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# Contextualization of the Study of Residual Lesions in Conized Patients

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**Abstract:** In the last years, it is evidenced of more remarkable way, an increment of the incidence of the cervical cancer and their lesions precursors in young patients. Conization, as an excisional method, is recommended in the treatment of high-grade epithelial lesions, as well as in the microinvasive stage of cervical cancer when satisfied parity has not yet been achieved. In Clinical Medicine, finding a balance between therapeutic effectiveness and iatrogenic intervention by exaggerated treatments is a challenge, a current scenario in which the probability of the appearance of residual lesions after conization is framed. Although factors related with the biggest probability of appearance of residual lesions are described in patient conizadas, models that demonstrate the interrelation between these variables don't exist; most of the studies are limited to the individual analysis of these factors. The current scientific evidences allow to state that the appearance of post-cone residual lesions is a multifactorial phenomenon dependent on elements related to the nature of the lesion, the surgical technique and the competence of the surgeon; even several of these predictive elements are interrelated in the same patient. The knowledge of these predictors factors of residual lesion, starting from the pattern of the three dimensions, allows to trace clinical and formative strategies of intervention.

**Keywords:** Conization, Residual Injury, Predictive Factors

## 1. Introduction

Cervical conization as a relatively simple therapeutic procedure was first described in 1810 in the "Medical Gacette" of Paris. Lisfranc uses it to treat cervical conditions of all kinds. In 1861 Sims sutured the neck with silver threads after a cone, achieving primary healing. Stumdorf in 1916 described a method to cover the bloody surfaces of the cervix with cervicovaginal epithelium. [1]

There is a coincidence in stating that after cervical conization, the risk of persistence-recurrence of the lesion is 5-30%; for this reason, post-cone cytocolpohistological follow-up is required. Recurrence is the appearance of the disease after its remission 12 months after treatment. Merlos Gutiérrez defines Persistence or Recurrence as the existence of an injury before 12 months after treatment. [2]

In 1992, Moradel defined that there are elements related to the success of conization based on the possibility or not of recurrence / persistence of the lesion and in this sense, he gives importance to the amplitude of the procedure, which will depend on the cervical anatomy, extension of injury, penetration into the cervical canal, suspected invasion, and degree of injury (histology).

This author reflects on his results, in the contributions of Bruxton, when they point out that up to half of the cases where injury of the surgical edges is reported do not have residual injury. [3]

From the author's perspective, residual lesion in a conized patient is defined as the presence of dysplastic or anaplastic tissue in a patient who has undergone a local surgical or destructive procedure, in which total remission of the disease has not been documented; and this injury is the cause that motivated the proceeding.

The concept implies that the presence of abnormal tissue that encompasses both the exocervical and the endocervical canal must be histologically demonstrated and that its nature is similar to the initial diagnosis and, therefore, it is discrepant if only a low-grade lesion in the neck is

demonstrated residual. The affected surgical margins in the specimen sent for histological study, by themselves, do not define the presence of residual lesion.

The evolution of the management of residual lesions of the cervix in conized patients has undergone an evolution, in line with scientific development. Several investigations of the first decade of the present century reflect the vision of the relevance of the state of the surgical margins in therapeutic decision-making, such as the article by Bermejo Bencomo and Martínez Hiriart where it is stated that the presence of positive edges was indicative of re-cone or hysterectomy. [4, 5]

The introduction of human papillomavirus typing and the introduction of video colposcopy in a generalized manner between 2009-2011 are two very relevant events in the diagnostic and therapeutic approach to cervical cancer, its precursor lesions and post-cervical residual disease. cone. The tendency to act whenever positive surgical margins are reported has been changing to more in-depth studies in relation to the pathophysiology of the residual lesion and the knowledge of the principles and scope of electrosurgical treatment.

In this article, the authors contextualize the factors related to the appearance of residual lesions in conized patients.

# 2. Developing

The definition of a post-cone residual epithelial lesion, from the author's perspective, obeys the interrelation of three fundamental elements: the factors related to the lesional and intrinsic characteristics of the patient, the factors related to the surgical technique and the factors related to the surgeon.

There are other factors associated with the persistence of the intraepithelial lesion, such as the existence of positive margins, a compromised cervical canal, the size of the lesion, and viral reinfection. However, it seems that the most important factor of all is the persistence of high-risk viruses, after conization.

### *2.1. Factors Related to the Patient*

The presence of high-risk human papillomavirus (HR-HPV) after conization has been associated with persistence and recurrence of high-grade lesions, which often requires the performance of a reconization or subsequent hysterectomy, the result of This can compromise the reproductive health of the woman who needs to take procedures.

In this sense, the presence alone of a serotype of high oncogenic risk of human papillomavirus should not be considered defining for deciding to reconize or perform hysterectomy, although it is related to a low probability of regression.

