XRCC1, XRCC3, XPD DNA repair gene polymorphisms as risk factors involved in colon cancer carcinogenesis. A Romanian case-control study

Introduction: Arg399Gln-XRCC1, Thr241Met-XRCC3 and Lys751Gln-XPD repair genes associated with genomic instability could represent risk factors involved in colon cancer carcinogenesis and cancer staging.

Methods: Genotyping of 40 male and 56 female patients with colon cancer and 62 male and 100 female controls was performed using PCR-RFLP analysis.

Results: The risk to develop colon cancer was 1.94 (55% vs. 38.7%, 95%CI [0.87-4.33]) in male and increased significantly to 2.24 (53.6% vs. 34%, 95%CI [1.15-4.37], p = 0.017) in female patients with at least one Gln751-XPD allele. The presence of the Gln399-XRCC1 allele was associated with a 2.49 (70% vs. 48.4%, 95%CI [1.075-5.77]) increased risk to develop colon cancer in males and 2.69 (67.9% vs. 44%, 95%CI [1.35-5.34]) in females. The risk to develop colon cancer was 4.75 (75% vs. 38.7%, 95%CI [1.97-11.45], p < 0.001) in male and 1.97 (60.7% vs. 44%, 95%CI [1.01-3.83], p = 0.045) in female carriers of the Met241-XRCC3 allele. pT analysis showed that in both males and females, the Gln399-XRCC1 allele was identified with a higher frequency in advanced stages (pT3 - 73.3%/100% and pT4 - 86.7%/84%) compared to early stages of colon cancer (pT1 - 50%/50% and pT2 - 0%/37.5%). There were differences of Gln399-XRCC1 allele frequency in male (Fisher’s exact test 7.31, df = 3, p = 0.04) and female patients (Fisher’s exact test 19.82, df = 3, p < 0.001). In both males and females, the Met241-XRCC3 allele was identified with a higher frequency in advanced stages (pT3 - 86.7%/68% and pT4 - 100%/100%) compared to early stages of colon cancer (pT1 -25%/50%). There were differences of Met241-XRCC3 allele frequency in male (Fisher’s exact test 20.16, df = 3, p < 0.001) and female patients (Fisher’s exact test 9.14, df = 3, p = 0.023). Male patients carriers of Gln751-XPD allele most frequently had pT1 stage (100%). There were differences of XPD allele frequency in male patients (Fisher’s exact test 11.53, df = 3, p = 0.005), but not in females (Fisher’s exact test 4.72, df = 3, p > 0.05). Dukes-Mac analysis showed that even though in both males and females the Gln399-XRCC1 allele was identified with a higher frequency in advanced stages (C -78.9%/70.4% and D - 100%/100%) compared to early stages of colon cancer (A - 50%/50% and B -55.6%/66.7%), there were no differences of Gln399-XRCC1 allele frequency in male (Fisher’s exact test 4.44, df = 3, p > 0.05) or in female patients (Fisher’s exact test 2.31, df = 3, p > 0.05). In both males and females, the Met241-XRCC3 allele was identified with a higher frequency in advanced stages (C -100%/77.8% and D - 100%/100%) compared to early stages of colon cancer (A -40%/25%). There were differences of Met241-XRCC3 allele frequency in male (Fisher’s exact test 28.54, df = 3, p < 0.001) and female patients (Fisher’s exact test 7.99, df = 3, p = 0.033). Male and female patients carriers of Gln751-XPD allele most frequently had stage A (53.3%/ 26.7%). There were differences of Gln751-XPD allele frequency in male (Fisher’s exact test 11.93, df = 3, p = 0.002), but not in females (Fisher’s exact test 8.75, df = 3, p = 0.029).

Conclusion: The study confirms the risk for colon cancer in both male and female carriers of XRCC1, XRCC3 and XPD polymorphisms. An association of cancer staging with XRCC1 and XRCC3, but not XPD polymorphisms in both males and females was observed.

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