TP53 Arg72Pro polymorphism and colorectal cancer risk: a systematic review and meta-analysis.

Dahabreh IJ, Linardou H, Bouzika P, Varvarigou V, Murray S.

Source

Center for Clinical Evidence Synthesis, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, 35 Kneeland Street, Boston, MA 02111, USA. issa.dahabreh@tufts.edu

Abstract

BACKGROUND:

The TP53 rs1042522 polymorphism (c.215C>G, Arg72Pro) has been extensively investigated as a potential risk factor for colorectal cancer, but the results have thus far been inconclusive.

METHODS:

We searched multiple electronic databases to identify studies investigating the association between the Arg72Pro polymorphism and colorectal cancer. Individual study odds ratios (OR) and their confidence intervals were estimated using allele-frequency, recessive, and dominant genetic models. Summary ORs where estimated using random effects models.

RESULTS:

We identified 23 eligible case-control studies, investigating 6,514 cases and 9,334 controls. There was significant between-study heterogeneity for all genetic models. The control group in one of the studies was not in Hardy-Weinberg equilibrium; only three studies reported that genotyping was blinded to case/control status and five studies used tumor tissue for case genotyping. Overall, we did not identify any association between rs1042522 and colorectal cancer risk under an allele-frequency comparison (OR, 0.99; 95% confidence interval, 0.89-1.09). Likewise, no association was evident under dominant or recessive models. Studies using tumor tissue for case genotyping found a protective effect for the Pro allele, compared with studies using somatic DNA (P(interaction) = 0.03). Results were also inconsistent between different genotyping methods (P(interaction) = 0.03).

CONCLUSION:

We did not identify an association between TP53 rs1042522 and colorectal cancer. Published results seem to be driven by technical artifacts rather than true biological effects.

IMPACT:

Future genetic association studies should use more rigorous genotyping methods and avoid the use of tumor tissue as a source of DNA to prevent genotype misclassification due to loss of heterozygosity.