According to the Sankasem results, age is defined as a predictive factor of residual disease, finding higher rates in patients older than 50 years of age and / or postmenopausal.[6] This difference is given, in other factors, by the relative difficulty in the approach to the neck due to genital atrophy, as well as the inversion of the transformation zone, to which the authors add the often deformed morphology of the cervix due to multiparity and previous tracheorrhaphy and the lower clearance rate of high risk serotypes oncogenic HPV.

Although obtaining healthy margins is a special point of excision treatments and requires the use of systematic direct colposcopic guidance, the risk of residual injury and recurrence remains minor if the margins are invaded. This is probably explained by the infectious (especially viral) nature of the intraepithelial lesions of the cervix.

On the other hand, as a complement to the destruction or excision of the lesion, the determining factor of therapeutic success is the possibility of achieving the elimination of the viral infection by the human papillomavirus (HPV). [7]

In this sense, the findings of Arbyn are interesting, who only found a residual lesion in 56% of the patients with compromised surgical margins in 18 months of follow-up, while a residual lesion was diagnosed in 16% of those who were declared healed. These authors highlight the greater sensitivity and similar specificity of the human papillomavirus high-risk serotype tests (HR-HPV DNA). [8]

The history of previous diagnosis and treatment of cervical lesions has been another variable related to the possibility of therapeutic failure or residual lesion; [9] another factor related to the patient is determined by her immunocompetence status. Regression of intraepithelial neoplasms is known to be slower in HIV-positive women.

*Long* recognizes that, according to Massad, 5.9% of HIV-positive women develop a high-grade lesion among 1,639 study candidates, even though progression rates are reported to be lower among young women. [10]

A study in Kenya demonstrated the highest prevalence of RA-HPV serotypes among women living with HIV, reporting that 61% of a series with high-grade lesions had serotypes 16 and / or 18. [11]

### *2.2. Factors Related to Surgical Technique*

During the treatment of an intraepithelial lesion of the cervix, the state of the resection margins directly influences the risk of residual lesion and recurrence. It is essential to remember that this risk exists even when the margins are healthy. In this case, it is estimated at 3% and rises to 18% if they are invaded. [12]

When ablative treatment is performed, the surgeon must strive to obtain healthy resection margins. This is one of the reasons why the therapeutic procedure must be performed by direct colposcopic guidance. If performed blindly and systematically, ablative treatment exposes the risk of incomplete resection, but also that of excision of an inadequate cervical volume, sometimes unnecessarily bulky, the obstetric consequences of which can be dramatic.

Only the colposcopic characterization of the lesion (exact position, extension, internal and external limits, as well as the appreciation of the cervical morphology) allows the surgeon to guarantee that a suitable and efficient procedure is carried out.

For many years, and even before the popularity of

colposcopy, cold knife conization was the standard treatment for cervical intraepithelial neoplasia when the uterus was desired.

Recently, due to the ease of conization using the Loop Electrosurgical Excision Procedure (LEEP), the fact that these interventions can be performed in the office, and their low morbidity compared to the cold conization technique, many specialists have limited the use of the latter to situations in which large conizations must be made or when histological evaluation is critical and the slightest artifact produced by heat in the samples cannot be tolerated.

The cold scalpel cone is currently conceived for the treatment of microinvasive lesions (Ia1) or extensive carcinoma in situ in patients without satisfied parity, where greater certainty is needed in the total removal of the lesion, although this implies a larger area of the surgical specimen. Furthermore, it is argued that the tissue margins tend to be affected by thermal artifacts in the LEEP method, which may interfere with the correct definition of the state of involvement of the surgical margins.

The risk of positivity of the endocervical margins is higher in the LEEP cone. At present, the conventional management of these injuries has been modified considering the scientific evidence, which shows that the risk of residual injury is similar in both methods. [13]

Another therapeutic trend is the central cone. This complementary method performed after conization by the diathermic loop markedly reduces the width of the endocervical margins in women with a type III transformation zone.

According to Carvajal Pliego, in his report, Kietpeerakool demonstrated that patients who underwent a cone by diathermic loop + central cone exhibited a reduction of approximately 65% in the risk of positivity in the endocervical margins compared to those in which it was not performed intervention. [14]

Even in those women who maintained positivity at the endocervical margin after the central cone, the benefit of a second procedure demonstrated a significant decrease in the risk of residual injury with a second excision compared to those who did not undergo a central cone (52, 2 vs. 84.1%).

About 50% of patients with positive margins in the cone will present a lesion in the central cone, as opposed to 6.6% when the margins are negative.

In the past, when an invasion of the margins was observed, a surgical reintervention was indicated to perform a new ablative treatment. Some authors even carried out an intraoperative study of the resection margins just after surgery.

At present, the knowledge of the low risk of residual injury, even in the case of positive margins, associated with the risk of obstetric and neonatal complications depending on the resected cervical volume, contraindicates the immediate performance of a second therapeutic intervention in these patients.

