

## Considerations related to radical fimbriectomy as an option in prophylaxis against serous carcinoma development

J. Markowska<sup>1</sup>, E. Nowak-Markwitz<sup>2</sup>, Z. Kojs<sup>3</sup>, W. Sawicki<sup>4</sup>

<sup>1</sup>Gynecological-Oncology, Poznań University of Medical Sciences, Poznań

<sup>2</sup>Department of Gynecologic Oncology, Poznań University of Medical Sciences, Poznań

<sup>3</sup>Department of Gynecology-Oncology, M. Skłodowska-Curie Institute, Cracow

<sup>4</sup>Chair and Department of Obstetrics and Gynecological Oncology, Medical University of Warsaw, Warsaw (Poland)

### Summary

Research has shown that papillary tubal hyperplasia may lead to the development of serous cancer in the fallopian tubes, ovaries, and peritoneum. According to numerous studies, opportunistic bilateral salpingectomy significantly reduces the risk of developing ovarian cancer. Recent data proves that radical fimbriectomy involving the tube and fimbrio-ovarian junction lowers ovarian, fallopian, and peritoneal serous cancer incidence. Risk-reducing salpingo-oophorectomy (RRSO) remains the gold-standard in prophylaxis regarding ovarian cancer in carriers of BRCA mutations, other options may exist – radical fimbriectomy which preserves function of the ovaries, observation in dedicated centers, and removal of the ovaries upon menopause.

*Key words:* Radical fimbriectomy; Risk-reducing salpingo-oophorectomy (RRSO) serous cancers in BRCA mutations.

Population studies prove that various methods are applied to reduce the risk of ovarian cancer including oral hormonal contraception, tubal ligation or excision [1-4]. Kurman *et al.* [5, 6] first proposed the dualistic theory of carcinogenesis, according to which ovarian cancers are divided into two groups: type I, linked to mutations in KRAS, BRAF, PTEN, in  $\beta$ -catenin and type II, serous cancers of an aggressive course in which TP53 mutations are noted (high grade serous ovarian cancer - HGSOC).

In the fallopian tubes, lesions, designated “papillary tubal hyperplasia” (PTH), have been identified. PTH may be induced by chronic inflammation and lead to the development of intraepithelial serous cancer of the fallopian tubes, which is also a precursor lesion associated with serous cancers of the ovary and peritoneum. Although, in around 30% of serous cancer cases, histological examination does not reveal any lesions in the fallopian tube, due to a similar clinical course such tumours should be classified as high grade serous cancer (HGSC) of the fallopian tube, ovary, and peritoneum [7, 8].

According to Chen *et al.* [4], a ten-year observation of over 1,800 patients, diagnosed and treated due to primary ovarian and peritoneal cancer provided evidence that incidence of ovarian cancer was significantly reduced ( $p < 0.05$ ) in the group of women who underwent prophylactic salpingectomy in comparison to the group whose fallopian tubes were preserved. The authors performed opportunistic salpingectomy in a population of over 4,300 women who

had surgical treatment for benign gynecological disease and consider it a preventative measure against serous tubal, ovarian, and peritoneal cancers.

An electronic meta-analysis included a population of 3,500 women who underwent bilateral salpingectomy (BS) and over 5,650,000 women in the control cohort without the procedure detected BS reduces the ovarian cancer risk by 49% ( $R=0.51$ ) [2]. Similar results were presented by Falconer *et al.* [3] in a group of over 251,000 women treated surgically compared to a control group of 5,449,000 women analyzed from 1973 to 2009. Bilateral salpingectomy reduced the risk of manifestation of ovarian cancer by 50% ( $HR=0.35$ ), as compared to unilateral salpingectomy ( $HR=0.71$ ). According to the authors, the results support the hypothesis that ovarian cancer originates from lesions in the fallopian tube and indicate the beneficial role of the procedure in the reduction of ovarian cancer in the general population.

According to Alvarez *et al.* [9], radical fimbriectomy involves the removal of the entire tube and the fimbrio-ovarian junction. In their study, Hasdemir *et al.* suggest this may be an implantation site of malignant cells and can initiate ovarian cancer [10]. Moreover, the authors are of the opinion that it is not necessary to radically excise the parauterine section of the fallopian tube since no cancer development has been described in the site. The procedure of BS does not result in early menopause since it does not reduce concentrations of secreted hormones [2, 10].

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Studies on a population of BRCA mutation carriers who had undergone bilateral salpingo-oophorectomy showed that serous intraepithelial cancer in the distal part of fallopian tube was detected [11]. Leblanc *et al.* [12], similarly to others, are of the opinion that the gold standard in prophylaxis of ovarian cancer in carriers of BRCA1/2 mutation involves bilateral excision of ovaries and fallopian tubes - risk-reducing salpingo-oophorectomy (RRSO). However, in such women, radical fimbriectomy should be considered a preventative procedure in the development of ovarian, tubal and peritoneal HGSC, while preserving ovarian hormonal function. The suggestion of the authors, based on pilot studies, requires further multi-center studies.

At the 2018 American Society of Clinical Oncology (ASCO) Congress, Leblanc *et al.* [13] presented histological results following radical fimbriectomy in 121 women: 106 were carriers of a BRCA mutation (75 with BRCA1 and 31 with BRCA2 mutations), while the remaining patients had a familial history of breast/ovarian cancer. In four patients, papillary tubal hyperplasia was revealed (HGSOC in one, serous tubal epithelial lesion (STIL) in two, and serous tubal intraepithelial carcinoma (STIC) in two), although none of these cases involved the fimbrio-ovarian junction. Additionally, TP53 mutation was disclosed in 21 cases (17.7%). In 11 patients, oophorectomy was conducted, mainly at the request of the patient, no pathological lesions were detected in the ovaries.

These studies shed new light on RRSO and could indicate an additional/new direction in possible reduction in the risk of development of ovarian and peritoneal cancer in carriers of BRCA mutations.

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Corresponding Author:  
J. MARKOWSKA, M.D.  
Poznan University of Medical Science  
Szamarzewskiego 82/84,  
Poznan, Wielkopolska 60-101 (Poland)  
e-mail: jmarkmed@poczta.onet.pl