

**Title:** Neutrophil-to-lymphocyte ratios in colorectal cancer patients treated with Selective Internal Radiotherapy with yttrium-90 resin microspheres

**Hypothesis:** NLR has a predictive significance in patients with unresectable metastatic colorectal cancer treated with SIRT

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**Purpose/Objective(s):**

Selective internal radiotherapy (SIRT) is a standard therapy option for patients with unresectable metastatic colorectal cancer (mCRC) to the liver. Elevated neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte ratios (PLR) have been shown to correlate with prognosis in multiple tumor types following different treatment modalities, including radiation therapy, and are potential predictors of survival following SIRT. We investigated the association of patient, tumor, and laboratory characteristics with overall survival (OS), progression-free survival (PFS), and liver-specific progression-free survival (LSPFS).

**Materials/Methods:**

We retrospectively analyzed blood results from 74 consecutive patients with mCRC treated with yttrium-90 resin microspheres from March 2011 to December 2015 at our institution. Patient, tumor and prior treatment characteristics were collected. Laboratory values for all patients at baseline included carcinoembryonic antigen (CEA), hemoglobin (Hgb), white blood cell (WBC), neutrophil, lymphocyte, platelet, hematocrit, NLR and PLR, change (baseline to 4 weeks) in NLR and PLR, bilirubin (Bili), alanine transferase (ALT), alkaline phosphatase (ALP), albumin, and creatinine. Univariate and multivariate Cox models were used with a 5% level for significance. Recursive partition analysis (RPA) was used to determine cutoff values associated with OS, PFS, and LSPFS.

**Results:**

All patients were refractory or intolerant of chemotherapy for mCRC; median OS was 9.8 months for those who received SIRT and 21 patients were alive on last follow-up. Median SIRT dose was 1.5 GBq (range 0.8 e 2.5 GBq). Statistically significant factors for worse OS upon multivariate analysis were previous chemotherapy, higher baseline Bili, lower albumin and higher CEA (all  $p$ 's<0.01), lower platelet (pZ0.02), higher NLR (pZ0.01), and lower creatinine (pZ0.03). Significant factors for worse PFS were previous chemotherapy, higher baseline Bili, lower albumin, higher CEA and higher NLR (all  $p$ 's<0.01). Significant factors for worse LSPFS were previous chemotherapy (pZ0.02), previous liverdirected therapy (0.02), higher baseline CEA (0.02), higher Bili, higher neutrophil, lower platelet and higher NLR (all  $p$ 's<0.01). RPA-derived cutoff value for NLR was 15.7. Pretreatment NLR 15.7 was associated with a worse OS (HR 3.3; 95% CI 1.3-7.1;  $p$ <0.01) when compared with those whose NLR < 15.7. PLR, change in NLR, and change in PLR were not significantly associated with OS, PFS or LSPFS (all  $p$ 's>0.05).

**Conclusion:**

Our results suggest that a higher pretreatment NLR is associated with worse OS in mCRC patients treated with SIRT in the salvage setting. The utility of analyzing baseline blood counts in potentially selecting patients for SIRT should be explored in retrospective data from larger clinical series.