SUMMARY

Ovarian cancer (OC) is the deadliest gynecologic malignancy with a substantial proportion of hereditary cases and a frequent association with breast cancer (BC). Genetic testing facilitates preventive management for carriers of mutations in OC-susceptibility genes. However, the prevalence of germline mutations varies among populations and many rarely mutated OC predisposition genes remain to be identified.

We analyzed 219 genes in 1333 Czech OC patients and 2278 population-matched controls (PMC) using next-generation sequencing. Altogether, 427/1333 (32%) patients and 58 /2278 (2,5%) PMC carried pathogenic mutations in 18 known/anticipated OC predisposition genes. Mutations in *BRCA1*, *BRCA2*, *RAD51C*, *RAD51D*, *BARD1* and mismatch repair genes conferred a high OC risk (with OR>5). Mutations in *BRIP1* and *NBN* were associated with moderate risk (both OR ≥2 - <5). *BRCA1/2* mutations dominated in almost all clinicopathological subgroups including sporadic borderline tumors of ovary (BTO). Analysis of remaining 201 genes revealed somatic mosaics in *PPM1D* and germline mutations in *SHPRH* and *NAT1* associating with a high/moderate OC risk significantly; however, further studies are warranted to delineate their contribution to OC development in other populations.

Results of this study demonstrate the high proportion of patients with hereditary OC in Slavic population justifying genetic testing in all patients with OC, including BTO.

Key words: genetic predisposition, mutation, next-generation sequencing, ovarian cancer, predisposition genes