

Fertility sparing approach in young patients with early stage cervical cancer

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Editorial

Cervical cancer (CC) represents the fourth most common malignancy in women worldwide, after breast, colorectal and lung cancer.^{1,2} The disease mainly affects young women at the reproductive age and is more common in developing countries, where CC accounts for approximately 12% of all female cancers.^{1,2} Furthermore, the mortality rate in developing countries is 10-14 times higher than in developed ones.^{1,2}

According to the recommendations of many international scientific societies, CC treatment depends on disease stage and consists of surgery, radiotherapy or combination of radiotherapy and chemotherapy.³⁻⁵ However, the extent of surgery should be carefully individualized based on the disease stage, the patient's general medical status and the desire of fertility preservation.^{3,4,6}

In this light, fertility sparing treatment should be offered in young patients with early stage disease and strong desire for fertility preservation.^{3,4,6,7} This is the reason why, recent guidelines incorporate conservative surgical treatment options in well selected patients after extensive counseling regarding risks for recurrence, anticipated future fertility, pregnancy issues and perinatal outcomes.^{3,6-8} Nevertheless, patients with aggressive (small cell neuroendocrine carcinoma) or potentially aggressive (gastric type adenocarcinoma, minimal deviation adenocarcinoma) histologic subtypes, are not eligible for fertility sparing management.^{3,9,10}

In CC patients with FIGO stage IA1 disease (stromal invasion of ≤ 3.0 mm in depth and extension of ≤ 7.0 mm) and no lymphovascular space invasion (LVSI), the risk of lymph node metastasis is almost 0.8% and the risk of recurrence is about 0.6%.¹¹⁻¹⁴ Those patients are eligible for conservative management with cervical conization only.^{3,4,6,15-17} The cone should have at least 3mm clear margins for invasive disease or high-grade squamous intraepithelial lesion (HSIL).^{3,4} Moreover, both the ectocervix and endocervical canal should be excised in a single specimen.^{3,4} For the procedure, cold knife conisation (CKC) is usually preferred, because it provides several advantages; especially in the evaluation of marginal involvement.¹⁸ If loop electro-surgical excision procedure (LEEP) is used, then additional care to minimize the electro-surgical effect in specimen's margins should be taken.^{18,19} In case of positive cone margins, either the procedure should be repeated or a radical trachelectomy should be performed.³

In CC patients with FIGO stage IA1 disease and LVSI, the risk of lymph node metastasis is nearly 8.2% and the risk of recurrence is approximately 3.1%.¹²⁻¹⁴ In those patients, either cervical conization or radical trachelectomy, with additional pelvic lymphadenectomy +/- para-aortic lymph node sampling should be performed.^{3,4,6,16,17,20-22} Particularly for patients with positive cone margins, either the conization procedure should be repeated or radical trachelectomy should be performed.^{3,21,22}

On the other hand, in FIGO stage IA2 patients (stromal invasion between 3.0 and 5.0 mm in depth and extension of ≤ 7.0 mm), the risk

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of lymph node metastasis is almost 8% and the risk of recurrence is substantially higher in patients with LVSI (15.7% vs 1.7%).^{11,12,14,23} Those patients are eligible for fertility sparing management with radical trachelectomy, pelvic lymphadenectomy +/- paraaortic lymph node sampling.^{3,4,6,8,21,24,25} Apart from that, cervical conization with additional pelvic lymphadenectomy +/- paraaortic lymph node sampling represents an alternative treatment choice, particularly in CC patients with stage IA2 disease, negative cone margins and negative lymph nodes.^{3,4,6,17,20,21}

Likewise, in CC patients with FIGO stage IB1 disease (clinically visible lesion ≤ 4.0 cm in greatest dimension), the risk of lymph node metastasis is about 14.9% and the risk of recurrence is significantly higher.^{11,26} Additionally, tumor size greater than 2 cm, deep stromal invasion (greater than 50% in depth) and LVSI, are negative prognostic factors.^{24,25} Patients with tumor size up to 2 cm, are eligible for fertility sparing management with radical trachelectomy, pelvic lymphadenectomy +/- paraaortic lymph node sampling.^{3,4,6,8,21,24,25,27} In those patients, radical trachelectomy could be performed either vaginally or abdominally, with no significant differences in long-term oncologic outcome.²⁸

The procedure of vaginal radical trachelectomy was first described by Dargent²⁹ and, in terms of surgical technique, shares many similarities with the type B radical hysterectomy.^{3,29-31} In particular, the cervix, the upper 1-2 cm of vagina and the supporting ligaments are being excised.^{3,30} Moreover, pelvic lymphadenectomy +/- paraaortic lymph node sampling are performed laparoscopically.³⁰ It is worth noting that vaginal radical trachelectomy should be used in well selected young CC patients with FIGO stage IA1 (with LVSI), IA2 and IB1 (with tumor size up to 2 cm) disease.^{3,22,27,32}

In contrast, abdominal radical trachelectomy provides a wider resection of parametria and represents a less conservative alternative, compared with vaginal radical trachelectomy.^{3,25,27,33,34} The procedure has many similarities with the type C radical hysterectomy, regarding surgical technique and oncologic outcome.^{3,25,31,33,35} The cervix, the upper 1-2 cm of vagina, the parametrium and the paracolpos are

being resected.^{3,33,36} It is interesting to note, that abdominal radical trachelectomy may be used in well selected young CC patients with FIGO stage IA1 (with LVSI), IA2 and IB1 (with tumor size up to 2cm) disease.^{3,22,27} However, recent studies evaluating the oncologic outcome of abdominal radical trachelectomy in CC patients with FIGO stage IB1 disease and tumor size between 2 and 4 cm, have shown promising results.^{35,36}

The abdominal radical trachelectomy can be performed either with the standard or the minimal invasive approach (laparoscopy, robotic assisted surgery).³⁷⁻³⁹ The minimal invasive approach, offers many advantages in terms of recovery, blood loss and total hospital stay, while there is no compromise in the oncologic outcome.^{3,37-39}

Additionally, the implementation of sentinel lymph node mapping and dissection is feasible in CC patients with early stage disease and decreases significantly the morbidity of systematic lymphadenectomy without affecting survival.^{40,41} The utilization of ultrastaging plays a crucial role in the detection of micro metastases in dissected lymph nodes.^{40,42} The procedure of sentinel lymph node mapping and dissection should be performed bilaterally, because it provides more reliable data regarding the sentinel lymph node metastases.^{40,41}

In general, fertility outcomes are better in CC patients treated with vaginal radical trachelectomy, when compared with others treated with the abdominal approach.^{22,27} This is mainly because the latter represents a less conservative approach.^{25,27,33,34} However, there is a wide variation in pregnancy rates among patients treated either with vaginal or abdominal radical trachelectomy.^{22,27,28,32,43-45} Furthermore, there is increased risk for miscarriages and preterm labors in both patient groups, mainly because of the impaired cervical function.^{3,22,27,28,43,44}

In conclusion, fertility sparing treatment is feasible in well selected young CC patients with early stage disease and strong desire for fertility preservation.^{3,46} However, all patients should have an adequate pretreatment assessment as well as a thorough counseling regarding risk for recurrence, future fertility, pregnancy issues and perinatal outcomes.⁸

Acknowledgments

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Conflicts of interest

None.

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