REVIEW

Lib Oncol. 2022;50(2-3):131–137

doi: 10.20471/LO.2022.50.02-03.20

FERTILITY PRESERVATION IN PATIENTS WITH GYNECOLOGICAL CANCER - IS IT POSSIBLE?

ZRINKA RENDIĆ-MIOČEVIĆ[1], MIRNA ALVIR[2], IVANA OREŠKOVIĆ[3] and LIDIJA BEKETIĆ-OREŠKOVIĆ[1,4]

[1]Division of Oncology and Radiotherapy, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[2]Emergency Department, Universitiy Hospital Center Zagreb, Zagreb, Croatia;
[3]School of Medicine, University of Zagreb, Zagreb, Croatia;
[4]Department of Clinical Oncology, School of Medicine, University of Zagreb, Zagreb, Croatia

Summary

The aim of this review article is to present current options for fertility preservation in young women with gynecological tumors (ovarian, endometrial or cervical cancer). An early pretreatment referral to multidisciplinary team which consists of general gynecologists, gynecologic oncologists, embryologists, radiologists, pathologists, and reproductive endocrinologists should be suggested to young women with gynecologic cancer, concerning the risks and benefits of fertility preservation options. Only a small percentage of patients with ovarian cancer and borderline ovarian tumors, are appropriate candidates for fertility preservation (FIGO stage IA and IC epithelial ovarian cancer). Following oophorectomy, ovarian tissue or oocytes are removed from the ovary for the use of cryopreservation; after completion of oncological treatment patient undergoes orthotopic retransplantation of ovarian tissue whereas oocytes may be used for in vitro fertilization. Live birth rates up to 53.8% have been reported after fertility preservation treatment in selected patients. In patients with endometrial cancer fertility preservation treatment means conserving of the uterus. Appropriate candidates for fertility preservation are younger women with well differentiated endometrial cancer, which does not invade the myometrium. Fertility preservation treatment in endometrial cancer is hormonal, based on progestins. After completion of fertility preservation treatment, frequent follow-ups are necessary, with tissue sampling (via curettage or endometrial biopsy) remaining standard approach in follow-up. Live birth rates after progestin therapy are around 60%, or even higher with the help of assisted reproductive procedures. In cervical cancer, fertility preservation treatment can be considered in women with early-stage disease (FIGO IA1, IA2, or IB1). Cone biopsy or conization followed by laparoscopic lymphadenectomy has been described as an appropriate procedure, with conception rates up to 47%.

KEYWORDS: *Fertility preservation – gynecological oncology; Ovarian cancer; Endometrial cancer; Cervical cancer*

INTRODUCTION

Gynecological malignancies are common in everyday clinical practice in oncology. With respect to vulvar cancer, which is diagnosed almost exclusively in older age, and primary vaginal cancer which is extremely rare entity, all other gynecologic malignant tumors including ovarian, endometrial and cervical cancer, in this patients can appear in women of reproductive age as well. According to the data from Croatian Cancer Registry in 2019, in Croatia there were 60 women younger than 45 diagnosed with cervical cancer (22,4% of all women diagnosed with cervical cancer in 2019.), 46 women with endometrial cancer younger than 45 (5,9%) and 34 women in reproductive

***Corresponding author**: Zrinka Rendić-Miočević, Division of Oncology and Radiotherapy, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Ilica 197, 10 000 Zagreb, Croatia. E-mail: zrinka.trstenjak@gmail.com*

age were diagnosed with ovarian cancer (7,4%) (1,2).

