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Titel des Beitrags: A retrospective comparative exploratory study on two Methylentetrahydrofolate Reductase (MTHFR) polymorphisms in esophagogastric cancer: the A1298C MTHFR polymorphism is an independent prognostic factor only in neoadjuvantly treated gastric cancer patient

Abstract:
Methylentetrahydrofolate reductase (MTHFR) plays a major role in folate metabolism and consequently could be an important factor for the efficacy of a treatment with 5-fluorouracil. Our aim was to evaluate the prognostic and predictive value of two well characterized constitutional MTHFR gene polymorphisms for primarily resected and neoadjuvantly treated esophagogastric adenocarcinomas. 569 patients from two centers were analyzed (gastric cancer: 218, carcinoma of the esophagogastric junction (AEG II, III): 208 and esophagus (AEG I): 143). 369 patients received neoadjuvant chemotherapy followed by surgery, 200 patients were resected without preoperative treatment. The MTHFR C677T and A1298C polymorphisms were determined in DNA from peripheral blood lymphocytes. Associations with prognosis, response and clinicopathological factors were analyzed retrospectively within a prospective database (chi-square, log-rank, cox regression). Only the MTHFR A1298C polymorphisms had prognostic relevance in neoadjuvantly treated patients but it was not a
The AC genotype of the MTHFR A1298C polymorphisms was significantly associated with worse outcome (p = 0.02, HR 1.47 (1.06-2.04). If neoadjuvantly treated patients were analyzed based on their tumor localization, the AC genotype of the MTHFR A1298C polymorphisms was a significant negative prognostic factor in patients with gastric cancer according to UICC 6th edition (gastric cancer including AEG type II, III: HR 2.0, 95% CI 1.3-2.0, p = 0.001) and 7th edition (gastric cancer without AEG II, III: HR 2.8, 95% CI 1.5-5.7, p = 0.003), not for AEG I. For both definitions of gastric cancer the AC genotype was confirmed as an independent negative prognostic factor in cox regression analysis. In primarily resected patients neither the MTHFR A1298C nor the MTHFR C677T polymorphisms had prognostic impact. The MTHFR A1298C polymorphisms was an independent prognostic factor in patients with neoadjuvantly treated gastric adenocarcinomas (according to both UICC 6th or 7th definitions for gastric cancer) but not in AEG I nor in primarily resected patients, which confirms the impact of this enzyme on chemotherapy associated outcome.