Abstract

Breast cancer is the most common serious cancer in women in the Czech Republic, with increasing incidence. Ovarian cancer, although rarer, has a significantly higher mortality rate due to the difficulty of diagnosis in the early stages. This study focuses on the identification of women at risk of these diseases based on the polygenic inheritance of low-penetrant SNP, expressed as polygenic risk score (PRS) using panel NGS.

In the breast cancer study, 1 329 patients (age at diagnosis 20–80) and 1 324 healthy women (age 20–80) without pathogenic variants in the predisposing genes were examined. The examination was performed using two PRS sets, PRS77 and PRS313. Both sets stratified women according to their disease risk. Women in the top decile had significantly higher risk of disease when compared to the middle quintile (PRS77: OR = 1.55; $p < 0.001$; PRS313: OR = 1.87, $p < 0.001$). Women in the top 2.5% of PRS313 had threefold risk (OR = 3.05, $p < 0.001$). Regarding continuous risk, PRS313 identified female patients more reliably ($HR_{per\ SD} = 1.64$; $p < 0.001$) than PRS77 ($HR_{per\ SD} = 1.40$; $p < 0.001$). The same was observed for continuous risk over time (PRS77: $p = 0.15$; PRS313: $p = 0.01$).

In the ovarian cancer study, 122 patients with early-onset disease (age at diagnosis 15–31), 85 stage- and histology-matched patients (age 40–86), and 78 patients with late-onset disease (age 33–79) were examined. The control group was identical to that of the breast cancer study. Women were examined using ovarian PRS sets and the PRS313 set. Ovarian sets discriminated only the late-onset patients ($p < 0.05$). Early-onset patients were discriminated only in PRS313 ($p < 0.05$).

The PRS313 set was identified as the more reliable risk indicator for both breast and early-onset ovarian cancer. In the future, this set can be considered as a possible screening tool to identify women who would benefit from an earlier initiation of preventive care.

Keywords: polygenic risk score, PRS, polygenic inheritance, breast carcinoma, ovarian carcinoma