Fertility preservation has become an important issue in the treatments of malignant diseases today. Some challenges and options of fertility preservation in young women with breast cancer were presented in our previous reports(3-8). In women with gynecological cancer fertility preservation treatment (FPT) is especially challenging because of tumor involvement of female reproductive system. The standard oncological treatment of gynaecological cancers can include radical surgical approach, chemotherapy and/or radiotherapy. All this treatment options can result in destroyed reproductive potential of these patients. FPT modalities can be considered only in women with very early stage disease who would like to preserve their fertility. Before starting the treatment, the patient should be referred to pretreatment counseling with reproductive medicine specialist, because some of these patients have impaired fertility even before cancer diagnosis. If it is estimated that patient has only a weak chance to conceive after completing FPT, standard oncological treatment should be reconsidered, rather than fertility preservation. The patient should be informed that FPT procedures are not considered to be standard oncological treatment because recurrence rates are significantly higher compared with standard treatment approach, and the patient should sign an informed consent prior to treatment induction. In addition, it is of utmost importance that patients who underwent FPT of gynecologic cancer are frequently followed up, so possible recurrence can be recognized as early as possible. If the patient is not motivated or for any reason cannot come to regular follow-up exams, she is not a good candidate for fertility preservation. Finally, the patient-must be aware that even if FPT is successful and patient conceives, these pregnancies are considered high-risk with higher rate of spontaneous abortions and premature deliveries. Also, although it is not mandatory, most obstetricians prefer to terminate these pregnancies with Cesarean section (especially after treatment of cervical or endometrial cancer) .

The purpose of this paper is to review the recent knowledge about fertility preservation in young patients treated for gynecological malignancies. PubMed browser was used to search leading medical databases (Medline, NCBI Entrez) with keywords: *fertility preservation*, *ovarian cancer*, *endometrial cancer*, *cervical cancer* and the results were summarized in this paper.

OVARIAN CANCER

Ovarian cancer is the second most common gynecologic cancer in Europe and North America and the leading cause of death among gynecological tumors. According to National Cancer Institute The Surveillance, Epidemiology, and End Results programme (NCI's SEER) database from 2012 to 2018, of all patients diagnosed with ovarian cancer, patients under 20 years of age represented 1.3% of new cases, those aged 20–34 represented 4,1% of new cases, while 6,6% of ovarian cancers were diagnosed in women aged 35–44. In summary, 12% of all ovarian cancers are diagnosed in women in reproductive age (age 20-44)(9). Vast majority (95%) of ovarian tumors are of epithelial origin (serous, mucinous, clear cell and endometrioid cancer) and they occur mostly in postmenopausal women. Unlike epithelial ovarian cancer (EOC), tumors that arise from ovarian stroma (granulosa cell tumor, thecoma, fibroma, Sertoli cell, and Sertoli–Leydig cell tumors) and the germ cell tumors (dysgerminoma, yolk sac and embryonal carcinoma, choriocarcinoma, and teratoma) are mostly diagnosed in premenopausal women in reproductive age(10). Treatment of ovarian tumors is dependent on histopathological type of tumor and FIGO stage of the disease, but in general it involves surgical removal of the ovary (or both) most often together with fallopian tubes and removal of the uterus. This procedure is standard oncosurgical approach in women with localized (FIGO I and II) and locally advanced (FIGO III) ovarian tumors, especially with epithelial histology. Even in advanced stage of the disease, surgery is often performed as cytoreductive and/or debulking procedure. Adjuvant oncological treatment is based on systemic cytotoxic treatment, usually platinum-doublet chemotherapy(11).

Some of younger, reproductive-aged women diagnosed with ovarian cancer can be interested in preserving their fertility. However, maintaining reproductive function in this patients is especially difficult because the ovary is the site of primary cancer. Thus, ovary containing tumor cells and follicles becomes a target to be both - treated (to remove/kill tumor cells) and protected (for the fer-

