research articles

The benefits of conization in histopathologic diagnosis and treatment of cervical intraepithelial neoplasia

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Abstract

The notion of cervical intraepithelial neoplasia (CIN) is the lesion of the cervix squamous epithelium, the precursor lesion of invasive cancer, diagnosed by biopsy and histopathological examination. The objective of the study is to evaluate the conization as a biopsy and treatment method, with the entire excision of the lesion together with a safe area in healthy tissue. We have studied a number of 46 patients between January 2017 and May 2018. The patients were between 21 and 70 years of age and were divided into 4 groups: 21-30 years old, 31-40 years old, 41-50 years old, older than 51 years old. The results of the cervical-vaginal cytology test were positive for epithelial cell abnormalities in the Bethesda classification, as follows: atypia of undetermined squamous cells in 8 cases (17%), atypia of squamous cells where a high grade lesion in 5 cases (11%), low-grade squamous intraepithelial lesions in 10 cases (22%), high-grade squamous intraepithelial lesions in 17 cases (37%), atypical glandular cells of undetermined significance in 1 case (2%), cells suggestive of squamous carcinoma in 5 cases (11%). Conization with cold scalp is preferred because it offers tissue samples without compromised edges for histopathological examination, and it is successfully applied in patients with high risk of invasive cancer, cervical carcinoma in situ, CIN 3, adenocarcinoma in situ, extensive lesions and high grade cancer.
Keywords: conization, biopsy, histopathological diagnosis, treatment

Introduction

The diagnosis of cervical cancer in the United States has an average age of 48 years and about 38 years for cervical intraepithelial neoplasia (CIN)[1]. Cervical and vaginal cytological screening determined a significant reduction in incidence and mortality rate by invasive cervical cancer[2].

The notion of CIN is the lesion of the cervical squamous epithelium, the precursor lesion of invasive cancer, diagnosed by biopsy and histopathological examination. The severity of the intraepithelial lesion is classified as: mild dysplasia or CIN 1, moderate dysplasia or CIN 2, severe dysplasia or CIN 3 and carcinoma *in situ* (CIS). Histological changes of the cylindrical epithelium areadenocarcinoma *in situ* (AIS) or adenocarcinoma. The concept of squamous intraepithelial lesion is used concomitantly with the term intraepithelial neoplasia and is used in histological diagnosis[3,4]. Histological changes in human papillomavirus infection (HPV) and CIN 1 infection are referred to as low-grade squamous intraepithelial lesions (L-SIL). CIN 2, CIN 3, CIS are referred to as high-grade squamous intraepithelial lesions (H-SIL). H-SIL lesions are more commonly associated with malignancy evolution[5]. Neoplastic potential increases with CIN[6]. The natural evolution of CIN lesions may be regressive, the persistence, CIS or invasion according to CIN grade[7]. Approximately 40% of CIN 2 lesions regress spontaneously in 2 years[8]. Biopsy with histopathological examination is used to diagnose the presence and severity of neoplasia and guide the therapies.

Most cervical neoplasias develop in the transformation zone (TZ), adjacent to squamous cylindrical junction[9]. Back up cervical cells and immature metaplasia cells are vulnerable to the oncogenic effects of HPV and carcinogens[10]. The highest risk for cervical neoplasia is caused by HPV high-risk persistence genital infection and old age[11,12,13,14].

The objective of the study is to evaluate the conization as a biopsy and treatment method, with the entire excision of the lesion together with a safe area in healthy tissue. This method applies to a cervical pathology, which can be properly traced and treated, can be satisfactorily cured, avoiding the evolution towards an invasive cancer.

Methods

We have studied a number of 46 patients between January 2017 and May 2018. The patients were between 21 and 70 years of age and were divided into 4 groups: 21-30 years old, 31-40 years old, 41-50 years old, older than 51 years old. The agreement of all patients was obtained prior to the inclusion in the study, also all the patients were informed regarding the scientific nature of the study. Preoperative investigations

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through cervical-vaginal cytology, colposcopy, and in 9 cases fragmented biopsy was performed in gynecology offices. The clinical study material was analyzed on a multivariate retrospective statistic, and Microsoft Excel (Microsoft Corp., Redmond, WA, USA) was used for data analysis, along with the XLSTAT 2014 add-on for MS Excel Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA).

