The prognostic role of KRAS and BRAF in patients undergoing surgical resection of colorectal cancer liver metastasis: a systematic review and meta-analysis

**Background:** Clinical trials investigated the potential role of both KRAS and BRAF mutations, as prognostic biomarkers, in colorectal cancer (CRC) patients who underwent surgical treatment of liver metastasis (CLM), showing conflicting results. This meta-analysis aims to review all the studies reporting survival outcomes (recurrence free survival (RFS), and/or overall survival (OS)) of patients undergoing resection of CLM, stratified according to KRAS and/or BRAF mutation status.

**Materials and Methods:** Data from all published studies reporting survival outcomes (RFS and/or OS) of CRC patients who received resection of CLM, stratified by KRAS and/or BRAF mutation status were collected by searching in PubMed, Cochrane Library, American Society of Clinical Oncology and European Society of Medical Oncology meeting proceedings. Pooled hazard ratios (HRs) and 95% confidence intervals (95% CIs) were calculated for both the OS and/or RFS.

**Results:** Seven eligible trials (1403 patients) were included. Pooled analysis showed that KRAS mutations predicted a significant worse both RFS (HR: 1.65; 95% CI: 1.23 – 2.21) and OS (HR: 1.86; 95% CI: 1.51 – 2.30) in patients who underwent surgical resection of CLM. BRAF mutations were also associated with a significant worse OS (HR: 3.90; 95% CI: 1.96 – 7.73) in this subgroup of patients.

**Conclusion:** This meta-analysis suggests both KRAS and BRAF mutations as negative prognostic biomarkers associated with worse survival outcomes in patients undergoing hepatic resection of CLM. Such evidences support the introduction of new treatment decision models, taking into account the tumor molecular profile in order to individualize both systemic and loco-regional treatment strategies.
Parole Chiave

1. KRAS/BRAF
2. prognostic biomarkers
3. colorectal cancer liver metastasis

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