tility) at the same time. Young woman with diagnosis of ovarian cancer who express their wish to preserve their reproductive potential should be referred to multidisciplinary team which consists of gynecologists, gynecologic oncologists, embryologists, radiologists, pathologists and reproductive endocrinologists. Only a small percentage of patients with ovarian cancer is considered to be appropriate candidates for FPT. Those are patients with early-stage EOC and borderline ovarian tumors, or those with juvenile granulosa cell tumors and germ cell tumors(12). Partial resection of the ovary is possible in benign subsets of ovarian tumors, such as benign teratomas which require only removal of the teratoma cyst. In many germ-cell tumors unilateral oophorectomy with frequent follow-ups can be definitive treatment. A study on 108 women with FIGO I EOC compared outcomes of fertility preservation and radical surgery(13). After a median follow-up of 83 months, there was no difference in disease-free interval and tumor specific overall survival in patients with stage I EOC, with exception of grade III tumors and clear-cell histology, as grade III and clear-cell histology were the only independent risk factors. Out of 52 patients treated with FPT, 34 (65.4%) attempted to get pregnant, and 28 (53.8%) achieved a successful pregnancy with a full-term delivery. Numerous studies yielded the same results: in young women with FIGO stage IA and IC epithelial ovarian cancer, conservative treatment (ovarian conserving surgery) is safe and can be considered in patients who wish to preserve fertility(13-18). After removal of the ovary, there are methods to preserve the healthy ovarian tissue, or only oocytes(15). In ovarian tissue cryopreservation, ovarian tissue is excised from the remaining healthy ovary and cryopreserved (usually frozen in liquid nitrogen) to be used in the future. After completion of oncological treatment, patient can undergo re-implantation of previously cryopreserved ovarian tissue. It is also possible to preserve oocytes rather than the full ovarian tissue. Usually it is done in women with unilateral ovarian tumor who are scheduled to undergo chemotherapy in order to spare oocytes in contralateral healthy ovary from the gonadotoxic effects of chemotherapy agents. Oocytes are usually retrieved from the contralateral ovary during oncological surgery, with or without prior hormonal controlled (hyper)stimulation of the ovaries(12).

ENDOMETRIAL CANCER

Although uterine (endometrial) cancer occurs most commonly in postmenopausal women, it can also occur in premenopausal women. Endometrial cancer is almost exclusively an adenocarcinoma, which develops as a result of unopposed estrogen exposure. So, in younger women, risk is increased in obesity, chronic anovulation (polycystic ovary disease) and some familial cancer syndromes, (such as HNPCC, Lynch syndrome etc.). It is important to emphasize that women diagnosed with endometrial cancer at a young age are at increased risk for a mismatch repair gene mutation associated with Lynch syndrome and should be referred for genetic counseling(19). According to the NCI's SEER database from 2012. to 2018., there were no patients younger than 20 diagnosed with endometrial cancer, 1.8% of patients were women aged 20-34, while patients aged 35–44 represented 5.3% of new cases (9,10). Standard treatment in stage I endometrial cancer (>70% patients) is radical surgery which entails removal of the cervix, uterus, both fallopian tubes and ovaries, and adjacent lymph nodes. Adjuvant oncological treatment is indicated in patients with higher risk of recurrence (more advanced cancer - higher stages and/or unfavorable histopathologic subtypes).

In women with endometrial cancer, fertility (and uterine) preservation options exist only for a special subset of patients with low-risk, localized endometrial carcinoma. Appropriate candidates for fertility preservation treatment are patients with low-grade endometrial cancer which does not invade the myometrium(20,21). These tumors are more likely to express progesterone receptors and respond to hormonal treatment(22). Clearly, there must be no evidence of extrauterine spread of the disease. It is strongly recommended that prior to definitive treatment decision, patients undergo a dilation and endometrial curettage, as it was shown to be more accurate in correlating with final pathology compared to endometrial biopsy. Also, the endometrial cancer is more likely to be removed with a curretage than with an endometrial biopsy(23). In assessment of myometrial invasion and lymph node involvement, MRI has an irreplaceable role and should be performed in all patients considered for FPT(24). Also, MRI can reveal synchronous ovarian tumor (in some studies

up to 25% of patients with endometrial cancer), which is a contraindication for fertility preservation(25). FPT in endometrial cancer is hormonal, based on progestins, which are given to stabilize and stop unopposed estrogen stimulation of the endometrium. There are numerous progesterone hormonal schemes used in endometrial cancer(21,26,27). The most commonly used agents are medroxyprogesterone acetate 200-400 mg/day (MPA; 44%) and megesterol acetate 160 mg/day (35%), for 9-12 months. Side-effects of oral progestins are thrombus formation, mood alterations, headaches, weight gain and breast pain and/or tenderness. Oral progestins are contraindicated in patients with a history of thromboembolism, breast cancer or hepatic dysfunction. In order to avoid adverse systemic effects of progestins, while maintaining localized effect on the endometrium, intrauterine devices with progesterones have been also used in young women with stage I endometrial cancer. Most common IUD is the levonorgestrel-releasing intrauterine system, which releases 20 mcg of levonorgestrel/day(28,29).

