ANGIOTENSIN-CONVERTING ENZYME GENE (*ACE*), ALDOSTERONE SYNTHASE GENE (*CYP11B2*) AND ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE (eNOS3) POLYMORPHISM AND CARDIAC REMODELING IN CHRONIC GLOMERULONEPHRITIS

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OBJECTIVES

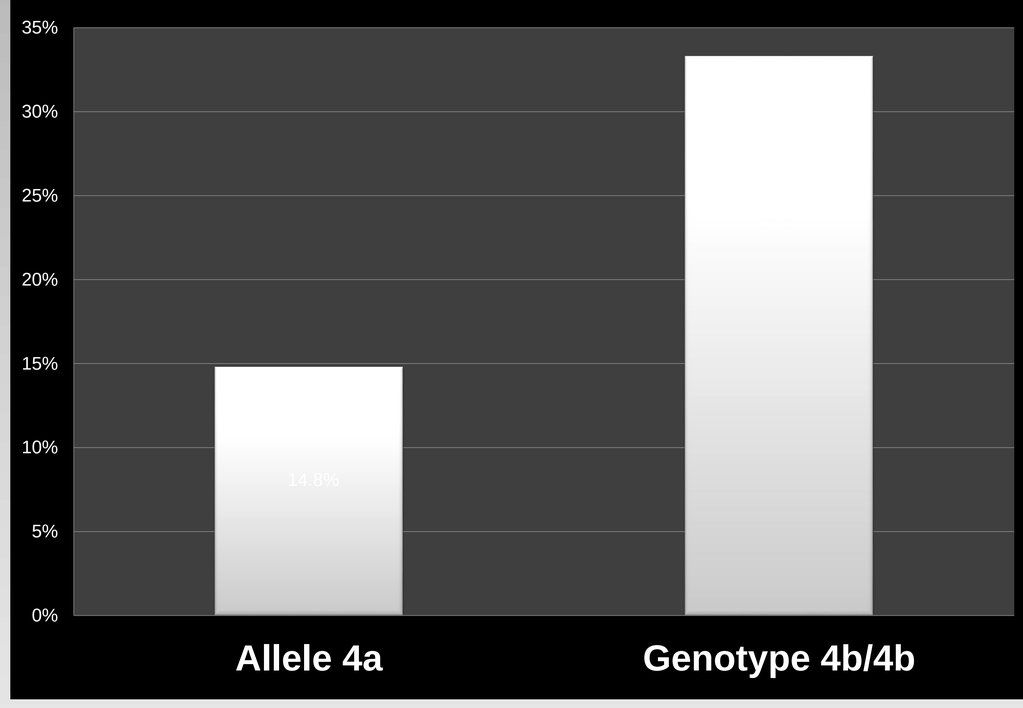
Patients with chronic kidney disease (CKD) are at a high risk of cardiovascular disease developing. It is considered, that genetic variants in the components of renin-angiotensin-aldosterone system and in nitric oxide synthase contribute to the development of cardiorenal syndrome, but results remain controversial.

The aim of the study was to evaluate the associations between the angiotensin-converting enzyme gene (*ACE*), aldosterone synthase gene (*CYP11B2*) and endothelial nitric oxide synthase gene (e*NOS3*) polymorphisms and cardiac remodeling in patients with chronic glomerulonephritis (CGN).

METHODS

80 CGN patients (mean age 37.3±13.9 years; 48% men) were examined. Mean duration of CKD was 8.1 [1.8:15.3] years. Arterial hypertension (AH) was revealed in 83%, its duration was 3.5 [1.3;3.9] years. 53% patients received ACE inhibitors. Body mass index (BMI) > 25 kg/m^2 was found in 36%, current smoking – in 28%, hereditary predisposal to cardiovascular diseases (CVD) – in 58%. Transthoracic Doppler echocardiography and genotyping by polymerase chain reaction-restriction length polymorphism were performed in all patients. Left ventricular hypertrophy (LVH) (left ventricular mass index ≥125 g/m^2 in men and ≥110 g/m^2 in women) and diastolic dysfunction (E/A≤1.0) were considered as measures of cardiac remodeling.

Frequency of the diastolic dysfunction in CGN patients according to *eNOS3 4a/4b* polymorphism



RESULTS

The frequency of LVH and E/A<1.0 was 21.7% and 26.3%, respectively. Both traditional (age, BMI, arterial blood pressure, smoking, dyslipidemia and hyperfibrinogenemia) and renal ($eGFR_{CKD-EPI}$, serum phosphate) risk factors (RF) were significantly associated with cardiac remodeling (p<0.05). The frequencies of genotypes were as follows: *ACE I/D* polymorphism (*II*-23.7%, *ID*-44.8%, *DD*-27.5%); *CYP11B2 C(-344)T* polymorphism (*CC*-18.8%, *CT*-53.8%, *TT*-27.5%); *eNOS3 4a/4b* polymorphism (*4b/4b*-65.4%, *4a/4b*-30.8%, *4a/4a*-3.8%). We did not found any correlations between LVH and *ACE*, *CYP11B2*, *eNOS* genotypes. There was a trend to more frequent diastolic dysfunction in patients with *4b/4b* genotypes of *eNOS* as compared with patients with *4a* allele (p=0.066). In CGN patients older 45 years, diastolic dysfunction was significantly more frequent in those with *4b/4b* genotype then in patients with *4a* allele (66.7% vs. 14.3%; p<0.05).

CONCLUSIONS

More then ¼ patients with CGN demonstrate signs of cardiac remodeling, strongly associated with clinical traditional and renal risk factors. Estimating of the *ACE*, *CYP11B2*, *eNOS* gene polymorphisms does not add any extra information for cardiac remodeling prediction in CGN.

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