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Alcohol, tobacco and genetic susceptibility in relation to cancers of the upper aerodigestive tract in northern Italy

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ABSTRACT

Aims and background. Each year in Italy there are approximately 14,000 new cases and 7,000 deaths from cancer of the upper aerodigestive tract, which includes malignant tumors originating from the oral cavity, pharynx, larynx and esophagus. Established etiological factors include tobacco consumption and heavy alcohol drinking. The study of single nucleotide polymorphisms in upper aerodigestive tract cancer etiology may help to identify high-risk subgroups and to better understand the pathways leading to the development of these cancers.

Methods. Italian results on about 500 cases and 500 controls from a large case-control study (ARCAGE) conducted in 10 European countries are presented with the major objectives of updating results on the effects of alcohol and tobacco consumptions in northern Italy, investigating the role of genetic variation with regard to the metabolism of alcohol and carcinogens from tobacco smoke, and evaluating possible interactions of these single nucleotide polymorphisms with these carcinogens.

Results. The present study confirmed the importance of tobacco smoking and alcohol drinking as the main risk factors for upper aerodigestive tract cancers, indicating that about 68% of cancers among populations in northern Italy can be attributed to the combination of these risk factors. Significant associations between metabolizing phase I genes (*CYP1A1* and *CYP2A6*), phase II genes (*GSTA2*) and upper aerodigestive tract cancers were found. A polymorphism of *ADH1C* has been associated with an increased risk of upper aerodigestive tract cancers, suggesting that the less rapid alcohol metabolizers are more susceptible to upper aerodigestive tract cancer risk.

Conclusions. Our results suggest that the *ADH1C* allele modifies the carcinogenic dose response for alcohol in the upper aerodigestive tract, giving rise to a gene-environment interaction. The role of genes as possible modifiers of life-style risks seems the most reliable.
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Key words: alcohol, case-control study, genetic susceptibility, Italy, single nucleotide polymorphisms, tobacco, upper aerodigestive cancer.

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