The importance of close surveillance of these patients cannot be overemphasized, as only regular and frequent follow-ups can enable the recognition of a non-hormonally responsive endometrial cancer relapse, in which cases patients are advised to go to standard treatment (radical surgery). Among the patients who respond to hormonal therapy, majority will respond within 16 weeks of therapy(30). Standardized surveillance protocol for follow-up after fertility preservation hormonal treatment in patients with stage I endometrial cancer does not exist. Although thinning of the endometrium on ultrasound scans is a good predictor of response to hormonal treatment, tissue sampling (via curettage or endometrial biopsy) remains standard approach in follow-up in these patients. First assessment of response, in the form of endometrial sampling, should be done 4 to 6 months after initiating hormonal therapy (most authors agree that optimal follow-up interval is 3 months)(31). Initial response rates are reported between 60% and 80% with recurrence rates between 25% and 40% (20).

Live birth rates after progestin therapy in women who pursue fertility after successful hormonal treatment, were reported around 60%. Women who used assisted reproductive procedures in the process of conception had higher live birth rates compared with women who conceived spontaneously, which is most probably an indicator of infertility or diminished fertility at baseline (prior to cancer diagnosis). It is impossible to predict the duration of remission after progestin therapy, so women who achieve complete response should be advised to try to conceive as soon as possible. Women not planning to attempt pregnancy immediately after achieving complete disease regression should continue using progestin therapy. In that case some authors suggest low-dose cyclic progestin or levonogestrel-IUD as maintenance hormonal therapy, as they lower the risk of recurrence after complete response among endometrial cancer patients who underwent FPT. As previously discussed, maintaining the patients on progesterone until pregnancy or hysterectomy, as well as between pregnancies, is of critical importance(31,32).

CERVICAL CANCER

Among gynecological malignancies, cervical cancer is the third cancer in terms of incidence and mortality. In the 'third world' countries, where screening programs don't exist at all, or aren't available to the majority of population, situation is significantly different: in these countries cervical cancer is the most common cancer and the leading cause of death among gynecologic malignancies. Because of the bigger proportion of the patients in their reproductive age, FPT treatment is more often desired and considered in treatment planning for cervical cancer, compared to other gynecologic cancers. According to the NCI's SEER database from 2012. to 2018., patients younger than 20 years represented 0.1% of all new cases of cervical cancer, 14,4% of patients were women 20-34 years old, while patients aged 35–44 made 23,8% of new cases (9,10). In summary, 38.3% patients with newly diagnosed cervical cancer were women in their fertile age, which is a much higher proportion compared to reproductive aged women with ovarian cancer (12%) or endometrial cancer (7.1%). Early-stage cervical cancer refers to FIGO stage IA1, IA2, IB1, and some small IIA1 tumors. Options for preservation of fertility are usually limited to women with FIGO stages IA1, IA2, or IB1 cervical cancer. Factors such as tumor size, tumor cell type, lymphovascular invasion, and lymph

node involvement also have to be considered when deciding about fertility-preservation treatment. Early stage cervical cancer can be treated with radical surgery (hysterectomy), conserving surgery (cone biopsy, trachelectomy) or chemoirradiation. For women who wish to preserve their fertility, hysterectomy and chemoradiotherapy are not suitable options. Treatments that allow a woman to carry a pregnancy after completion of oncological treatment include(33,34):

