BRCA1 4153delA and 5382insC Mutations Confer Different Risks of Contralateral Breast and Second Primary Malignancies in Breast Cancer Patients

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Introduction. Genotype-phenotype correlation effect has been already described among carriers of BRCA1 mutations located in different parts of the BRCA1 gene. It was shown that risk of development of breast and ovarian cancers can differ significantly among carriers of the BRCA1 4153delA and 5382insC mutations. In addition, several retrospective studies have demonstrated that the age of onset and clinical outcome of breast cancer can be dependent on the type of BRCA1 mutations. The impact of the specific BRCA1 mutations on risk of development of contralateral breast and second primary malignancies in primary breast cancer patients has not been investigated yet.

Aim, material and methods. Prospective cohort study evaluating cancer-related events and risk of development of contralateral breast and second primary malignancies in carriers of the BRCA1 4153delA and 5382insC mutations and non-carriers, diagnosed with primary non-metastatic breast cancer.

Results. The median follow-up period was 87 months (range 36–144 months). A total of 131 patients were included in the study. During the follow-up period, cancer related events were observed more frequently among carriers of the 4153delA than 5382insC mutations (RR = 2.30, 95%CI 1.18 to 4.50, p = 0.03). Relative risk of contralateral breast and other second primary cancers development was significantly higher among carriers of the 4153delA mutation in comparison with carriers of the 5382insC mutation (RR = 4.69, 95% CI 1.26 to 17.42, p = 0.023) and non-carriers (RR = 7.29, 95% CI 1.94 to 27.41, p = 0.005). Event-free survival ($\chi 2$ = 6.53, DF = 1, p= 0.011) and overall survival (χ^2 = 3.87, DF = 1, p = 0.049) were significantly worse among carriers of the 4153delA in comparison with carriers of the 5382insC mutation.

Conclusions. BRCA1 4153delA mutation carriers have an increased risk of contralateral breast and second primary cancer development after primary breast cancer in comparison with 5382insC mutation carriers which is associated with significant survival differences in these groups of patients.