

Cryosurgery for Cervical Intraepithelial Neoplasia: Follow-Up a 7 Year

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Abstract

We studied 1450 patients in our Colposcopy Unit for either a gynecological check-up or due to a positive Pap smear. We attempted to diagnose and localize HPV(human papillomavirus) of the lower genital tract through colposcopy, biopsy, endocervical curettage, vaginoscopy or vulvoscopy. We did not use typing methods due to costs. Cervical HPV was confirmed in 130 patients. The patients' ages ranged from 25 to 65.

Possible risk factors were evaluated such as number of partners, frequency of sexual intercourse and birth control methods. The patients were treated with topical applications, cryosurgery or loop conization.

A 3 years later the results show that 82 cases (63%) were negative, 30 cases (23%) were LGSIL and 18 cases (13.8%) were HGSIL.

A 5 years of follow the results show 85 cases were negative,30 cases were LGSIL and 18 cases were HGSIL

A 7 years later of study, 88 cases (71.5%) were negative and 35 cases were LGSIL (28.4%) (Table 1).

Time follow after-treatment	Negative	L-SIL	H-SIL
3 years	82 (63%)	30 (23 %)	18 (13.8%)
5 years	85 (63.9%)	30 (22.5%)	18 (13.5%)
7 years	88 (71.5%)	35 (28.4%)	--

Table 1

European guidelines recommend primary HPV testing for cervical cancer screening. However, the starting age remains to be defined, with an undecided window between 30 and 35 years. This pilot study compares the effectiveness of primary HPV testing to that of cytology for the detection of high-grade (CIN2+) lesions stratified by age.

Keywords: Human Papillomavirus; Epidemiology; Cervical Intraepithelial Neoplasia; Cryosurgery; Loop Conization; Cotesting

Introduction

From the introduction by Since in the 60's of the cryosurgery for the CIN treatment multiple articles have been published that enclose the therapeutic efficacy so the patient's tolerance in the ambulatory application [1].

There is a preferential though not an exclusive relationship between different types of HPV and clinical lesions, anatomical localizations and genital tropism. In susceptible subjects they cause tumors in the squamous epithelium, cutaneous and mucous, called warts and condylomas respectively [2].

Andersen in a study about the follow-up in ten years post-cryosurgery obtained a curation rate of 90% in patient well selectionated, anyway in his study included the CIN III so the atypical image that affect the canal [3].

Condylomas, especially those of the uterine cervix, present different degrees of cervical intraepithelial dysplasia or neoplasia (SIL). LGSIL (lesion squamous intraepithelial low grade) is related to HPV-6 and 11. HGSIL (lesion squamous intraepithelial high grade) are associated with HPV-16 and 18 and less often to 31, 33 and 51 [4].

Cervical HPV (human papillomavirus), causes lesions in the epithelium which are seen on the Pap smear (Papanicolaou test), colposcopy or the cervical biopsy with or without special stains [5].

In order to ensure correct diagnosis, endocervical curettage was performed on all patients with diagnosed HPV infection [6].

We consider that if we are more selective the failure rates with this treatment technique is lower.

Material and Methods

Out of 1450 colposcopies referred to us for either gynecological check-up or because of a positive Pap smear (Papanicolaou test), between 2010 and 2016, HPV infection was confirmed in 130 by Pap smear, test HPV (Aptima), colposcopy, vaginoscopy or colposcopically directed cervical biopsy. To confirm cervical HPV, at least two of the methods had to prove positive.

Cryosurgery was performed on those patients with low grade squamous intraepithelial lesions (LGSIL) who presented a visible lesion confirmed through biopsy, a visible squamous-columnar junction and negative cervical curettage.

Loop conization was performed on high grade squamous intraepithelial lesions (HGSIL). Cryotherapy was performed as a double-freeze technique, 3 minutes freeze-2 min thaw-3 min freeze, nitrous oxide was used as refrigerant.

We established as exclusion criteria:

1. The patient with CIN III.
2. When the colposcopy image invade the canal.
3. Large CIN with an extension bigger than 2 cms.

The age of our patients ranged from 25 to 65. The average age of the LGSIL patients was 28.6 +/- 4.2. Thirty percent were nulliparas, 42% primiparas and 28% multiparas.

The patients were followed up for at least a year. The data was analysed with Access program for doctors.

In the follow-up the first control was in three months and after each 6 months during the first two years and later yearly, realized cytology, colposcopy and directed biopsy in the required cases. We release the follow-up during a mean time of five years.

