



Monocyte-to-lymphocyte ratio in metastatic colorectal cancer: Prognostic role evaluation and cut-off definition

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Background: Changes in peripheral blood cells composition may reflect tumor immune microenvironment and its role in cancer growth control. High monocyte-tolymphocyte ratio (MLR) could be a sign of tumor's recruitment of suppressive cells, showing a prognostic role in many cancer types. This study aimed to evaluate the prognostic role of MLR in metastatic colorectal cancer (MCRC).

Methods: This retrospective study analyzed a consecutive cohort of 392 patients (pts) with MCRC treated in 2004-2017 at the Oncology Departments of Aviano and Udine (Italy). The prognostic impact of MLR on overall survival (OS) was evaluated with uniand multivariate Cox regression analyses. The best cut-off value to predict survival was defined through ROC analysis.

Results: Before first line therapy, 269 pts (69%) were aged <70, 120 pts (31%) had a right tumor, 150 pts (38%) a left tumor and 117 pts (30%) a rectal one. Of note, 105 pts (27%) received metastasectomy and 142 pts had >1 metastasis. Metastasis were more frequent in liver (40%), lung (20%) and peritoneum (20%) Overall, 57% had a KRAS mutation (m) and 11% had a BRAFm. At median follow-up of 60 months, median OS was 26 months. At univariate analysis, older age (HR 1.61, p < 0.001), nodes (pN2 HR $1.48, p = 0.036; pN3 \ HR \ 2.52, p = 0.001), KRASm \ (HR \ 1.36, p = 0.020) \ and \ MLR \ (HR \ 1.36, p = 0.020)$ 3.32, p < 0.001) were associated with worse OS. Conversely, sidedness (left HR 0.65, p=0.003; rectum HR 0.73, p=0.042), metastasectomy (HR 0.36, p<0.001) and adjuvant chemotherapy (HR 0.66, p = 0.008) were associated with better OS. By multivariate analysis, sidedness and metastasectomy confirmed a better OS, while MLR (HR 3.20, p < 0.001), nodes (pN2 HR 1.89, p = 0.006; pN3 HR 2.25, p = 0.014), and KRASm (HR 1.50, p < 0.001) were associated with worse OS. The adoption of the cutoff value for MLR (i.e. 0.44) predicted worse OS both in univariate (HR 2.23, p < 0.001) and multivariate (HR 2.41; p < 0.001) analyses. Moreover, MLR was associated with number of metastatic sites (p < 0.001), type of sites (p < 0.001), sidedness (p = 0.001) and LDH level (p < 0.001).

Conclusions: High MLR is an independent prognostic factor associated with worse OS and pathological features of MCRC. Further studies are needed to confirm these data. Legal entity responsible for the study: University of Udine.

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