– conization/cone biopsy of the cervix - surgical removal of a cone-shaped portion of the cervix, including the cancerous area. Cone biopsy in combination with laparoscopic lymphadenectomy has been described as an appropriate procedure in strictly selected patients with early-stage cervical cancer (FIGO IA2 and IB1) and tumors < 20 mm(35). After FPT, 47% patients have succeeded in conceiving, with the 5-year DFS of 97%(36).
– trachelectomy – more extensive removal of the cervical tissue than in cone biopsy, with or without removing the surrounding parametrium (simple vs.radical trachelectomy). Radical trachelectomy can be performed as radical vaginal (more often) or radical abdominal trachelectomy. It is an acceptable treatment option for women with early stage disease (FIGO IA1, IA2, and small IB1 lesions <2 cm)(27). A laparoscopy for removal of the lymph nodes is performed prior to the trachelectomy to make sure cancer cells have not spread to the lymph nodes(37). Lymph node sampling is mandatory, with exception of patients in FIGO IA1 stage without cancer cells in the lymphatic channels. In order to reduce complications associated with radical pelvic lymph node dissection, there is increasing use of sentinel lymph node biopsy. However, this procedure is not yet considered *standard of care* but it can be considered and performed by surgeons experienced with the technique. Women who underwent conization or trachelectomy are advised to wait 6 to 12 months to allow tissue to fully heal, before attempting to conceive(38,39).
– neoadjuvant chemotherapy followed by radical trachelectomy and lymphadenectomy has been suggested by some authors for patients with more advanced disease (tumor size >2 cm)(40). Although this approach showed high fertility rates and similar oncologic outcomes compared to upfront trachelectomy without chemotherapy, it should still be regarded as experimental because of small number of reported cases and no long-term follow-up outcomes(41).

CONCLUSION

Fertility preservation in young women treated for malignant diseases is very important issue. Fertility preservation options in women with gynecological cancer can be considered only in patients with very early stages of cancer (FIGO IA and IC in ovarian cancer, FIGO IA in endometrial cancer, and FIGO IA1, IA2 and IB1 in cervical cancer). Pretreatment patient's counseling with collaboration of multidisciplinary team in highly specialized clinical hospitals is obligatory. The patients who underwent fertility preservation treatment of gynecological cancer should be regularly followed up, so possible recurrence could be recognized as early as possible. However, in the situations where there is no patient's motivation for frequent follow-up exams, or there is only a weak chance for the patient to conceive after completing fertility preservation oncological treatment, the patient and her oncologist should reconsider standard oncological approach.

REFERENCES

1. Hrvatski zavod za javno zdravstvo, Registar za rak Republike Hrvatske. Incidencija raka u Hrvatskoj 2019. Bilten HZJZ. 2021;44. Available from: https://www.hzjz.hr/wp-content/uploads/2021/12/Bilten44_2019.pdf. Accessed on: October 6th, 2022.
2. Šekerija M, Čukelj P. Epidemiology of ovarian cancer in Croatia. Libri Oncol. 2015;43(1-3):3-83.
3. Kasum M, Šimunić V, Orešković S, Beketić-Orešković L. Fertility preservation with ovarian stimulation protocols prior to cancer treatment. Gynecol Endocrinol. 2014;30(3):182-6. doi: 10.3109/09513590.2013.860123.
4. Kasum M, Beketić-Orešković L, Orešković S. Subsequent pregnancy and prognosis in breast cancer survivors. Acta Clin Croat. 2014;53(3):334-41.
5. Kasum M, Beketić-Orešković L, Peddi PF, Orešković S, Johnson RH. Fertility after breast cancer treatment. Eur J Obstet Gynecol Reprod Biol. 2014;173:13-8. doi: 10.1016/j.ejogrb.2013.11.009.
6. Vuković P, Raguž J, Beketić-Orešković L. Management of young women with early breast cancer-focus on fertiliy preservation. Libri Oncol 2018; 46(2-3):78-82. https://doi.org/10.20471/LO.2018.46.02-03.13
7. Vuković P, Kasum M, Orešković D, Čehić E, Raguž J, Elezaj S, Beketić-Orešković L. Importance of ovarian

