



MTHFR 677CT Gene Polymorphism is not a Risk Factor for Venous Thromboembolism

MTHFR 677CT Gen Polimorfizmi Venöz Tromboembolizm İçin Bir Risk Faktörü Değildir.

Cengiz Beyan¹, Esin Beyan²

¹Gulhane Military Medical Academy, Department of Hematology; ANKARA

²Kecioren Training and Research Hospital, Department of Internal Medicine, ANKARA

Cukurova Medical Journal 2014;39(1):188-189.

Dear Editor,

We read with great interest the article by Ilhan about descriptive data of patients with venous thromboembolism (VTE)¹. The author evaluated the archive records of patients diagnosed with deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE) excluding patients with splanchnic vein thrombosis. Fifty percent heterozygous factor V Leiden mutation, 4.5% homozygous factor V Leiden mutation, 5.8% prothrombin 20210GA mutation and 66.6% methylene tetrahydrofolate reductase (MTHFR) mutation were found as risk factors of inherited thrombophilia. The author was not used the data of protein C, S and antithrombin because these tests were applied during acute phase of thrombosis in this study. We would like to comment on this study.

The most common form of genetic hyperhomocysteinemia results from production of a thermolabile variant of MTHFR with reduced enzymatic activity (T mutation). The gene encoding for this variant contains a cytosine to thymine substitution at nucleotide 677 (677CT)². The MTHFR 677CT gene is common in population. Sazci et al. calculated as 42.9% and 9.6% the population frequency of the MTHFR 677CT

(heterozygosity) and 677TT (homozygosity) in Turkey, respectively³.

There is increasing evidence that hyperhomocysteinemia is a risk factor for VTE; but, most studies that have examined patients with the thermolabile variant of MTHFR have not found that this genotype increases the risk of VTE when found alone or combined with risk factors of thrombophilia⁴⁻⁷. It was collected DNA from 4375 patients with a first DVT of the leg or PTE and from 4856 control subjects in the Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA Study). The results of MEGA study showed that MTHFR 677CT polymorphism was not associated with the risk of venous thrombosis (odds ratio [95% confidence interval] 0.99 [0.91-1.08] for the CT genotype and 0.94 [0.81-1.08] for the TT genotype)⁴. The narrow confidence interval in this study excluded even a small effect relationship between MTHFR 677CT and the risk of VTE.

According to current literature, it recommends that the patients with a strong family history of VTE should undergo testing for the five major inherited defects of thrombophilia (factor V Leiden, prothrombin gene mutation, protein C, S and

antithrombin deficiency) and MTHFR 677CT polymorphism should not be used for thrombophilia screening⁸.

As a result, there is no rationale for measuring the MTHFR 677CT polymorphism for clinical purposes in patients with VTE.

REFERENCES

1. Ilhan G. Descriptive data of patients with venous thromboembolism. *Cukurova Medical Journal*. 2013;38:610-6.
2. Rosenson RS, Kang DS. Overview of homocysteine. <http://www.uptodate.com/contents/overview-of-homocysteine.htm> (accessed 2013 Aug 16).
3. Sazci A, Ergul E, Kaya G, Kara I. Genotype and allele frequencies of the polymorphic methylenetetrahydrofolate reductase gene in Turkey. *Cell Biochem Funct*. 2005;23:51-4.
4. Bezemer ID, Doggen CJ, Vos HL, Rosendaal FR. No association between the common MTHFR 677C->T polymorphism and venous thrombosis: results from the MEGA study. *Arch Intern Med*. 2007;167:497-501.
5. De Stefano V, Casorelli I, Rossi E, Zappacosta B, Leone G. Interaction between hyperhomocysteinemia and inherited thrombophilic factors in venous thromboembolism. *Semin Thromb Hemost*. 2000;26:305-11.
6. Tsai AW, Cushman M, Tsai MY, Heckbert SR, Rosamond WD, Aleksic N, et al. Serum homocysteine, thermolabile variant of methylene tetrahydrofolate reductase (MTHFR), and venous thromboembolism: Longitudinal Investigation of Thromboembolism Etiology (LITE). *Am J Hematol*. 2003;72:192-200.
7. Naess IA, Christiansen SC, Romundstad PR, Cannegieter SC, Blom HJ, Rosendaal FR, et al. Prospective study of homocysteine and MTHFR 677TT genotype and risk for venous thrombosis in a general population--results from the HUNT 2 study. *Br J Haematol*. 2008;141:529-35.
8. Bauer KA, Lip GYH. Evaluation of the patient with established venous thrombosis. <http://www.uptodate.com/contents/evaluation-of-the-patient-with-established-venous-thrombosis.htm> (accessed 2013 Aug 16).

Yazışma Adresi / Address for Correspondence:

Dr. Cengiz Beyan
Gülhane Military Medical Academy
Department of Hematology
Etlik, 06018 ANKARA
E-mail: cengizbeyan@hotmail.com; cbeyan@gata.edu.tr

geliş tarihi/received :29.08.2013

kabul tarihi/accepted:18.09.2013