

Summary

Novák P.: Tumor infiltrating lymphocytes as prognostic factor of colorectal cancer after radical surgical treatment

Background: Colorectal cancer (CRC) belongs among the most frequent malignant diseases and represents worldwide problem. Czech Republic has one of the highest incidence of CRC. The fight against this disease is kept in many lines as preventive, surgical and oncological treatment and very important part is also the estimation of prognosis and suggestion of individual treatment.

Aim: The aim of this study was to analyze the relation of contemporary clinical and histopathological factors and tumor infiltrating lymphocytes, dendritic and natural killer cells. The next aim was to differentiate the patients with high risk of shortened overall survival and tendency to early recurrence of CRC after radical surgical treatment.

Methods: We analyzed the group of 150 patients (93 men, 57 women) that were operated on at the Department of Surgery of Teaching Hospital in Pilsen between 2004 and 2007. The important condition for inclusion into the study was radical operation. We excluded patients with any disease that could influence immunological reactivity. We examined endovascular, endolymphatic, perineural infiltration by tumor cells (0 – none, 1 positive). Infiltrations of tumor by lymphatic cells were intratumoral, intrastromal, peritumoral and Crohn-like reaction. The scale for evaluation was: none (0), mild (1), medium (2) and severe (3). Reactive histological changes in lymphatic nodes were described as follicular hyperplasia, sinuses histiocytosis and presence of granulomas. We quantified also immunohistochemical expression of CD4+, CD8+, CD57+ and S100 patterns on immune cells. All these parameters were analyzed by statistical examination in relation to overall and disease free survival.

Discussion: We proved that negative prognostic factors of overall survival are metastatic proves in lymph nodes, N2 status of affliction of lymph nodes, endovascular infiltration and extension of intratumoral infiltration by CD+ lymphocytes. Positive prognostic factors of overall survival were presence of peritumoral lymphocytes, Crohn-like peritumoral lymphocytes, follicular hyperplasia of lymph nodes, the extension of intratumoral infiltration by CD8+ lymphocytes and CD57+. Perineural infiltration, metastatic infiltration of lymph nodes and N2 status of lymph nodes were proved as negative prognostic factors of disease free survival. Intratumoral infiltration by CD8+ is factor that prolongs disease free survival. Multivariate analysis proved combination of CD8+ infiltration and lymph node affliction by metastatic process as most important for prediction of risk of early recurrence ($p < 0,05$).

Conclusion: Tumor infiltrating lymphocytes and NK cells seems to be promising prognostic factors that could find their application in colorectal surgery and following oncological treatment as key indicator for individualized treatment. The status of tumor infiltrating lymphocytes reflects immune system from the view of tumor control.

Key words: tumor infiltrating lymphocytes, CD4+, CD8+, CD57+, dendritic cells, prognostic factors, overall survival, disease free survival.