Abstract

Telomeres are non-coding nucleoprotein structures that make up the very end of each linear chromosome. They stabilize chromosome structure and thus prevent the ends from being recognized by DNA damage response machinery. Telomere shortening in the synthesis phase of the cell cycle is related to the loss of protective ability and the finite replicative potential of the cell. The environmental factors, impaired DNA repair pathways, and loss of telomeric DNA-binding proteins exert negative effects on telomere function. Telomere dysfunction instigates chromosomal rearrangements and together with telomere erosion precedes tumorigenesis. Extension of telomeric DNA is catalyzed by the enzyme telomerase, whose activity is repressed in most adult somatic cells, except for stem cells, lymphocytes, and some cancer cell types.

Colorectal cancer comprises malignant tumors of the colon and rectum. It is the second most common cancer in both sexes in the Czech Republic, with over 81,000 cases diagnosed in 2013 and 55.2% overall survival at 5 years. This study focuses on the association of telomere length to clinico-pathological features of the colorectal cancer patients and investigates also the effect of cancer treatment on telomere length. Further, it compares two methods of telomere length measurement; the quantitative polymerase chain reaction and the multiplex quantitative polymerase chain reaction. Relative telomere length was evaluated in peripheral blood lymphocytes in repeated samples from 193 patients. We have observed significant telomere shortening in time period 0 - 1 year after diagnosis ($\chi^2(2) = 17.59$, $P = 0.0002$, $N = 74$, the 1^{st} - 3^{rd} sampling). Regarding telomere length and clinico-pathological and molecular traits of colorectal cancer, the shortest telomere length was observed in patients with proximal colon cancer (mean relative telomere length ± standard deviation in the 1^{st} sampling: 0.77 ± 0.31), followed by rectal (0.92 ± 0.32) and distal colon (1.00 ± 0.40) cancer patients. In all the patients we found a consistent decreasing trend in telomere length over time irrespectively of tumor stage and location. Moderately shorter telomere length was recorded in patients with high microsatellite instability. Regarding the treatment response, poor responders had on average longer telomeres in the 1^{st} (1.15 ± 0.29) and the 2^{nd} sampling (1.01 ± 0.25) compared to good responders (1.00 ± 0.33 in the 1^{st} sampling and 0.82 ± 0.30 in the 2^{nd} sampling).

Key Words: colorectal cancer, telomeres, telomerase, peripheral blood lymphocytes