation processes.**
- **The CGM with time in ranges and GV analysis should be considered for assessment of glycemic control in T1D subjects with eGFR <60 ml/min/1.73 m2, taking into account the limited value of HbA1c in this group.**

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