This is only indicated if a residual lesion or recurrence is discovered during post-therapeutic follow-up. The only indication of a new entry excision is the existence or suspicion of a microinvasive lesion in unhealthy margins. [12]

From the authors' perspective, the positivity of the endocervical margins is of greater relevance in the therapeutic decision when there is a suspicion of residual lesion. The diagnosis of glandular injury is notably difficult when compared with exocervical injuries and, therefore, more difficult to determine its magnitude and evolution.

For more than 20 years, several authors such as Manchanda, have insisted on the value of cytology, colposcopy and biopsy in demonstrating the presence of residual lesion in patients with compromised surgical margins. [15] It is known that organic cytology has sensitivity between 40-70% and the false positive and negative rates can be really significant.

The authors agree with the approaches described by Manchanda by suggesting post-cone cytological and colposcopic follow-up before raising the possibility of residual lesion according to the surgical specimen report and never taking action, only based on cytology.

The strong prognostic value of the association between positive endocervical margins and residual lesion suggests the importance of studying the cervical canal during the procedure, mainly in patients with severe intraepithelial neoplasia. Both cervical canal curettage and the "second pass" or central cone are currently used to examine the status of the cervical canal in women conized by LEEP. [16]

In this sense, the type of diathermic loop to be used also influences since those of triangular shape tend to go deeper into the stroma and affect more frequently the functional capacity of the internal cervical os, even though they allow obtaining a more comprehensive and reliable evaluation of the status of the endocervical epithelium.

Its complement with the study of the cervical canal before the surgical procedure and of the postcone residual canal will allow to better prepare the surgery and choose the most appropriate volume to remove, in terms of area and depth.

Another variable to be considered as a predictor of residual injury is the size or extent of the injury area. A study by Munmany reported a statistical relationship between this variable and the frequency of residual injury, considering that the chances of therapeutic failure in patients with a lesion $<12mm^2$ was less than 5%. [17] Even though this assessment seems to be obvious, a relationship should not be established Direct mathematics, since in healthcare practice patients with extensive lesions that may represent cervical' ectopy and circumscribed lesions that express a microinvasive carcinoma are assisted.

Related to this age variable, other factors such as the unifocality or multifocality of the lesion, its relationship with the transformation zone and its topographic location, should be evaluated. Lesions that involve more than two-thirds of the cervix and are excised by LEEP are more likely to be positive for the surgical margins. Diffuse, multifocal, or extensive lesions require conizations with large areas of removed tissue guided by colposcopies or the cold knife technique.

Several factors can influence the adequacy of diagnostic colposcopy in relation to the squamocolumnar junction, the

main site of epithelial lesions. Incomplete visualization of the transformation zone can lead to an imprecise and erroneous estimation of the limits of the lesion, increasing the probability of incomplete resection, compromise of the surgical margins and residual disease. A single excision may be insufficient in extensive or diffuse lesions.

### *2.3. Surgeon Dependent Factors*

One of the prognostic elements of therapeutic success in LEEP conization for patients with high-grade lesions that is currently discussed in the specialized literature is related to the use of intraoperative colposcopy.

Performing conization under colposcopic guidance is related to a lower probability of positivity of the surgical margins, as shown by authors such as Demarquet. [18] The authors consider this element relevant and its systematic use in healthcare practice offers advantages in this regard, since it is possible to count today with software such as SPIC that allows to measure the lesion area and select the appropriate size of the diathermic loop for each case.

If performing an insufficient excision can obviously result in a residual lesion, removing an excessive amount of tissue also increases the risks of negative consequences, especially related to future reproduction.

An example that illustrates the value of intraoperative colposcopy is the study by Zhang, which in 2015 showed a significant difference in the frequency of residual injury in the use or not of this guide (18 vs 27%). [19]

Another element related to the surgeon's skill is the fragmentation of the sample. In fact, it is possible to consider that this is not an unequivocal element that depends only on surgical skill and skill. The cooperation of the patient during the intraoperative procedure performed under local anesthesia and the anatomical and morphological characteristics (especially in large multiparous women or patients with previous tracheloplasties) may influence the fragmentation of the surgical specimen.

A study by Grubman-Lea exemplifies the influence of this phenomenon on decision-making in a series of 300 patients who underwent conization by LEEP or scalpel, in whom the positivity status of the surgical margins was uncertain. It is considered that addressing this issue in an elementary or superficial way can lead to an increase in the rate of residual injury or an increase in the frequency of overtreatment. [20]

## 3. Conclusions

Current trends in the treatment of high-grade epithelial lesions of the cervix and early stages of cervical cancer - in patients without satisfied parity - are related to cervical conization and the use of radiosurgery.

The closed electrode electrosurgical procedure has displaced the traditional cold scalpel method by offering fewer complications, hospital stays and resources, and similar rates of residual injury; which proves to be a multifactorial element where factors related to the patient, the surgical technique and the surgeon are integrated.

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