# ASSOCIATION OF THE VASCULAR ENDOTHELIAL GROWTH FACTOR (*VEGF*) GENE *C(-460)T* POLYMORPHISM WITH URINARY VEGF-A EXCRETION IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS

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## OBJECTIVES

Vascular endothelial growth factor A (VEGF-A) plays an important role in the maintenance of the glomerular filtration barrier (GFB) function. Both the overexpression and the downregulation of VEGF-A could cause GFB injury and the development of proteinuria – an important marker of kidney injury and a risk factor of renal diseases progression. It is considered, that the *VEGF* gene polymorphism may be associated with the production of VEGF protein.

**The aim of the study** was to investigate the associations between *VEGF* gene *C(-460)T* polymorphism and urinary VEGF-A level, which reflects its local kidney production, proteinuria (PU) as the main sign of CGN activity and urinary excretion of neutrophil gelatinase-associated lipocalin (NGAL) and type IV collagen (COL4) as biomarkers of kidney injure and fibrogenesis.

## METHODS

68 CGN patients (mean age 42.2±16.6 yrs; 47.1% men) were examined. 88.2% patients developed arterial hypertension; nephrotic syndrome was revealed in 27.9%; $eGFR_{CKD\text{-}EPI}$ < 60 ml/min/1.73 $m^2$ was found in 29.4% of the study patients. Mesangioproliferative GN was revealed in 34.6%, membranoproliferative GN – in 15.4%, minimal change disease – in 15.4%, focal segmental glomerular sclerosis – in 7.7%, membranous nephropathy – in 19.2%, diffuse nephrosclerosis – in 7.7%. Genotyping was performed by polymerase chain reaction-restriction length polymorphism. Morning urine samples were analyzed by ELISA to determine the excretion of VEGF-A, NGAL and COL4.

## RESULTS

The frequencies of genotypes were as follows: *CC*-29.4%, *CT*-50.0%, *TT*-20.6%. For further analysis patients with CGN were grouped according to the presence of *VEGF* -460*T*-allele: *CC* group (20 patients) and *CT+TT* group (48 patients). The median urinary level of VEGF-A was significantly higher in *CT+TT* group compared with *CC* group (Table). Moreover we found, that PU in *CT+TT* group also was higher, then in *CC* group. *VEGF* gene variants were not associated with other clinical signs of CGN activity as well as morphological changes. But we found statistically significant higher urinary excretion of NGAL and COL4 in *CT+TT* group compared with *CC* group.

**Table: eGFR, PU and urinary excretion of biomarkers according to *VEGF C(-460)T* genotypes**

| | CC genotype | *CT+TT* genotypes | p value |
|---|---|---|---|
| eGFR, ml/min/1.73 $m^2$ | 78,6 (52,1; 99,9) | 80,6 (54,6; 103,4) | 0,882 |
| PU, g/24h | 0,5 (0,2; 2,2) | 1,5 (0,5; 3,9) | 0,074 |
| VEGF-A, ng/l | 184,8 (137,5; 592,0) | 454,8 (202,2; 803,7) | 0,016 |
| NGAL, μg/l | 0,2 (0; 0,9) | 2,5 (0,4; 12,9) | 0,003 |
| COL4, μg/l | 1,8 (1,5; 2,5) | 2,9 (1,9; 4,0) | 0,010 |

## CONCLUSIONS

In this study we have demonstrated the associations between the *VEGF C(-460)T* polymorphism and urinary excretion of kidney injury and fibrogenesis biomarkers with the higher urine level of VEGF-A, NGAL, COL4 and total protein in carrier of *VEGF -460T* allele. Although the association of this polymorphism with renal dysfunction was not found, the association of *-460T* allele with biomarkers of renal injury could be an argument to discuss its possible unfavorable prognostic role in CGN. But we need prospective trials to test it.

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