The cervical-vaginal cytology was reported in the Bethesda system and according to the Babes-Papanicolau classification. The colposcopic examination included the description of the examined cervix, the possibility of examining the junction area, the description of the normal and pathological colposcopic aspects, the assessment of the possibility of examining the entire lesion area. To quantify the colposcopic examination we have used the Reid Colposcopic Index.

The indications for practicing conization have been: positive cytology or suspected for epithelial cell abnormalities with non-totally visualized collagen TZ, inconsistency between the cytology exam and histopathological examination of the piece obtained by fragment biopsy, H-SIL cytology and multiple extended lesions, some positioned to the vaginal sac bottoms for therapeutic purposes for CIN II or CIN III lesions diagnosed by anterior biopsy, a positive result for dysplasia after endocervical curettage. In 9 cases, the histopathological examination of the piece obtained by fragmentary biopsy was not consistent with the cytological examination and for the elucidation of the diagnosis it was decided to practice the conization with the removal of the entire lesion area followed by a thorough histopathological examination.

The patients were hospitalized immediately after menstruation. The preoperative preparation consisted of sanitizing of the vagina and easy sedation of the patient the evening before surgery. Spinal anesthesia or general anesthesia was performed.

The conization with the scalpel consisted of the incision of the exocervical mucous in healthy tissue and the cross-section of the oblique circumference in the depth of the cervical tissue. A broad cone of cervical tissue was extirpated, with the exocolus base and the height of the cervical canal. For the orientation of the piece were set marking threads in the 12th and 15th hours at the exocolus level. The hemostasis was performed by suture, using the Sturmdorf method. There have been situations in which the hemostasis was achieved by cauterization of the excision bed which was then left beant. An endocervical and endovaginal piece was left for 24 hours. Electroexcision was practiced as an alternative technique.

Postoperatively, daily vulvar-vaginal cleaning with light antiseptic solutions was practised, antibiotic therapy was not systematically prescribed, bed rest on the day of surgery. Postoperative complications of the conization, bleeding, pain and leucorrhea were reported in 28 patients. Postoperative monitoring was performed by 2 to 6 weeks re-examination, clinical, cytological and periodic examination, depending on the outcome of the histopathological examination.

Results

From the distribution analysis by age group we found that the maximum incidence of conizationwas recorded in the age group of 31-40 years old (24 cases, 52%), followed by the age group 21-30 years (11 cases, 24 %). In the age group 41-50 years old there were 9 cases (20%), the lowest incidence of conization being in the age group of over 51 years old (2 cases, 4%) (Table 1).

The results of the cervical-vaginal cytology test were positive for epithelial cell abnormalities in the Bethesda classification, as follows: atypia of undetermined squamous cells (ASC-US) in 8 cases (17%), atypia of squamous cells where a high grade lesion (ASC-H) in 5 cases (11%), L-SIL in 10 cases (22%), H-SIL in 17 cases (37%), atypical

Table 1 Distribution of patients by age group

Age group	21-30 years	31-40 years	41-50 years	>50 years	Total
Nr. cases	11	24	9	2	46
%Percentage	24%	52%	20%	4%	100%

Table 2 Distribution of patients by results of the cervical-vaginal cytology test

Cytology	ASCUS	ASC-H	LSIL	HSIL	AGUS	Squamos Carcinoma	Total
Nr. cases	8	5	10	17	1	5	46
Percentage	17%	11%	22%	37%	2%	11%	100%

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glandular cells of undetermined significance in 1 case (2%), cells suggestive of squamous carcinoma in 5 cases (11%) (Table 2).

