ASSOCIATION OF FETUIN GENE POLYMORPHISMS WITH CORONARY ARTERY CALCIFICATIONS AND MORTALITY IN RENAL TRANSPLANT AND CHRONIC KIDNEY DISEASE PATIENTS

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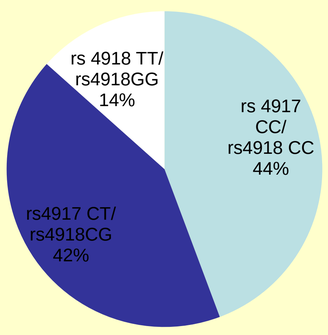
Objectives:

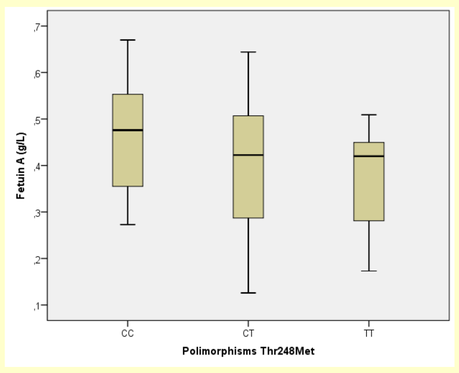
The present prospective study evaluated the association of single nucleotide polymorphisms in the genes for fetuin-A: Thr248Met C>T (rs4917) and Thr256Ser C>G (rs4918) with fetuin-A serum levels, coronary arteries calcification (CAC) and mortality in renal transplant (RT) and chronic kidney (CKD) patients.

Methods:

METHODS: During the period of 72 months 97 patients, regularly monitored at Clinic of nephrology CCS, were examined (49 stable RT patients, 31 males, at least 6 months after transplantation and 48 CKD patients, 25 males, stage 2-5 not requiring dialysis). Demographic (age and gender), clinical (dialysis and transplant duration, BMI, hypertension) parameters and serum creatinine, high sensitive C reactive protein (hs-CRP), interleukin-6, serum amyloid A, as well as fetuin-A (ELISA Epitope Diagnostics, Inc., San Diego, California, USA) concentration were determined. CAC score was evaluated using multi-detector row spiral computed tomography (MSCT). Detection and analysis of single nucleotide polymorphisms SNP were performed using PCR method.



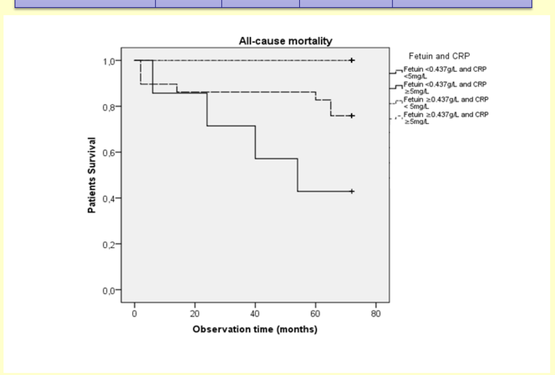
Graph. 1.Distribution of genotypes rs4917 and 4918



Graph. 2. Serum fetuin A levels according rs4917 genotypes

Tab.1 Logistic univariate analysis with presence of CAC as dependent variable

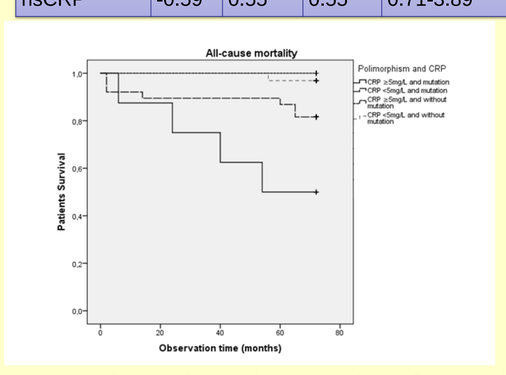
Varijable	p	Exp(B)	OR	95% CI Exp(B)
Age	0.000	1,156	1.17	1.09-1.24
Fetuin-A	0,011	3,238	4.77	1.31-8.01
Rs 4917	0.021	2.801	1.16	1.17-6.69



Graf.3. Kaplan-Meier analysis - influence of serum fetuin A and inflammation on mortality

Tab.2 Logistic multivariate analysis with presence of CAC as dependent variable

Variable	B	p	OR	OR 95% CI
Age	0.15	0.001*	1.17	1.09-1.24
Fetuin-A	1.56	0.03*	4.77	1.15-19.74
Rs 4917	0.15	0.82	1.16	0.30-4.47
hsCRP	-0.59	0.55	0.55	0.71-3.89



Graf. 4.Kaplan-Meier analysis - influence of rs4917 polymorfism and inflammation on mortality

Results:

RESULTS: Genotype rs4917 CC was found in 43 (44.3%), CT in 41 (42.3%) and TT in 13 (13.4%) of examined patients. Because of a fact that a complete linkage disequilibrium rs4917 with rs4918 was found, in further analysis only data for rs4917 polymorphism will be reported. Median of serum fetuin-A level was 0.437 g/L. Patients with serum fetuin-A level ≤0.437 g/L had rs4917 TT genotype significantly more frequent than the ones with serum fetuin-A level >0.437 g/L (18.6% vs. 8.9%, p=0.019). Univariate logistic analysis determined age (p=0,000), serum fetuin-A levels (p=0,011) and rs 4917 polymorphism (p=0.021) while multivariate determined only age (p=0,001) and fetuin-A levels (p=0,031) as significant predictors of CAC. During the observation period 11 patients died. Kaplan–Meier survival analysis revealed that patients with variant rs4917 T allele and CRP ≥5mg/L had the survival rate of only 50 %, but the patients without rs4917 T allele and CRP<5mg/L had survival rate of 100% (p=0.001).

Conclusions:

CONCLUSIONS: The present study confirms that variant alleles for single nucleotide polymorphisms in genes for fetuin-A: Thr248Met C>T (rs 4917) and Thr256 Ser C>G (rs 4918) were associated with lower serum fetuin-A levels and higher mortality rate in RT and CKD patients.

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