SUMMARY

Colorectal carcinoma (CRC) ranks high in mortality and morbidity in most developed countries. Following theses focus on specific aspects of colorectal carcinoma pathogenesis including the issue of screening. The goal of the first study was assessment of expression of epithelial markers of colorectal carcinogenesis p53, COX-2, bcl-2. The study included patients with active ulcerative colitis (UCA), ulcerative colitis in remission (UCR), primary sclerosing cholangitis with ulcerative colitis (PSC-UC) (PSC), patients after liver transplantation for PSC (OLT) and a control group (N). We found significantly increased expression of tumour suppressor gene p53 in non-dysplastic mucosae in PSC-UC compared with UCA, UCR, OLT, and N, which may indicate higher neoplastic potential of PSC. Statistically significant correlation was found between PSC incidence and p53 expression. Surprisingly, OLT showed no p53 expression in non-dysplastic mucosa compared with PSC-UC. This indicates that PSC may contribute to increased expression of p53 and p53-induced colorectal carcinogenesis. Furthermore, a correlation between expression of p53 and COX-2 together with the increased expression of bcl-2 in UCA compared to N can support the role of inflammation in colorectal carcinogenesis.

The goal of the second study was comparison of 4 screening programs using the Markov model. In this study we investigated CRC screening from the perspective of screening method optimalization and timing of colonoscopy examination as a primary screening methods. In our model, two colonoscopy examinations during lifetime turn out to be the most effective strategy to reduce CRC mortality depending on appropriate timing. However, when CRC treatment costs are included, it represents the most cost-effective strategy. The output of our model demonstrated that optimum timing of the first colonoscopy in life falls before 50 years of age. It is desirable to time also the second colonoscopy in life because it is non-random and displays specific time-dependance. The optimum timing strongly depends on statistical parameters incorporated into the model, which are specific for different populations defying universal reccomendations. According to our model, the dependance is non-monotonous but represents a minimum from the timing perspective. The model suggests that optimum timing of the second colonoscopy is 59 years of age.

Keywords : Colorectal carcinoma – carcinogenesis – ulcerative colitis – PSC – p53 – Screening strategies – Markov chain