The colposcopic examination was unsatisfactory – the scuamo-cylindrical junction could not be fully or inconclusively visualized – a large lesion or invasive cancer could not be excluded in 12 patients (26%). The Reid score was 0-4 points in 17 patients (37%), which would correspond to CIN of low grade and between 5-8 points in 15 patients (33%), which correspond to high grade CIN. Signs suggestive of cancer in 2 patients (4%) were identified.

In 9 cases fractional biopsy of the uterine cervix was performed before conization. We have found that only 4 cases (45%) were consistent, in 2 patients the

histopathological diagnosis of fractured biopsy was overestimated (22%) and in 3 cases (33%) the injuries were undervalued. In the 3 undervalued cases they were diagnosed by the histopathological examination of the invasive cancer conization piece.

As surgical technique, in 37 patients (80%) the conization was performed by the classic scalpel technique and in 9 patients (20%) the conization with the electric scalpel was made (Figure 1).

In terms of complications, bleeding occurred in 5 cases (11%), 14 cases complained about pain (30%), and leucorrhea was recorded in 9 cases (19%) (Figure 2).

The results of histopathological examinations of conization pieces were: 15 cases (33%) of low grade CIN (CIN 1) including HPV infection lesions, 23 cases
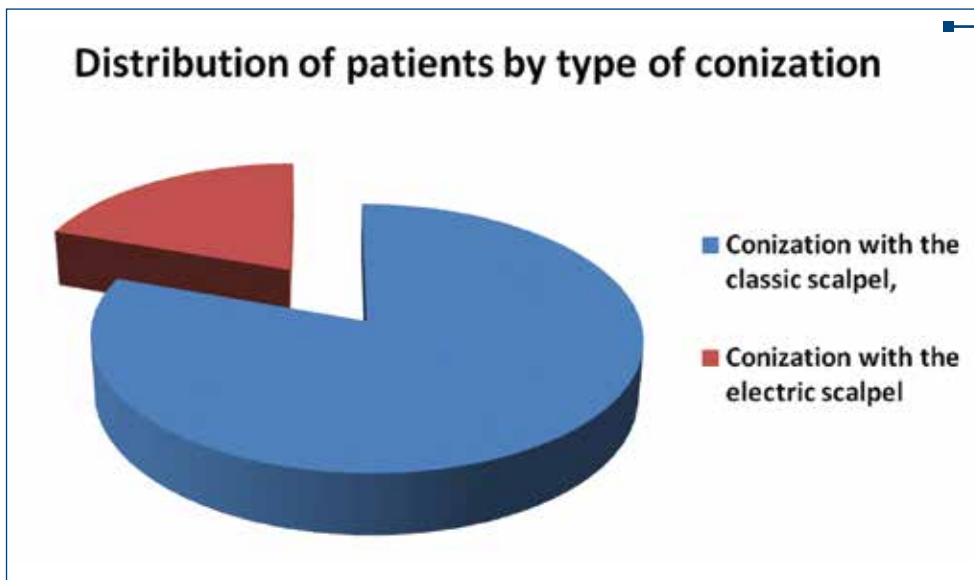

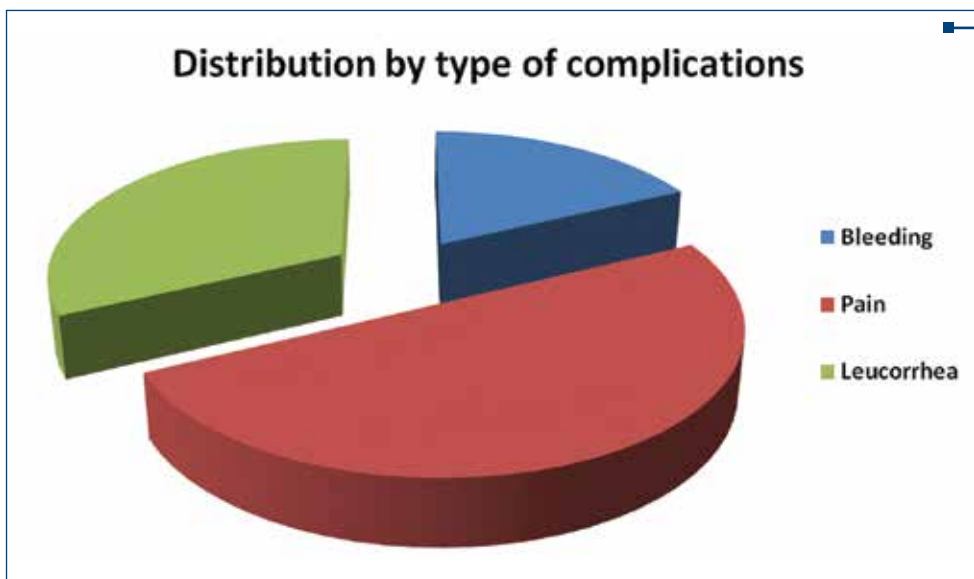**Figure 1.** *Distribution of patients by type of conization*

