Abstract:

Introduction: About 5 - 10% of breast carcinomas are caused by genetic mutations. The most common genetic mutation that is involved in the development of this malignancy is a mutation in the tumor suppressor genes BRCA1/2 whose carriers have approximately a 70% lifetime risk of developing breast cancer. The prognosis of patients with BRCA1/2-asociated breast carcinoma, compared to patients with sporadic breast carcinoma is the subject of many studies with ambiguous results.

Aim: The aim of the theoretical part of this work was to approach the issue of breast cancer and the most common genetic syndromes associated with it. In the practical part of this work a retrospective study was carried out in order to compare BRCA1/2 mutated breast cancer patients with non-mutated breast cancer patients in the tumor profile, methods of treatment and prognosis.

Methods: We retrospectively analyzed the data of 134 patients who were tested for the presence of BRCA1/2 mutation at the Institute of Medical Genetics, University Hospital in Pilsen during the years 2013-2018 and at the same time were treated for early breast cancer at the University Hospital in Pilsen during the years 2000-2020. 32 patients were BRCA1 positive (24%), 10 BRCA2 positive (7%) and 92 without BRCA1/2 mutation (69%). The follow-up time was set from the date of surgery up to 1/2020.

Results: Women with the BRCA1/2 mutation developed breast cancer at a statistically significantly younger age than women without the BRCA1/2 mutation, the difference was more significant in the BRCA1 mutated group ($p = 0.0005$). Breast carcinomas in BRCA1/2 mutated patients were more likely to have worse prognostic markers such as higher grade ($p < 0.0001$), higher proliferative activity ($p < 0.0001$) and hormone receptor negativity ($p < 0.0001$). On the contrary no statistically significant difference was found in tumor size (T) or lymph node positivity (N) at the time of diagnosis. Despite the negative prognostic markers of BRCA1/2 mutated breast carcinomas the prognosis of mutated patients in our cohort did not appear worse than in non-mutated patients. In BRCA2 mutated group the prognosis was even better but the results were not statistically significant. 5-year DFS in BRCA1 mut. group was 93%, in BRCA2 mut. 100% and in non-mutated 90% ($p = 0.3293$), 5-year OS in BRCA1 mut. group was 96.7%, in BRCA2 mut. 100% and 94.3% for non-mutated ($p = 0.5205$). One of the possible explanations of relatively good prognosis of patients with BRCA1/2 mutation is higher intensity of treatment. BRCA1/2 mutated patients in our study underwent total mastectomy rather then breast-conserving surgery ($p = 0.0003$) and more frequently have been treated with adjuvant chemotherapy ($p = 0.0004$). On average they received higher number of adjuvant chemotherapy cycles ($p = 0.0008$) and because of their genetic burden prophylactic contralateral mastectomy was performed more frequently ($p < 0.0001$).

Conclusion: In our work, in accordance with available literature, we confirmed that BRCA1/2 mutated breast carcinomas have worse prognostic markers. Despite the worse prognostic markers the prognosis of these patients does not differ significantly from patients without this mutation. One of possible explanations may be higher radicality of treatment of mutated patients. Results of our study are another argument for testing healthy women with a positive family history which will allow us to provide most effective treatment for BRCA1/2 mutated patients who develop cancer.