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The Contribution of *MTHFR* C677T Polymorphism to Peripheral Artery Disease in Diabetic Patients

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Background & Hypothesis:

Disorders in blood coagulation may play a role in peripheral artery disease. The aim of this study was to investigate the association between functional polymorphism C677T (*rs1801133*) of *methylenetetrahydrofolate reductase* (*MTHFR*) gene for and risk of peripheral artery disease in diabetes patients.

Methods:

The study sample included 434 unrelated Russian patients (50 patients with diabetic angiopathy of lower limbs and 384 healthy subjects). Genotyping of the polymorphism was performed by TaqMan assay.

Results:

No statistically significant differences in frequencies of the *MTHFR* alleles and genotypes were found between the study groups, as between entire groups as well as between gender stratified groups ($P > 0.05$). However, we found that the 677TT genotype showed an association with increased risk of the disease in male smokers (OR = 4.2 95% CI 1.28-13.79, $P = 0.01$), whereas non-smoker carriers of the 677TT genotype did not exert the disease risk.

Discussion & Conclusion:

Thus, increased risk of peripheral artery disease (diabetic angiopathy) is attributed to the interaction between the *MTHFR* gene polymorphism and tobacco smoking, pointing out to an importance of gene-environment interactions in disease susceptibility. We suggest that disease risk in patients with "thrombotic genotype" of the *MTHFR* gene is triggered by tobacco smoking exposure. The study was supported by the Russian Research Foundation (No.-15-15-10010).