tissue cryopreservation in fertility preservation and anti-aging treatment. Gynecol Endocrinol. 2019;35(11): 919-923. doi: 10.1080/09513590.2019.1611763.
8. Vuković P, Kasum M, Raguz J, Lonjak N, Bilic Knezevic S, Oreskovic I, Beketic- Oreskovic L, Cehic E. Fertility preservation in young women with early-stage breast cancer. Acta Clin Croat 2019; 58(1):147-156. Doi: 10.20471/acc.2019.58.01.19.
9. https://seer.cancer.gov/statistics-network/ Accessed on October 6th, 2022.
10. Franasiak JM, Scott RT Jr. Demographics of cancer in the reproductive age female. In: Sabanegh, ES Jr, editor. Cancer and Fertility; Current Clinical Urology. Springer International Publishing, Humana Press; 2016. p 11-19.
11. Ledermann JA, Raja FA, Fotopoulou C, Gonzalez-Martin A, Colombo N, Sessa C, ESMO Guidelines Working Group. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(Suppl 6):vi24–vi32, doi: 10.1093/annonc/mdt333.
12. So-Youn K, Jung Ryeol L. Fertility preservation option in young women with ovarian cancer. Future Oncol. 2016;12(14):1695–8, doi: 10.2217/fon-2016-0181.
13. Jiang X, Yang J, Yu M, Xie W, Cao D, Wu M, et al. Oncofertility in patients with stage I epithelial ovarian cancer: fertility-sparing surgery in young women of reproductive age. World J Surg Oncol. 2017;15:154, doi: 10.1186/s12957-017-1222-4.
14. Wright JD, Shah M, Mathew L, Burke WM, Culhane J, Goldman J, et al. Fertility preservation in young women with epithelial ovarian cancer. Cancer. 2009;115: 4118-26, doi: 10.1002/cncr.24461.
15. Santos ML, Pais AS, Santos TA. Fertility preservation in ovarian cancer patients. Gynecological Endocrinology. 2021;37(6):483-9. doi.org/10.1080/09513590.2021.1872534.
16. Bentivegna E, Gouy S, Maulard A, Pautier P, Leary A, Colombo N, et al. Fertility-sparing surgery in epithelial ovarian cancer: a systematic review of oncological issues. Ann Oncol. 2016;27(11):1994–2004, doi: 10.1093/annonc/mdw311.
17. Fruscio R, Ceppi L, Corso S, Galli F, Dell'Anna T, Dell' Orto F, et al. Long-term results of fertility-sparing treatment compared with standard radical surgery for early-stage epithelial ovarian cancer. Br J Cancer. 2016; 115:641-8, doi: 10.1038/bjc.2016.254.
18. Taylan E, Oktay K. Fertility preservation in gynecologic cancers. Gynecologic Oncology. 2019;155(3):522-9. doi.org/10.1016/j.ygyno.2019.09.012.
19. Kauff ND. How should women with early-onset endometrial cancer be evaluated for lynch syndrome? J Clin Oncol. 2007;25(33):5143–6, doi:10.1200/JCO.2007.13.4940.
20. Kalogera E, Dowdy SC, Bakkum-Gamez JN. Preserving fertility in young patients with endometrial cancer: current perspectives. Int J Womens Health. 2014; 6:691-701, doi: 10.2147/IJWH.S47232.
21. Kesterson JP, Fanning J. Fertility-sparing treatment of endometrial cancer: options, outcomes and pitfalls. J Gynecol Oncol. 2012;23(2):120-4, doi: 10.3802/jgo.2012.23.2.120.
22. Park JY, Nam JH. Progestins in the fertility-sparing treatment and retreatment of patients with primary and recurrent endometrial cancer. Oncologist. 2015; 20(3):270-8, doi: 10.1634/theoncologist.2013-0445.
23. Leitao MM Jr, Kehoe S, Barakat RR, Alektiar K, Gattoc LP, Rabbitt C, et al. Comparison of D&C and office endometrial biopsy accuracy in patients with FIGO grade 1 endometrial adenocarcinoma. Gynecol Oncol. 2009;113(1):105-8, doi: 10.1016/j.ygyno.2008.12.017.
24. Bolanča Čulo K, Pedišić I, Herceg Ž. MRI in gynecological oncology. Lib Oncol. 2015;43(1-3):29-32.
25. Walsh C, Holschneider C, Hoang Y, Tieu K, Karlan B, Cass I. Coexisting ovarian malignancy in young women with endometrial cancer. Obstet Gynecol. 2005;106 (4):693–9, doi: 10.1097/01.AOG.0000172423.64995.6f.
26. Ramirez PT, Frumovitz M, Bodurka DC, Sun CC, Levenback C. Hormonal therapy for the management of grade 1 endometrial adenocarcinoma: a literature review. Gynecol Oncol. 2004;95(1):133–8, doi: 10.1016/j.ygyno.2004.06.045.
27. Maggiore U, Khamisy-Farah R, et al. Fertility-Sparing Treatment of Patients with Endometrial Cancer: A Review of the Literature. J Clin Med. 2021;10:4784; doi: 10.3390/jcm10204784.
28. Pal N, Broaddus RR, Urbauer DL, Balakrishnan N, Milbourne A, Schmeler KM, et al. Treatment of low-risk endometrial cancer and complex atypical hyperplasia with the levonorgestrel-releasing intrauterine device. Obstet Gynecol. 2018;131(1):109-16, doi: 10.1097/AOG.0000000000002390.
29. Baker WD, Pierce SR, Mills AM, Gehrig PA, Duska LR. Nonoperative management of atypical endometrial hyperplasia and grade 1 endometrial cancer with the levonorgestrel intrauterine device in medically ill post-menopausal women. Gynecol Oncol. 2017;146(1): 34-8, doi: 10.1016/j.ygyno.2017.04.006.
30. Won S, Kim MK, Seong SJ. Fertility-sparing treatment in women with endometrial cancer. Clin Exp Reprod Med. 2020;47(4):237–244, doi: 10.5653/cerm.2020.03629.
31. Gunderson CC, Fader AN, Carson KA, Bristow RE. Oncologic and reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 adenocarcinoma: a systematic review. Gynecol Oncol. 2012;125(2):477-82, doi: 10.1016/j.ygyno.2012.01.003.
32. Park H, Seok JM, Yoon BS, Seonq SJ, Kim jY, Shim jY, et al. Effectiveness of high-dose progestin and long-term outcomes in young women with early-stage, well-differentiated endometrioid adenocarcinoma of uterine endometrium. Arch Gynecol Obstet. 2012;285: 473–478, doi: 10.1007/s00404-011-1959-x.
33. Gien LT, Covens A. Fertility-sparing options for early stage cervical cancer. Gynecol Oncol. 2010;117(2):350–7, doi: 10.1016/j.ygyno.2010.01.039.

