The End of a Long Debate: Methylene tetrahydrofolate Reductase Gene Polymorphisms do not Increase Thrombosis Risk

Eski Bir Tartışmanın Sonu: Metilentetrahidrofolat Redüktaz Gen Polimorfizmeleri Tromboz Riskini Artırmamaktadır

Ugur Sahin, Muhit Ozcan

To the Editor,

We read the article by Ozturk et al. [1], in which they reported the frequency of some thrombophilic mutations in eastern Turkey. The authors have defined single nucleotide gene variations of factor V Leiden, prothrombin G20210A, and methylenetetrahydrofolate reductase (MTHFR) C677T as thrombophilic mutations. However, as current scientific data do not support an increased risk of thrombosis in the presence of MTHFR gene polymorphisms, MTHFR C677T is not presently regarded as a thrombophilic mutation. In a recent meta-analysis involving over 11,000 cases and 21,000 controls, a significant association with venous thromboembolism was not observed for homozygous MTHFR C677T, whereas carriers of either heterozygous factor V Leiden or prothrombin G20210A, double heterozygotes and homozygous factor V Leiden or prothrombin G20210A exhibited an increased risk of thrombosis [2].

The misclassification of these gene variations is a commonly encountered problem. By definition, a polymorphism is a variation in a gene sequence, which is observed with a frequency of 1% or higher in a population, that leads to either neutral or favorable outcomes [3]. Although the aforementioned 1% cut-off is arbitrary and the classification is dependent on the definition of the studied population and is subject to some exceptions, the term “mutation” refers to an infrequent variation in a gene sequence associated with a disease-causing capacity. Thus, in daily jargon, variations in factor V Leiden and prothrombin G20210A are traditionally referred to as mutations, whereas those in MTHFR are referred to as polymorphisms.

The authors have denied the necessity of ethical approval with respect to the retrospective study design. This might be generally acceptable. However, the decision depends on the type of data being processed. Ethical committee approval should be strongly considered in such studies, which cover analyses of sensitive data, including DNA test results. Even in the absence of formal ethical committee approval, the authors should have at least declared that the study had been conducted in accordance with the Helsinki Declaration as revised in 2013 [4].

In conclusion, MTHFR gene polymorphisms, including MTHFR C677T, are definitely not related to an increased risk of thrombosis, and their diagnostic testing in the clinical evaluation of inherited thrombophilia should be strongly discouraged.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.O.; Design - U.S.; Supervision - M.O.; Literature Review - U.S., M.O.; Writing - U.S.; Critical Review - M.O.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.
References


