Genetic Polymorphisms CYP2J2*7 and CYP2C8*3 and Effects on the Level of Risk for Coronary Artery Disease

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Abstract
In the present study we analyzed the impact of a genetic variant in CYP2C8 on coronary artery disease (CAD) in Bulgarian population. We conducted a case-control study to determine whether the common genetic variation rs890293 (CYP2J2*7) in CYP2J2 gene was associated with the risk of CAD.

Methods
We analyzed 99 patients with CAD and 377 controls for a potential correlation of the CYP2J2 polymorphism G-50T. 96 of these 99 patients were tested for the presence of polymorphisms CYP2C8. To evaluate the genotypes of the samples real time PCR with predesigned TaqMan SNP Genotyping Assays (Applied Biosystem) for rs890293 was used. The deviation of allele polymorphism CYP2J2*7 and CYP2C8*3 on the balance of Hardy-Weinberg are greater than 0.05 and, therefore, for all groups distribution of the T-allele in CYP2J2*7 corresponds to the balance Hardy-Weinberg and the frequency of the T allele with $\chi^2$ test was studied.

Results
The main dichotomous and nondichotomous and clinical characteristics of the study group are shown in the Table 1 and 2.

The frequency of genotypes of the T allele CYP2J2*7 and CYP2C8*3 is shown on the Tables 3 and 4. In the group of people with MI, the percentage of this T-allele is slightly greater than in the control group (14.14% versus 12.10% of patients with T-allele (Table 3). The resulting p-values for both polymorphism (for CYP2C8*3, $p = 0.0670$) and (CYP2J2*7) indicates that the distribution of T allele CYP2C8*3 with high probability close to balance Hardy Weinberg, than in the CYP2J2*7 (Table 3 and 4).

An analysis of the connection between gender and the likelihood of CAD among polymorphisms in the CYP2J2*7 and CYP2C8*3 is made. The results are shown in Table 5 and Table 6.

The obtained p-value is $p=0.3656$ which show that the hypothesis of no association have to be rejected. The chances for people with T-allele polymorphism in the CYP2C8*3, CAD occur on average 1.7 times higher than those who did not carry this allele. CI of OR (1.0334÷2.8746) with 95% probability. CI indicated that it could be argued with a 95% probability that the presence of T allele in CYP2C8*3 increases the risk of CAD.

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The obtained p-value is $p=0.0356$ which show that the hypothesis of no association have to be rejected. The chances for people with T-allele polymorphism in the CYP2C8*3, CAD occur on average 1.7 times higher than those who did not carry this allele. CI of OR (1.0334÷2.8746) with 95% probability. CI indicated that it could be argued with a 95% probability that the presence of T allele in CYP2C8*3 increases the risk of CAD.

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Table 10: Association between gender and CAD among participants without T-allele in CYP2J2*7.

<table>
<thead>
<tr>
<th>Group with coronary artery disease - 99</th>
<th>Control group - 377</th>
<th>Total – 459</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT</td>
<td>Number 2</td>
<td>2.08%</td>
</tr>
<tr>
<td>TG or TG</td>
<td>26</td>
<td>27.08%</td>
</tr>
<tr>
<td>GG</td>
<td>68</td>
<td>70.84%</td>
</tr>
<tr>
<td>Frequency</td>
<td>0.1562</td>
<td>15.62%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.7901</td>
<td>0.6974</td>
</tr>
</tbody>
</table>

The obtained p-value and OR are p=0.8085 and OR=1.1719 with CI=0.3423÷4.011. The analysis shows that sex doesn’t influence on CAD chances among T allele CYP2J2*7 carriers.

The obtained statistical parameters are p=0.4780 and OR=0.6553 with CI=0.2027÷2.1187. The obtained values shows that there isn’t association between smoking and CAD among T allele CYP2J2*7 carriers.

The obtained statistical parameters are p=0.0441 and consequently there is statistical significant association between smoking and CAD among T allele CYP2C8*3 carriers. The odds ratio is 2.4965 with CI 1.0125÷6.1555. The results indicate that the chances for CAD are 2.5 times greater to smokers.

The obtained p-value and OR are p=0.9489 and OR=0.9717 with CI=0.4034÷2.3404. The analysis shows that sex doesn’t influence on CAD chances among T allele CYP2C8*3 carriers.

The obtained statistical parameters are p=0.1091 and OR=1.4917 with CI=0.9130÷2.4374. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2J2*7 carriers.

The obtained statistical parameters are p=0.1547 and OR=1.4781 with CI=0.8612÷2.5369. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2C8*3 carriers.

The obtained p-value is p=0.0441 and consequently there is statistical significant association between smoking and CAD among T allele CYP2J2*7 carriers.

Table 11: Association between the T allele in the CYP2J2*7 and smoking in the group with CAD.

<table>
<thead>
<tr>
<th>Smoker</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>5</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>No</td>
<td>39</td>
<td>46</td>
<td>85</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>55</td>
<td>99</td>
</tr>
</tbody>
</table>

Table 12: Association between the T - allele in CYP2C8*3 and smoking group with CAD.

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Conclusions

The analysis of results shows that polymorphism CYP2C8*3 is more important for the occurrence of CAD compared with CYP2J2*7 in the study. Demonstrates a statistically significant association between the presence of the T allele and smoking respectively CYP2J2*7 and CYP2C8*3.

Acknowledgement

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References
