

Depth of glandular crypts and its involvement in squamous intraepithelial cervical neoplasia submitted to large loop excision of transformation zone (LLETZ)

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Summary

Background: The authors aimed to confirm the depth of six mm in order to achieve an optimal eradication of the lesion. **Materials and Methods:** This is a retrospective observational study of 94 cervical surgical pieces from women aged 17 to 22 years with a cyto-colpo-histopathological diagnosis of high-grade squamous cervical intraepithelial neoplasia (CIN II and/or CIN III) submitted to large loop excision of transformation zone (LLETZ). The glandular crypts and margins, both exposed or not to CIN, were assessed. The compromise and the maximum depth of the glandular crypts were noticed. **Results:** After LLETZ, 23 (24.47%) cases presented a neoplastic impairment of endocervical margin and ten (10.64%) of the ectocervical margin. The largest noticed crypt measured 4.500 mm and the shortest 0.100 mm, with an average of 2.148 mm. **Conclusions:** Squamous CIN more frequently show the exposure of surgical margins to LLETZ. The deeper location of glandular crypts in the cases studied was 4.500 mm, while the largest neoplastic extension was 3.000 mm. The therapeutic method depends on this knowledge.

Key words: Glandular crypt; Cervical intraepithelial neoplasia; LLETZ; Cervix.

Introduction

The cervix is lined by two different epithelia: squamous and columnar: the squamous epithelium is pluristratified and nonkeratinized and the monostratified columnar epithelium comprises of a single layer of muco-secreting cylindrical cells, and runs a sinuous trajectory, delimitating structures named glandular crypts. The transformation zone is a squamous epithelium and comprises of the area between the original squamous epithelium and the glandular one as a consequence of a metaplastic process

Cervical epithelia, more specifically its transformation zone, might shelter cervical intraepithelial neoplasias (CIN), also known as low- mid- and high-grade lesions, at any portion of its extension. The knowledge of the cervical lining structure leads to the compliance with rigid precepts in choosing the destructive treatment for low-grade intraepithelial lesions. Since high-grade intraepithelial lesions, have a higher potential of evolution to invasive lesions, due to the larger action on glandular crypts in its depth, and an option is made for the surgical excision of loops with large loop excision of transformation zone (LLETZ) [1-3].

In a histopathological analysis conducted by Anderson and Hartley, the depth of glandular crypts, both free or presenting neoplasia, was measured. Eighty-five percent of the pieces presented involvement of crypt by neoplasia,

and their depth ranged from 1.24 to 5.22 mm. For this reason, authors should consider a depth of six mm in order to achieve an optimal and safe eradication of the lesion [4].

The authors aimed in assessing the exposure of crypts by CIN, in order to confirm or not these findings.

Materials and Methods

This is a retrospective observational study performed at the Gynecologic Diseases Prevention Center, Gynecology Department of Escola Paulista de Medicina, Federal University of São Paulo - EPM-UNIFESP, from August 2019 to June 2011.

Many surgical cervical pieces originated from women with a cyto-colpo-histopathological diagnosis of high-grade squamous intraepithelial neoplasia (HSIL) (CIN II and/or III). The clinical findings were obtained from an analysis of clinical records and these women were submitted to large loop exeresis of transformation zone or conization as a complementary diagnostic conduct, after a colposcopic analysis and conducted biopsy. The entire project was presented to the Research Ethics Committee of Hospital São Paulo - UNIFESP, and was approved under the number 0178/09.

Upon study of histopathological views, stained through the Hematoxylin and Eosin (H&E) method, [5] the glandular crypts and margins, both exposed or not to high-grade squamous intraepithelial neoplasia, were assessed and were divided into two groups of analysis. Through the histopathological measuring technique with a Breslow microscopic rule, the glandular crypt depth in each group was measured. The exposure of surgical margins was also noticed in each group and was related to the histopathological diagnosis and to the maximum depth of glandular crypt.

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Results

Only 94 pieces out of the initially-selected 104 products of LLETZ, could be measured. The other pieces presented tangential sections, which rendered it impossible to take precise measurements. The patients age ranged from 17 to 72 years, with an average of 33.7 years. The ethnic groups were as follows: 38 (40.4%) women were white, 54 (57.4%), afro-descendents, and the remaining two were Indians. The initial cytopathological results were the following: 55 (58.51%) of cases were compatible with high-grade lesion/invasive spinocellular carcinoma (ISC); low-grade lesions occurred in 13 (13.82%) cases, and ISC were seen in three (3.19%) cases.

In 56 (59.57%) patients, the abnormal colposcopic aspect noticed was unique, with the associated aspects noticed in other 36 (38.30%) women. After LLETZ, the definite histopathological diagnosis was of grade III intraepithelial neoplasia (CIN III) in 42 (44.68%) cases; 30 (31.92%) cases, the result was grade-II intraepithelial neoplasia (CIN II); 22 cases comprised of six (6.38%) cases with spinocellular carcinoma, and 16 (17.02%) cases with grade-I (CIN I) intraepithelial neoplasia.

In the 48 cases with initial diagnosis of CIN II, an agreement was noticed with the LLETZ diagnosis in 23 (47.92%) cases and a final diagnosis of CIN III in 18 (37.50%) cases. In 21 (67.74%) biopsy cases of CIN III, histopathological agreement in the surgical piece was achieved.