34. Somigliana E, Mangli G, Martinelli F, Noli S, Filippi F, Bergamini A,et al. Fertility preservation in women with cervical cancer. Critical Reviews in Oncology/ Hematology. 2020; 154:103092. doi: 10.1016/j.critrevonc.2020.103092
35. Martinelli F, Ditto A, Filippi F, Vinti D, Bogani G, et al. Conization and lymph node evaluation as a fertility-sparing treatment for early stage cervical cancer. Intl J Gynecol Cancer 2021;31(3):457-461. doi: 10.1136/ijgc-2020-001740
36. Fagotti A, Gagliardi ML, Moruzzi C, Carone V, Scambia G, Fanfani F. Excisional cone as fertility-sparing treatment in early-stage cervical cancer. Fertil Steril. 2011;95(3):1109-12, doi: 10.1016/j.fertnstert.2010.11.010.
37. Plante M, Renaud MC, Sebastianelli A, Gregoire J. Simple vaginal trachelectomy: a valuable fertility-preserving option in early-stage cervical cancer. Int J Gynecol Cancer 2017;27(5):1021-7, doi: 10.1097/IGC.0000000000000989.
38. Salvo G, Ramirez PT, Levenback CF, Munsell MF, Euscher ED, Soliman PT, et al. Sensitivity and negative predictive value for sentinel lymph node biopsy in women with early-stage cervical cancer. Gynecol Oncol 2017;145(1):96-101, doi: 10.1016/j.ygyno.2017.02.005.
39. Bréban-Kehl M, Zaccarini F, Sanson C, Maulard A, Scherier S, Genestie C, et al. Fertility preservation in cervical cancer, analysis of 30 years of practice and immersion in future developments. Gynecologie, Obstetrique, Fertilite & Senologie. 2022;50(1):62-68. doi: 10.1016/j.gofs.2021.09.001.
40. Robova H, Halaska MJ, Pluta M, Skapa P, Matecha J, Lisy J, et al. Oncological and pregnancy outcomes after high-dose density neoadjuvant chemotherapy and fertility-sparing surgery in cervical cancer. Gynecol Oncol. 2014;135(2):213–6, doi: 10.1016/j.ygyno.2014.08.021.
41. Pareja R, Rendon GJ, Vasquez M, Echeverri L, Sanz-Lomana CM, et al. Immediate radical trachelectomy versus neoadjuvant chemotherapy followed by conservative surgery for patients with stage IB1 cervical cancer with tumors 2cm or larger: a literature review and analysis of oncological and obstetrical outcomes. Gynecol Oncol. 2015;137(3):574–80, doi: 10.1016/j.ygyno.2015.03.051.

