

32. Gene polymorphism as riskfactors for predicting the cardiovascular manifestations in marfan syndrome

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Background: Folic acid metabolism enzymes polymorphisms are believed to be responsible for the elevation of homocysteine (Hcy) concentration in the blood plasma, which correlates to the formation of certain cardiovascular diseases such as aortic aneurysms and dissection.

Purpose: Our aim was to investigate the four gene polymorphisms of Methylenetetrahydrofolate reductase (MTHFR), Methionine synthase (MTR) and Methionine synthase reductase (MTRR) in patients with Marfan syndrome.

Methods: We studied 78 Marfan patients divided into groups based on the severity of cardiovascular manifestations: no involvement n=34 (Group A); mild involvement required intervention n=17 (Group B); severe cardiovascular involvement n=27 (Group C) subdivided into aortic dilatation n=14 and aortic dissection n=13 (Group C1 and C2), and 117 control subjects. We evaluated Hcy, folate, vitamin B12 and the polymorphisms of MTHFR C677T and A1298C, MTR A2576G and MTRR A66G.

Results: Multiple comparisons showed significantly higher levels of Hcy in Group C2 compared to Group A, B, C1 and control group ($P<0.0001$, $P<0.0001$, $P=0.001$ and $P=0.003$, respectively). Similarly, folate differed significantly, being lower in Group C2 than in Group A, B, C1 and control subjects ($P<0.0001$, $P=0.02$, $P<0.0001$ and $P<0.0001$). Multivariate logistic regression analysis revealed, that homocysteine plasma level was an independent risk factor for the severe cardiovascular involvement (Group C; OR 1.85, 95% CI 1.28-2.66, $P=0.001$) as well as for aortic dissection (Group C2; OR 2.49, 95% CI 1.29-4.78, $P=0.006$).

Conclusions: Our findings indicate that patients with more severe cardiovascular involvements in Marfan syndrome, and in particular with aortic dissection are associated with higher Hcy plasma levels and prevalence of homozygous genotypes of folic acid metabolism enzymes' than in patients with mild or no cardiovascular manifestations. These results suggest an important role for the proper homeostasis of folic acid metabolism in the development and remodelling of the extracellular matrix of the aorta, and could indicate a preventional supplementation of folic acid and vitamin B12 for Marfan patients.