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Abstract: The present study retrospectively examined the correlation between the outcome of patients with locally advanced oesophageal squamous cell carcinoma (cT3-4 cN0-1 cM0) after multimodal treatment (radiochemotherapy+/surgical resection), and the presence of genetic polymorphisms in genes involved in folate metabolism. In total, 68 patients who took part in a prospective multicentric trial received 5-fluorouracil (FU)-based radiochemotherapy, optionally followed by surgery. DNA was extracted from pretherapeutic tumour biopsies and was subsequently genotyped for common genetic polymorphisms of three genes (MTHFR C677T, MTR A2756G, TS tandem repeat polymorphism) involved in folate metabolism and potentially in sensitivity to 5-FU-based chemotherapy. The genotypes were correlated with tumour response to polychemotherapy, radiochemotherapy and with overall survival. Tumours with the MTR wild-type genotype (2756AA) showed a median survival time of 16 months, whereas tumours with an MTR variant genotype (2756AG/2756GG) showed a median survival time of 42 months (P=0.0463). No prognostic impact could be verified for the genotypes of the MTHFR genes and the TS gene.
Among tumours treated with radiochemotherapy and subsequent resection, MTR variant genotype showed higher histopathological response rate than tumours with MTR wild-type genotype (P=0.0442). In contrast, no significant relationship between clinically determined tumour regression after polychemotherapy and polymorphisms of the three genes under analysis was observed. In conclusion, pretherapeutical determination of the MTR A2756G polymorphism may predict survival of multimodally treated oesophageal squamous cell carcinomas. Determination of MTHFR C677T and TS tandem repeat polymorphism has no predictive value.