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Effects of the Ser326Cys Polymorphism in the DNA Repair OGG1 Gene on Cancer, Cardiovascular, and All-Cause Mortality in the PREDIMED Study: Modulation by Diet.

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Abstract

BACKGROUND: Oxidatively induced DNA damage, an important factor in cancer etiology, is repaired by oxyguanine glycosylase 1 (OGG1). The lower repair capacity genotype (homozygote Cys326Cys) in the OGG1-rs1052133 (Ser326Cys) polymorphism has been associated with cancer risk. However, no information is available in relation to cancer mortality, other causes of death, and modulation by diet.

OBJECTIVE: Our aim was to evaluate the association of the OGG1-rs1052133 with total, cancer, and cardiovascular disease (CVD) mortality and to analyze its modulation by the Mediterranean diet, focusing especially on total vegetable intake as one of the main characteristics of this diet.

DESIGN: Secondary analysis in the PREDIMED (Prevención con Dieta Mediterránea) trial is a randomized, controlled trial conducted in Spain from 2003 to 2010.

PARTICIPANTS/SETTING: Study participants (n=7,170) were at high risk for CVD and were aged 55 to 80 years.

INTERVENTION: Participants were randomly allocated to two groups with a Mediterranean diet intervention or a control diet. Vegetable intake was measured at baseline.

MAIN OUTCOME MEASURES: Main outcomes were all-cause, cancer, and CVD mortality after a median follow-up of 4.8 years.

STATISTICAL ANALYSES: Multivariable-adjusted Cox regression models were fitted.

RESULTS: Three hundred eighteen deaths were detected (cancer, n=127; CVD, n=81; and other, n=110). Cys326Cys individuals (prevalence 4.2%) presented higher total mortality rates than Ser326-carriers (P=0.009). The multivariable-adjusted hazard ratio for Cys326Cys vs Ser326-carriers was 1.69 (95% CI 1.09 to 2.62; P=0.018). This association was greater for CVD mortality (P=0.001). No relationship was detected for cancer mortality in the whole population (hazard ratio 1.07; 95% CI 0.47 to 2.45; P=0.867), but a significant age interaction (P=0.048) was observed, as Cys326Cys was associated with cancer mortality in participants <66.5 years (P=0.029). Recessive effects limited our ability to investigate Cys326Cys×diet interactions for cancer mortality. No statistically significant interactions for total or CVD mortality were found for the Mediterranean diet intervention. However, significant protective interactions for CVD mortality were found for vegetable intake (hazard ratio interaction per standard deviation 0.42; 95% CI 0.18 to 0.98; P=0.046).

CONCLUSIONS: In this population, the Cys326Cys-OGG1 genotype was associated with all-cause mortality, mainly CVD instead of cancer mortality. Additional studies are needed to provide further evidence on its dietary modulation.

KEYWORDS: Cancer; Cardiovascular; Mortality; Nutrigenetics; Vegetables

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