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

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\textbf{Background:} Changes in peripheral blood cells composition may reflect tumor immune microenvironment and its role in cancer growth control. High monocyte-to-lymphocyte 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).

\textbf{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 univariate and multivariate Cox regression analyses. The best cut-off value to predict survival was defined through ROC analysis.

\textbf{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, \textit{p} < 0.001), nodes (pN2 HR 1.48, \textit{p} = 0.036; pN3 HR 2.52, \textit{p} = 0.001), KRASm (HR 1.36, \textit{p} = 0.026) and MLR (HR 3.32, \textit{p} < 0.001) were associated with worse OS. Conversely, sidedness (left HR 0.65, \textit{p} = 0.003; rectum HR 0.73, \textit{p} = 0.042), metastasectomy (HR 0.36, \textit{p} < 0.001) and adjuvant chemotherapy (HR 0.66, \textit{p} = 0.008) were associated with better OS. By multivariate analysis, sidedness and metastasectomy confirmed a better OS, while MLR (HR 3.20, \textit{p} < 0.001), nodes (pN2 HR 1.89, \textit{p} = 0.006; pN3 HR 2.25, \textit{p} = 0.014), and KRASm (HR 1.50, \textit{p} < 0.001) were associated with worse OS. The adoption of the cut-off value for MLR (i.e. 0.44) predicted worse OS both in univariate (HR 2.23, \textit{p} < 0.001) and multivariate (HR 2.41; \textit{p} < 0.001) analyses. Moreover, MLR was associated with number of metastatic sites (\textit{p} < 0.001), type of sites (\textit{p} < 0.001), sidedness (\textit{p} = 0.001) and LDH level (\textit{p} < 0.001).

\textbf{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.

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