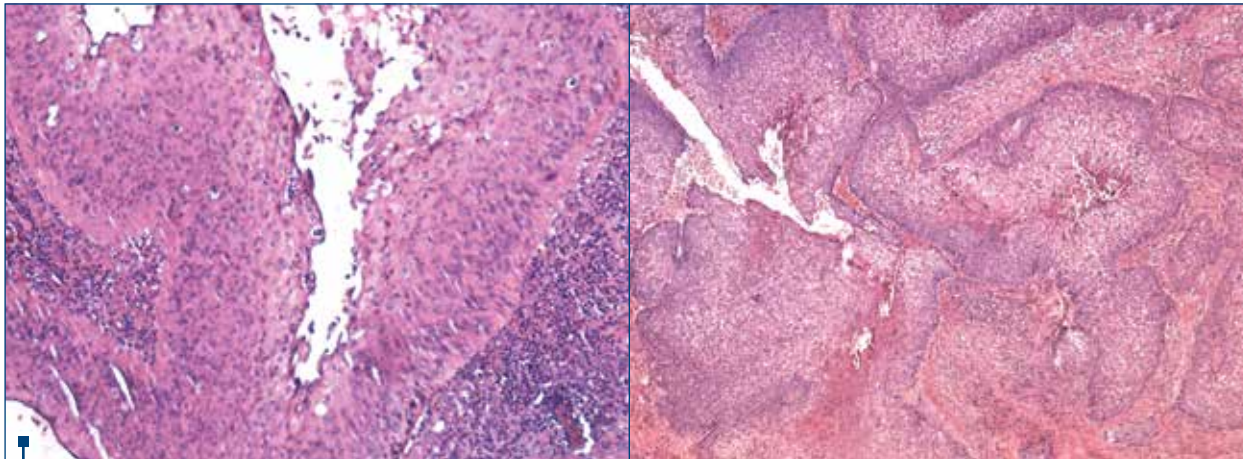**Figure 2.** *Distribution by type of complications*

Figure 3. *Carcinoma "in situ" of the cervix (CIS), intraepithelial lesion grade dysplasia cells have lost the polarity shows the ratio between the nucleus/cytoplasm enlarged nuclei pleomorphic the whole thickness of the epithelium, but not on the cell membrane*
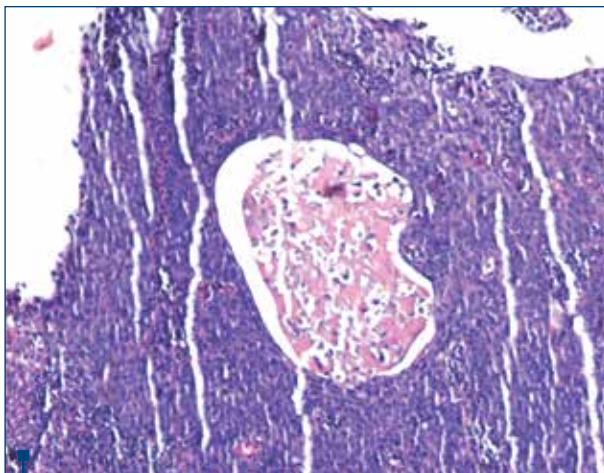

