

## LETTER TO THE EDITOR

### State of the art on HPV-related cervical lesions

*Short title: Latest advances in HPV cervical lesions*

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## Key words

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To the Editor,

cervical carcinoma is the third most common cancer by incidence and mortality in the female population, with over 600,000 new cases per year and more than 340,000 deaths. There are over 200 strains of human papillomavirus (HPV), but most cervical neoplasia cases are attributable to persistent sexually transmitted infections caused by oncogenic strains, such as HPV-16, HPV-33, HPV-18, HPV-31, HPV-45, HPV-52, HPV-58 [1]. This disease can manifest in a severe form, but is susceptible to highly effective treatment, especially when early detected through prevention strategies, early diagnosis and appropriate therapies. Currently, in comparison to other gynecological malignancies, several prevention modalities are available for cervical carcinoma. First, abstention from smoking and the use of barrier contraception methods may contribute to the prevention of acquiring HPV infection. Moreover, available scientific evidence indicates that HPV vaccination, recommended during adolescence for both sexes, can limit the incidence of infection and reduce the occurrence of precancerous lesions and cervical carcinoma [2-4]. Screening methods, such as cervical cytology and human papillomavirus testing, and colposcopy allow the detection of cervical dysplasia and early-stage cervical carcinoma, guiding patients toward appropriate management modalities and follow-up. Finally, tertiary prevention focuses on the treatment of previously identified lesions through surgery and other therapeutic strategies. DTC (electrocoagulation diathermy) is a safe, widespread and effective therapeutic approach for the management of non-invasive lesions, instead, the therapeutic approach to cervical carcinoma varies depending on the diagnostic stage at the time of evaluation. In recent years, several studies have analyzed the safety and efficacy of minimally invasive surgery (MIS), highlighting its benefits [5,6]. The 2023 guidelines issued by the European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO) and the European Society of Pathology (ESP), supported the MIS as a potential option for low-risk tumors (with a diameter of less than 2 cm and negative margins after conization), considering it acceptable for lymph node staging [7]. However, to date, the selection of the most appropriate surgical approach for the treatment of cervical carcinoma remains a matter of debate. The LACC study (Laparoscopic Approach to Carcinoma of the Cervix) raised questions about the oncological outcomes of MIS, showing a four-fold higher recurrence rate and a six-fold higher all-cause mortality rate compared to laparotomy [8]. The risk of recurrence following surgery for cervical intraepithelial lesions of grade 2 (CIN 2) or grade 3 (CIN 3) cannot be underestimated, and therefore, several studies have

performed an in-depth analysis to identify the main determinants of the risk of recurrence. Following primary conization, patients who retained the presence of the human papillomavirus six months after the procedure had a 7.46% probability of recurrence. However, the persistence of HPV at twelve months is strongly associated with a significantly increased risk of disease recurrence (risk of recurrence: 13.1%). The magnitude of the risk of CIN2+ recurrence increases proportionally to the duration of HPV persistence up to one year, whereas HPV persistence beyond the first year does not appear to be a significant risk factor [9, 10]. In addition, a retrospective survey conducted on a sample of 2966 patients who underwent conization for high-grade cervical lesions showed that the presence of positive endocervical margins is one of the main risk determinants associated with a five-year probability of recurrence. Despite the inherent importance of surgical treatment of cervical intraepithelial lesions in preventing progression to cervical carcinoma, it may result in adverse outcomes for pregnant women, increasing the risk of preterm delivery, low birth weight and premature rupture of membranes before 37 weeks of gestation. Indeed, the postponement of treatment for cervical dysplastic lesions identified during pregnancy until the postpartum period is a safe and well-established practice for both maternal and neonatal health. The management of cervical carcinoma remains a subject of growing concern. As this disease can also affect young women who are seeking pregnancy, early diagnosis and implementation of highly personalized treatment approaches are of crucial importance.

### **Abbreviations**

CIN 2: cervical intraepithelial lesions of grade 2

CIN 3: cervical intraepithelial lesions of grade 3

ESGO: European Society of Gynaecological Oncology

ESP: European Society of Pathology

ESTRO: European Society for Radiotherapy and Oncology

HPV: human papillomavirus

LACC: Laparoscopic Approach to Carcinoma of the Cervix

MIS: minimally invasive surgery

### **COMPLIANCE WITH ETHICAL STANDARDS**

#### **Authors contribution**

T.G.D. and A.G.: Conceptualization, Resources, Software and Project administration;

I.C., A.E and A.D: Data curation and Writing – original draft; A.S.L. and O.D.:

Investigation and Methodology, V.D.D., G.B. and L.M: Supervision, Validation and Writing – review & editing.

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### **Disclosure of interests**

The authors declare that they have no conflicts of interest.

### **Ethical approval**

Not applicable.

### **Informed consent**

Not applicable.

### **Data sharing**

Not applicable.

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