Effect of the polymorphism rs2470893 of the CYP1A1 gene on ovarian and endometrial cancer in Mediterranean women

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Background: The CYP1A1 gene is located on chromosome 15 (15q22-q24.1) and is part of the cytochrome P450 family. This catabolizing enzyme has an important role in the activation/deactivation of various chemical agents, including xenobiotics and sex hormones. It is related to the synthesis of cholesterol and steroids, and to the metabolism of drugs, coffee, or different metabolites such as those of tobacco. It is found mainly in extrahepatic tissues such as lung, breast or ovarian follicles, and participates in the metabolism of a large number of xenobiotics as well as one of endogenous substrates. Human cytochrome P450 1A1 is one of the most important enzymes involved in the human carcinogenesis because it metabolizes several procarcinogens to active carcinogens. There are previous studies that have linked rs2470893 with ovarian cancer. Our aim has been to estimate the association between polymorphism rs2470893 of the CYP1A1 gene on ovarian and endometrial cancer in a Mediterranean population.

Methods: We have carried out an observational study at baseline and longitudinally in the PREDIMED-Valencia study including 696 women at high cardiovascular risk. We prospectively analyzed cancer incidence as a secondary outcome in this study. Lifestyle, clinical and biochemical variables were assessed by standardized methods. DNA was isolated from blood and the selected polymorphisms were determined.

Results: We detected 8 new cases of ovarian and endometrial cancer from 2003 to 2014, representing 0.6% and 0.1% respectively, of all cancers. In our study it was observed that the variant rs2470893 was related to ovarian and endometrial cancer. The allelic frequency of the A allele was 0.246. The carriers of the G allele were grouped in front of the AA carriers. When assessing the risk of having suffered from ovarian or endometrial cancer according to the genotype of this variant, it was observed that the individuals carrying the AA allele presented a higher risk OR = 8.7; CI 95% (2.4-31.9); P = 0.001 after adjustment for age, intervention group, tobacco smoking and obesity (BMI ≥ 30 Kg/m²).

Conclusions: rs2470893of the CYP1A1 gene could be associated with ovarian and endometrial cancer in a high cardiovascular risk population.