Mutations of RAS/RAF Proto-oncogenes Impair Survival After Cytoreductive Surgery and HIPEC for Peritoneal Metastasis of Colorectal Origin.

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Abstract

BACKGROUND:

Adequate selection of patients with peritoneal metastasis (PM) for cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) remains critical for successful long-term outcomes. Factors reflecting tumor biology are currently poorly represented in the selection process. The prognostic relevance of RAS/RAF mutations in patients with PM remains unclear.

METHODS:

Survival data of patients with colorectal PM operated in 6 European tertiary centers were retrospectively collected and predictive factors for survival identified by Cox regression analyses. A simple point-based risk score was developed to allow patient selection and outcome prediction.

RESULTS:

Data of 524 patients with a median age of 59 years and a median peritoneal cancer index of 7 (interquartile range: 3-12) were collected. A complete resection was possible in 505 patients; overall morbidity and 90-day mortality were 50.9% and 2.1%, respectively. PCI [hazard ratio (HR): 1.08], N1 stage (HR: 2.15), N2 stage (HR: 2.57), G3 stage (HR: 1.80) as well as KRAS (HR: 1.46) and BRAF (HR: 3.97) mutations were found to significantly impair survival after CRS/HIPEC on multivariate analyses. Mutations of RAS/RAF impaired survival independently of targeted treatment against EGFR. Consequently, a simple point-based risk score termed BIOSCOPE (BIOlogical Score of COlorectal PEritoneal metastasis) based on PCI, N-, G-, and RAS/RAF status was developed, which showed good discrimination [development area under the curve (AUC) = 0.72, validation AUC = 0.70], calibration (P = 0.401) and allowed categorization of patients into 4 groups with strongly divergent survival outcomes.

CONCLUSION:

RAS/RAF mutations impair survival after CRS/HIPEC. The novel BIOSCOPE score reflects tumor biology, adequately stratifies long-term outcomes, and improves patient assessment and selection.