In the 94 operated cases, 23 (24.47%) presented a neoplastic impairment of endocervical margin, and ten (10.64%) cases of the ectocervical margin. Both surgical margins were exposed in eight (8.51%) cases, and the assessment was not possible in one CIN III case. The higher exposure index of surgical margins was noticed in CIN III cases (20 out of 40 cases), as seen in Table 1. This Table allows an assessment of the higher impairment of margins in CIN II, CIN III, and ISC cases ($p = 0.007$).

Ninety-four cases were submitted for glandular crypt measurement. The largest noticeable crypt measured 4.500 mm, and the shortest 0.100 mm, with an average of 2.148 mm (Table 2).

No significant statistics were found among the crypt extension, neoplastic extension, and histopathological diagnoses in LLETZ. In 53 (56.38%) cases, the neoplastic extension into the glandular crypts was noticed. In Table 3, the histological types (CIN II, III, and ISC) more often presented the neoplastic extension for crypts ($p = 0.001$).

No significant statistics were seen in comparing the impairment of surgical margins with the neoplastic extension for crypts (Table 4).

Discussion

In 94 patients with CIN submitted to LLETZ, a prevalence of high-grade squamous lesions was noticed in women living their fourth decade of life. These findings are similar to those referred to by other authors [1, 2]. With regards to colposcopy, most of the cases presented a unique and abnormal aspect.

Table 1. — Relationship between histopathological diagnosis (LLETZ) and neoplastic exposure of surgical margins in 94 patients bearing intraepithelial neoplasia, submitted to LLETZ.

Cytopathological diagnosis	Impairment of surgical margin											
	Endocervical		Ectocervical		Both		Not involved		No assessment		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
CIN I	1	6.25	0	0.00	1	6.25	14	87.50	0	0.00	16	100.00
CIN II	9	30.00	4	13.33	2	6.66	15	50.00	0	0.00	30	100.00
CIN III	11	26.19	6	14.28	3	7.14	21	50.00	1	2.38	42	100.00
ISC	2	33.33	0	0.00	1	16.66	3	50.00	0	0.00	6	100.00
Total	23	24.47	10	10.64	7	7.45	53	56.38	1	1.06	94	100.00

CIN I: intraepithelial neoplasia grade I; CIN II: intraepithelial neoplasia grade 2; CIN III: intraepithelial neoplasia grade 3; ISC: invasive spinocellular carcinoma. Chi-square test (Pearson) $\chi^2 = 7.339 p = 0.007$. N = cases number.

Table 2. — Assessment of crypts depth in 92 cases and 60 cases of neoplastic extension into crypts, in 94 patients bearing intraepithelial neoplasia, submitted to LLETZ.

Depth (mm)	Glandular crypts	
	Neoplastic extension (60 cases)	Maximum depth (94 cases)
Larger	3.000	4.500
Smaller	0.100	0.700
Medium	0.950	2.200
Average	1.075	2.148
Standard deviation	0.703	0.845

Table 3. — Relationship between histopathological diagnosis (LLETZ) and exposure of crypts in 94 patients bearing intraepithelial neoplasia, submitted to LLETZ.

Cytopathological Diagnosis	Neoplastic extension into crypt					
	Present		Absent		Total	
	N	%	N	%	N	%
CIN I	2	12.50	14	87.50	16	100.00
CIN II	18	60.00	12	40.00	30	100.00
CIN III	28	66.66	14	33.33	42	100.00
ISC	5	83.33	1	16.66	6	100.00
Total	53	56.38	41	43.62	94	100.00

CIN I: intraepithelial neoplasia grade I; CIN II: intraepithelial neoplasia grade 2; CIN III: intraepithelial neoplasia grade 3; ISC: invasive spinocellular carcinoma. Chi-square test (Pearson) $\chi^2 = 11.509 p = 0.001$.

Table 4. — Relationship between neoplastic extension into glandular crypts and exposure of surgical margin in 93 cases (one of them not assessed, in view of an improper piece).

Exposure of Crypts	Exposure of surgical margin									
	Endocervical		Ectocervical		Both		Free		Total	
	N	%	N	%	N	%	N	%	N	%
Present	14	26.41	7	13.21	4	7.55	28	52.83	53	100.00
Absent	9	22.50	3	7.50	3	7.50	25	62.50	40	100.00
Total	34	25.73	10	10.75	7	7.53	53	56.00	93	100.00

Chi-square test (Pearson) $\chi^2 = 0.870 p = 0.351$.

Sixteen out of 94 cases presented negative cytology, but the conducted biopsies revealed CIN II involved in nine cases and CIN III in five cases. The histopathological results of biopsies agreed with those from a cytopathological exam compatible with HSIL.

The LLETZ conduct had grounds on the diagnostic agreement of HSIL, the cytohistopathological disagree-

ment, and/or the persistence of CIN I. Similarly to literature, a diagnostic agreement among the products of biopsies and LLETZ was reached, mainly in CIN II/III case [1]. The CIN III cases prevailed among those allowing the identification of exposed surgical margins. These facts suggest that CIN III lesions have larger dimensions and are frequently more involved in the endocervical channel. The measurement of columnar epithelium crypts were smaller compared to those referred by Anderson and Hartley [4]. The agreement of neoplastic extension to glandular crypts, the exposure of surgical margins, and the higher severity of lesion became evident.

Conclusion

In view of their features of dimension and location, CINs more frequently show exposure of surgical margins to LLETZ. Likewise, they extend more often into the glandular crypts. The deeper location of glandular crypts in the cases studied was 4.500 mm, while the largest neoplastic extension was 3.000 mm. The choice of the therapeutic method adopted depends on this knowledge.

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