



ESGO/ESTRO/ESP updated guidelines in cervical cancer

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New and exciting data continue to emerge in the management of patients with cervical cancer. To that end, the European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology (ESGO/ESTRO/ESP) groups have come together to deliver a comprehensive new set of guidelines in order to give clinicians a valuable resource aimed at providing the most sound and evidenced-based recommendations to patients diagnosed with cervical cancer.¹ The members of the societies who worked to develop such guidelines ought to be commended for their effort and time devoted to an extensive review of the literature and detailed process to achieve consensus and target all facets of the management of patients with cervical cancer.

The updated guidelines continue to stress the value of centralization of care and decision-making based on discussions in a multidisciplinary team. In addition, the guidelines highlight the critical importance of patient accrual to clinical trials. The adherence to standardized processes of documentation pertaining to tumor characteristics and initial patient evaluation is paramount for the accurate diagnosis and treatment of this disease.

There are a number of items in these revised guidelines worth highlighting that could be viewed as debatable or even controversial. First, in the setting of early-stage disease, patients with International Federation of Gynecology and Obstetrics (FIGO) 2019 stage IA2 disease who are not interested in fertility preservation are candidates for a simple, rather than the traditional radical, hysterectomy, albeit with a firm recommendation for lymph node assessment by sentinel lymph node mapping in those patients with lymphovascular invasion. This is consistent with the results of the ConCerv trial,² where investigators demonstrated the safety and feasibility of either cone or simple hysterectomy in the setting of low-risk disease.

For more advanced tumors (FIGO 2019 stage IB1, IB2, and IIA1), the surgical standard of care remains an open radical hysterectomy. However, the minimally invasive approach is proposed in these new guidelines as an option in patients with 'low risk' tumors (<2 cm and free margins on cone), performed in high-volume

centers that meet ESGO quality criteria for surgery, and after extensive patient counseling. This should be interpreted with caution, as such a recommendation is not based on properly conducted prospective evaluation and patients should be informed of this fact. Another area of contention is the evaluation of lymph nodes. Contrary to the approach in many institutions outside of Europe, these current guidelines support the use of frozen section for intra-operative assessment of sentinel lymph nodes. This has been refuted by many, given the low likelihood of detecting micrometastases and isolated tumor cells by frozen section evaluation.³ Interestingly, it is also notable that if the sentinel lymph nodes are negative by frozen section, a pelvic lymphadenectomy is recommended. If performing frozen section and considering that this is a reliable technique, one would wonder as to the rationale for a lymphadenectomy after negative frozen section, particularly given the low likelihood of positive non-sentinel lymph nodes in the setting of a negative sentinel lymph node.⁴

For patients interested in future fertility, the options range from simple conization to abdominal radical trachelectomy in those with tumor size <2 cm. The management of tumors >2 cm is less well defined and the guidelines highlight the concern for higher recurrence rates when considering fertility-sparing options in that setting. Similarly, the option of neoadjuvant chemotherapy is recommended in selected patients. However, it should be noted that use of neoadjuvant chemotherapy is currently being evaluated in the CONTESSA trial.⁵ Of note, there is no clear recommendation as to the surgical approach (open vs minimally invasive) when performing radical trachelectomy.

In patients with locally advanced cervical cancer, the guidelines propose that para-aortic lymph node dissection at least up to the inferior mesenteric artery may be considered. This recommendation despite the results of the Uterus-11 trial,⁶ which showed no difference in disease-free survival between surgical staging and clinical staging, highlights that perhaps further studies are needed to address the question of surgical staging in the setting of locally advanced disease. For recurrent disease, pelvic exenteration remains an option in carefully selected patients.



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Interestingly, surgery is still being considered in the setting of disease extension to the pelvic sidewall (the laterally extended endopelvic resection (LEER) procedure). Herein lies a recommendation where the bulk of the literature is restricted to retrospective studies of small patient cohorts and in very select centers. Thus, such patients should be counseled regarding these limitations. For patients with recurrent or widely metastatic disease at time of diagnosis, based on the exciting data of the KEYNOTE-826 trial,⁷ the combination of platinum, taxane, bevacizumab, and pembrolizumab (PDL1+) is considered the new standard of care. Lastly, the guidelines touch on the topics of cancer in pregnancy and rare tumors; however, these topics are addressed without extensive details and further in-depth recommendations are needed, particularly on the management of pregnancy at different gestation times or for specific rare histologic subtypes.

As it pertains to surveillance, the guidelines stress on monitoring quality of life in order to assure that patients provide critical information pertaining to short- and long-term side effects. In addition, the emphasis on early access to palliative care should be commended as this has been shown to offer patients relief from cancer-related pain, symptoms secondary to malignant bowel obstruction, and psychological suffering.

These updated guidelines provide an extensive outline on principles of radiotherapy, as well as a detailed discussion regarding specimen grossing and sampling for conization, radical hysterectomy, and radical trachelectomy. In addition, as anticipated, there is a broad discussion regarding the pathological processing of sentinel lymph nodes. Similarly, the authors stress a critically important element for gynecologic oncologists addressing here the specific details expected in the pathology report of patients with carcinoma of the cervix. This will allow for institutions, physicians, and patients to have an extensive amount of crucial information in deciding whether to recommend adjuvant treatment.

In summary, these guidelines will be of great value in the current management of patients with cervical cancer. Such resources are of paramount importance in assuring that as clinicians and surgeons we are aligned to provide consistent recommendations for our patients, that our multidisciplinary approach continues to evolve in

creating clear and strict criteria for reporting and analyzing tissue, and that we continue to focus not only on the surgical and therapeutic approach but also on key elements such as quality of life and palliative care for our patients. We must strive to continue developing and updating such guidelines and to that end we must once again congratulate the members of the ESGO/ESTRO/ESP societies for such outstanding work.

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