THE INACTIVE FORM OF MATRIX GLA PROTEIN (MGP) IS NOT ASSOCIATED WITH MGP GENE PROMOTER T-138C POLYMORPHISM IN PATIENTS WITH DIABETIC NEPHROPATHY

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INTRODUCTION and AIMS

Vitamin K-dependent matrix Gla protein (MGP) is an important inhibitor of vessel and cartilage calcification. Modification by γ- carboxylation is necessary for MGP to become biologically active. Vitamin K deficiency leads to accumulation of high levels of inactive uncarboxylated MGP (dpucMGP) in calcified vessels. Plasma dpucMGP increases progressively in a chronic kidney disease (CKD) setting and is associated with the severity of aortic calcification. Single nucleotide polymorphism (SNP) of the promoter region of MGP gene, *MGP T-138C*, leads to alteration of the binding of transcription factors, affects transcriptional regulation and probably results to higher levels of dpucMGP. We sought to determine the association of dpucMGP levels with *MGP T-138C* polymorphism in patients with diabetic nephropathy.

METHODS

Plasma dpucMGP levels were measured in 71 patients in different stages of diabetic nephropathy (mean age 67.99±8.48 years) using ELISA. *MGP T-138C* polymorphism was determined using PCR-RFLP (Table 1).

RESULTS

The frequencies of the *MGP T-138C* genotypes were: TT (n=34) 47.9%, TC (n=23) 32.4%, CC (n=14) 19.7%. The inactive dpucMGP was not significantly higher in patients with the *MGP T-138C* TC or CC genotype compared with the TT genotype (773±535 pM vs 725±542 pM, p=0.68) (Table 2). Additionally, dpucMGP was positively correlated with the stage of diabetic nephropathy (Figure 1), the presence of peripheral artery disease (PAD), triglycerides, BMI, and HbA1c levels (p<0.0001, <0.001, 0.004, 0.048, and 0.01 respectively).

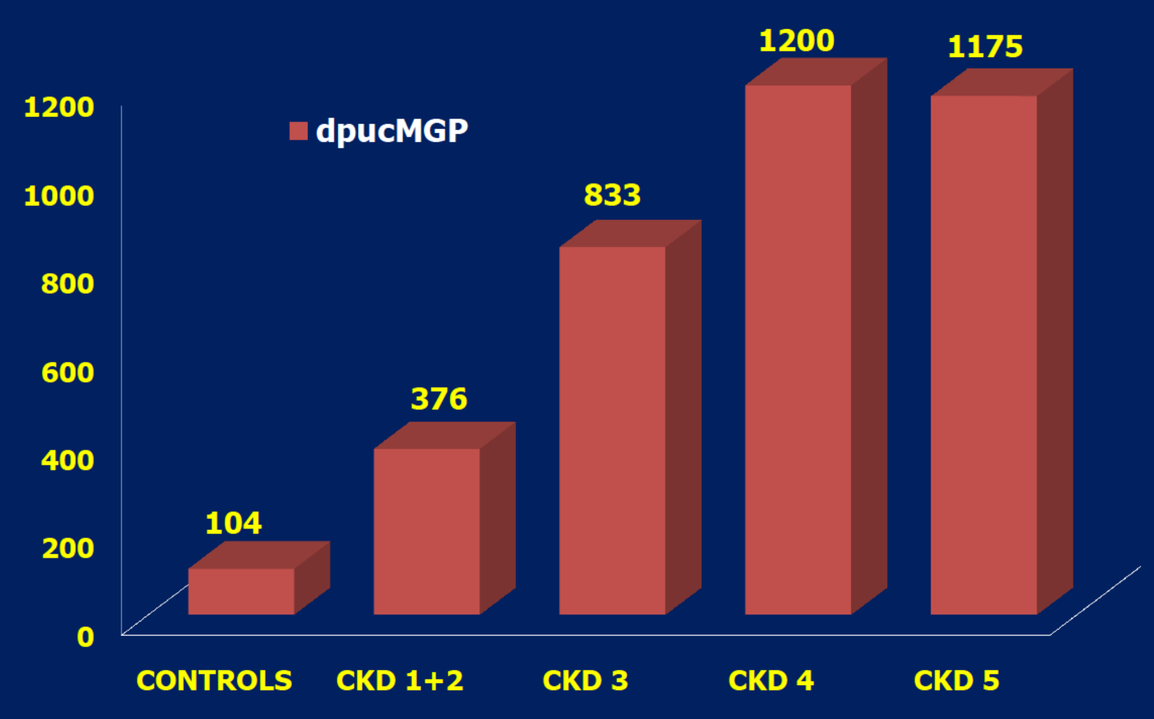
***Table 1:* Anthropometric, clinical and biochemical parameters**

n=71 patients (37 M & 34 F)	*Mean value ± SD*
Age (y)	67.99 (8.48)
SBP (mm Hg)	141.1 (16.0)
DBP (mm Hg)	79.1 (7.0)
BMI (kg/m^2)	31.2 (4.7)
Duration of T2DM (y)	15.6 (8.2)
Fasting glucose (mg/dl)	153.7 (50)
HbA1c (%)	7.4 (1.1)
eGFR (ml/min/1.73m^2)	48.9 (27.5)
Total cholesterol (mg/dl)	183.5 (40.3)
LDL-cholesterol (mg/dl)	104.4 (32.8)
HDL-cholesterol (mg/dl)	46.7 (12.7)
Triglycerides (mg/dl)	170.0 (74.2)
dpucMGP (pM)	765.94 (543.84)

***Table 2:* MGP T-138C genotypes and dpucMGP**

MGP T-138C genotypes	N (%)	dpucMGP (pM)	p
TT/TC	34/23 (80.3%)	773±535	0.68
CC	14 (19.7%)	725±542	

***Figure 1:* dpucMGP in different stages of T2DM CKD**



CONCLUSIONS

Plasma dpucMGP levels were not associated with MGP gene promoter *T-138C* polymorphism in patients with diabetic nephropathy. Advanced stage of diabetic nephropathy, severe PAD, high levels of triglycerides, increased BMI and poor glycemic control (high levels of HbA1c) were significantly associated with dpucMGP in diabetic nephropathy.

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