Sažetak

JE LI MOGUĆE OČUVANJE PLODNOSTI KOD BOLESNICA S GINEKOLOŠKIM RAKOM?

Z. Rendić-Miočević, M. Alvir, I. Orešković. L. Beketić-Orešković

Cilj ovog preglednog rada je prikazati suvremene mogućnosti očuvanja plodnosti kod mladih žena s ginekološkim tumorima (rakom jajnika, trupa maternice ili vrata maternice). S obzirom na rizike i koristi metoda za očuvanje plodnosti, preporuča se bolesnicu prijeterapijski prezentirati na multidisciplinarnom timu koji uključuje ginekologa, ginekološkog onkologa, embriologa, radiologa, patologa i reprodukcijskog endokrinologa. Samo je mali udio bolesnica s epitelnim rakom jajnika ili granično malignim tumorom janika prikladan za očuvanje plodnosti (FIGO IA I IC). Nakon operacijskog uklanjanja jajnika, tkivo jajnika ili jajne stanice se krioprezervaju; nakon završetka onkološkog liječenja obično slijedi ortotopična retransplantacija ovarijskog tkiva bolesnici, dok se jajne stanice mogu koristiti u postupku izvantjelesne oplodnje. Nakon liječenja uz očuvanje plodnosti kod odabranih bolesnica rakom jajnika stopa živorođenih kretala se do 53,8%. Kod bolesnica s rakom endometrija očuvanje plodnosti podrazumijeva očuvanje maternice. Bolesnice pogodne za očuvanje plodnosti su mlađe žene sa dobro diferenciranim tumorom koji ne prodire u miometrij. Za očuvanje plodnosti kod raka endometrija primjenjuje se hormonsko liječenje, utemeljeno na gestagenima, koji stabiliziraju i zaustavljaju nekontroliranu estrogensku stimulaciju endometrija. Po završetku liječenja potrebni su učestali kontrolni pregledi, a uzimanje tkiva sluznice (kiretaža ili biopsija endometrija) predstavljaju standard u praćenju ovih bolesnica. Nakon liječenja gestagenima stopa živorođenih kreće se oko 60% ili čak više kod primjene postupaka potpomognute oplodnje. Očuvanje plodnosti kod karcinoma vrata maternice moguće je kod strogo odabrane skupine bolesnica (FIGO IA1, IA2 ili IB1) motiviranih za trudnoću; kod tih bolesnica konizacija ili biopsija konizata u kombinaciji s laparoskopskom limfadenektomijom predstavlja najprikladniji zahvat sa stopom trudnoća do 47%.

KLJUČNE RIJEČI: *Očuvanje plodnosti – ginekološka onkologija; Rak jajnika; Rak endometrija; Rak vrata maternice*