Figure 4. *Squamous carcinoma, proliferated tumor cells, located in islands, groups and solid masses, separated by fine fibrous bands, invasive*
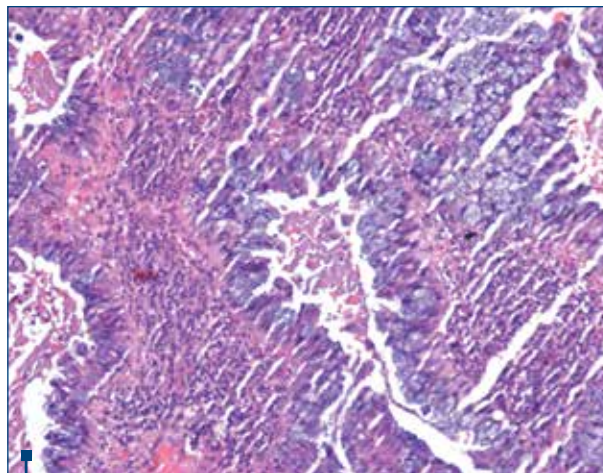

Figure 5. *Mucinous endocervical adenocarcinoma, glandulariformes and muco-secretory cell islets and increased nucleus/cytoplasm ratio, invading subjacent stroma*

(50%) of high grade CIN (8 cases – 17% CIN 2, 10 cases – 22% CIN 3 and 5 cases – 11% CIS) (Figure 3), 7 cases (15%) of invasive epidermoid carcinoma (Figure 4) and 1 case (2%) of adenocarcinoma (Figures 5 and 6; Tabel 3).

Discussion

The conization was preferred to other excisional biopsy methods in situations where their use was susceptible to fragmentation of the lesion area in the case of large extension lesions in patients resulting from the H-SIL cytology test because it was considered that it allows a good histopathological examination of the margins of the lesion which they do not thermally distort.

The postoperative bleeding was of low intensity, requiring hemostatic tamponing and in one case hemostasis had to be performed by suture. The pain recorded postoperatively had a duration of 3-5 days. Leucorrhea was reported in patients who had undergone electroexcision, hemostasis through electrocoagulation and beant cervix leaving.

Although epithelial cellular changes were observed in 15 cases, it was not possible to accurately determine their type and the smear was classified in the class of epithelial cellular atypias: 8 cases with cellular ASC-US and 5 cases with cellular ASC-H cannot be excluded.

The concordance between the cervical-vaginal cytological examination and the histopathological diagnosis ascertained by the examination of conization pieces was partial, which confirms the specialization literature studies according to which that the cytological examination is a test with great sensitivity and specificity in the detection of CIN and cervical cancer in infra-clinical
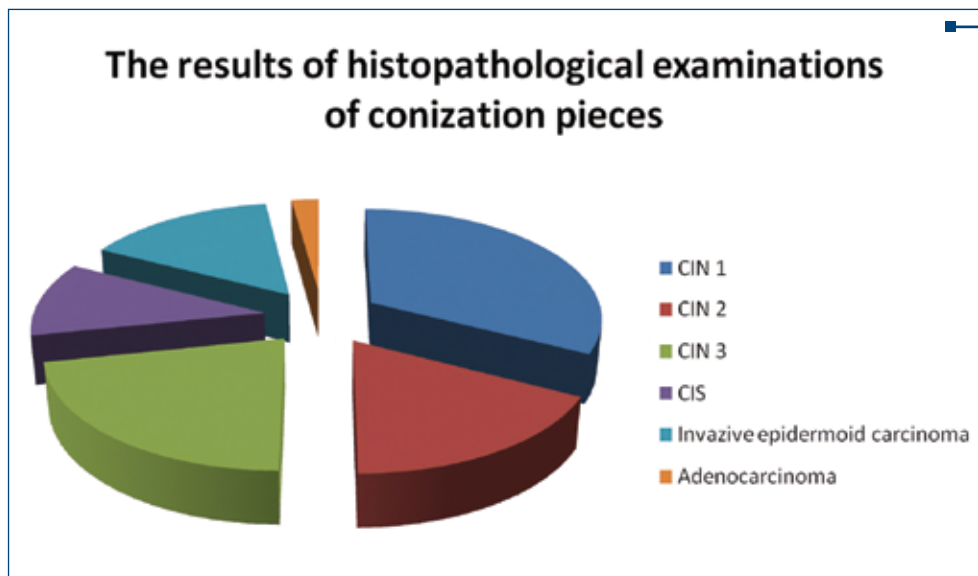
Figure 6. *The results of histopathological examinations of conization pieces*

