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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).