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LUNG ALERT

Folate metabolism gene polymorphisms may influence lung cancer prognosis

▲ Matakidou A, el Galta R, Rudd MF, *et al*. Prognostic significance of folate metabolism polymorphisms for lung cancer. *Br J Cancer* 2007;**97**:247–52.

Aberrant DNA methylation is a common feature of human neoplasia, including lung cancer. Folate metabolism pathway variants affect DNA methylation and tumour suppressor genes and may impact tumour behaviour. In this study the association between selected polymorphic variants of folate metabolism genes and overall survival of 619 Caucasian female patients with lung cancer was assessed.

Patients were included from the Genetic Lung Cancer Predisposition Study (GELCAPS) with non-small cell and small cell lung cancer at variable staging following standard UK management regimes. Associations between survival and clinical and demographic variables were assessed with overall survival as the primary endpoint.

A reduced overall survival was observed for single polymorphisms of *MTHFS, MTHFR* and *MTRR* genes. Specifically, associations with *MTHFS* Thr202Ala were related to reduced survival for all lung cancers for heterozygosity, homozygosity and carrier status. Carrier status for *MTRR* Ser175Leu was associated with a poorer outcome in all lung cancers, and homozygosity for the polymorphism *MTHFR* Ala222Val in small cell lung cancer. Carriers of *MTHFR* Arg594Gln with non-small cell lung cancer had a slightly longer overall survival. Staging and histology, both very important prognostic indicators, had no correlation with polymorphisms tested.

This study provides evidence for associations between survival and variation in three genes of folate metabolism; however, some of the associations may be false positives due to the methods used. Further genetic studies are needed to truly assess the influence of folate metabolism gene polymorphisms on clinical outcomes of survival and prognosis of lung cancer.

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