Table 3 Distribution of patients by results of histopathological examinations

HP results	CIN low grade	CIN high grade	Invasive epidermoid carcinoma	Adeno carcinoma	**Total**
Nr. cases	15	23	7	1	46
Percentage	33%	50%	15%	2%	100%

stages, but of little value in terms of the degree of squamous lesion or invasion[15,16].

For a more accurate quantification of colposcopic lesions, several grading systems have been developed[17,18]. The most common is the Reid Colposcopic Index, which is based on four features of colposcopic lesions: lesion contour, colour, lesion vascularization and iodine impregnation. Each lesion feature was marked from 0 to 2, their sum determines a score that can be correlated with histological changes. According to this score between 0 and 2 points corresponds to CIN I, 3-4 points CIN I or CIN II, from 5 to 8 points for CIN II or CIN III[19]. It was appreciated that between 0 and 4 points according to the Reid score would correspond to low grade CIN and between 5 and 8 points for high-grade CIN[20].

Comparatively analyzing the concordance of the colposcopic examination with the histopathological diagnosis established by examining the conization pieces, we have found that for L-SIL there is a difference in favour of the colposcopic examination, while for the H-SIL the difference is in favour of the histopathological examination, the case of squamous cancer.

The practice of fraction cervical biopsy prior to conization in the 9 patients allowed the assessment of the degree of accuracy of the fractional biopsy compared to the histopathological result obtained after the examination of the conization piece. The concordance was observed in about half of the cases, the underestimation and overevaluation of histopathological diagnosis in fractional biopsy was observed in about a quarter of the cases. Usually the biopsy is harvested from the most severe aspect, but there is evidence that the detection of the disease correlates with the number of biopsies performed[21,22,23]. The biopsies performed under colposcopic guidance may only account for 60-70% of high-grade lesions. The detection of the disease can increase by increasing the number of biopsies and adding random biopsies to the seemingly normal epithelium[24,25,26]. The American College of Obstetricians and Gynecologists concluded that these studies recommend biopsy of all lesions regardless of the result of the colposcopic examination. The risk of residual adenocarcinoma is about 80% and therefore the remaking of the conization is necessary[27], the hysterectomy being recommended after the end of maternity[27,28].

Conclusions

Conization is a safe method of diagnosis and treatment in cervical CIN. Compared to fractional biopsy, conization provides the benefit of a diagnosis certainty by full excision of the lesion and the detailed histopathological examination. It is a particularly necessary

method in discordant cytology, colposcopy, fractional biopsy and in situations involving a long-term follow-up and further investigation.

There is a method that establishes the histopathological diagnosis of endocervical lesions associated or simultaneous with CIN due to the fact that the extirpated piece contains both the lesion and the adjacent area. If the cytological examination revealed atypical glandular cells, as an expression of an endocervix adenocarcinoma, the conization may be considered the best investigative procedure.

While the use of electricity for surgical excision can cause histological artifacts by partial thermal confinement of resection edges, the conization with cold scalpel is preferred because it provides tissue samples without compromised edges for histopathological examination, and is applied successfully in particular in the case of high risk patients with invasive cancer, CIS, CIN 3, AIS, extensive lesions and high grade cancer. ■

Conflict of interests: The authors declare no conflict of interests.

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