

Recommendation for preventive adnexectomy in MLH1 and MSH2 mutation carriers.

Magdalena Kuświk¹, Tomasz Gromowski², Tadeusz Dębniak¹, Grzegorz Kurzawski¹, Cezary Cybulski¹, Jacek Gronwald¹, Tomasz Huzarski¹, Jan Lubiński¹

1 Department of Genetics and Pathology, Pomeranian Medical University, Szczecin, Poland

2 Human Genome Variation Research Group & Genomics Centre, Malopolska Centre of Biotechnology, Jagiellonian University, Cracow, Poland

Abstract:

Lynch syndrome (LS) is a common hereditary cancer predisposition syndrome. It is caused by mutation in one of four DNA mismatch repair (MMR) genes: *MLH1*, *MSH2*, *MSH6*, *PMS2* or deletion of last exons in *EPCAM* gene. Mutation carriers are at high risk of developing colorectal cancer (CRC) and endometrial cancer (EC). They have also increased risk of some extra-colonic cancers such as ovarian, small bowel, urinary, biliary tract, gastric, and brain tumors.

Ovarian cancer (OC) is third most common cancer in Polish LS women constitutes about 5% of all LS cancer. There is no consensus guidelines for OC prevention in LS women.

The aim of this study was to evaluate and compare ovarian cancer risk in our series of 289 families with identified pathogenic mutations (referred as Lynch syndrome families) to the general population.

We observed increased risk of OC in Polish LS families in comparison to the general population. Moreover, high risk of ovarian cancer was found for LS women under 50 years of age. Furthermore 6 out of 17 (35%) early-onset patients from LS families died from ovarian cancer within 2 years of diagnosis.

Due to the increased risk of ovarian cancer in LS women and low efficiency of the gynecological screening, for female carriers of a pathogenic variant in *MLH1* and *MSH2* genes prophylactic adnexectomy should be recommended after 35 years of age. Additionally because of the small number of cases of pathogenic mutations in the *MSH6*, *PMS2* and *EPCAM* gene, the validity of prophylactic adnexectomy cannot be demonstrated.