We consider a therapeutic failure only the presence of histologic CIN during the first year and the lesion recurrence. There was not significant different between CIN I and CIN II (p < 0.05).

Cotesting with LBC cytology and APTIMA® HPV Hologic Inc, was performed in women aged 25 - 65 in an opportunistic screening program in Madrid. Aptime HPV-positive cases were referred to colposcopy and genotyped for HPV 16 and 18/45 (Aptime HPV).

Results

The pill was the preferred method by 66 women (50.7%), the IUD (Intrauterine device) was used by 18 (13.8), barrier methods were used by 32 women (24.6%) and coitus interruptus and or no birth control in 14 women (10.7%).

Pap smears (Papanicolaou test) prior to treatment were negative in 20 women (16.6%), LGSIL in 78 women (56.6%) and HGSIL in 32 women (26.3%) (Figure 1).

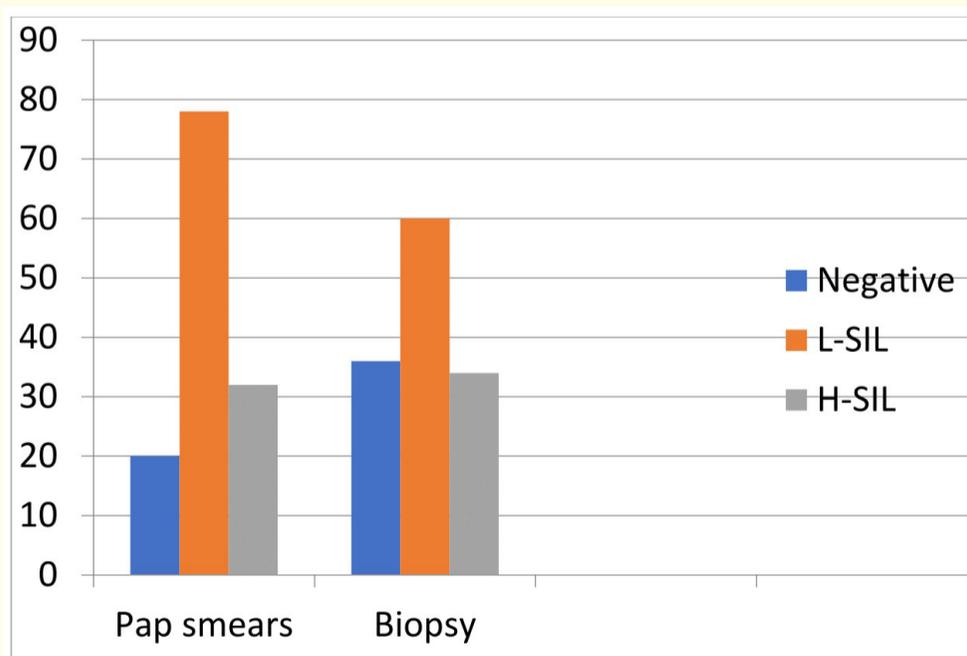


Figure 1: Prior to treatment.

Cervical biopsy was performed in all cases either on the atypical image or on the squamous columnar junction. It was negative in 36 cases (31.3%), LGSIL in 60 cases (52.3%) and HGSIL in 34 cases (26.3%) (Table 2).

Pap smears prior treatment	Negative: 20 (16.6%)	L-SIL: 78 (56.6%)	H-SIL: 32 (26.3%)
Cervical biopsy	Negative: 36 (31.3%)	L-SIL: 60 (52.3%)	H-SIL: 34 (26.3%)

Table 2

Conservative treatment was prescribed to 25 patients (12.5%), cryosurgery was performed on 75 patients (62.5%) and loop conization on 30 patients (25%).

The follow ups were: Pap smear at 6 weeks (negative in 70 women (54.1%), LGSIL in 35 women (26.6%) and HGSIL in 25 cases (19.1%), biopsy was performed at 6 weeks in 28 cases with HGSIL and those with LGSIL with unsatisfactory colposcopy (negative 17 cases (60.7%), LGSIL in 6 (21.4%) and HGSIL in 5 (17.8%), and Pap smear at a year was negative in 80 cases (62.5%), LGSIL in 30 cases (22.5%) and HGSIL in 20 cases (14.9%).

Cervical biopsy was performed one year later in 35 cases, the indications the same as at 6 weeks and the results were negative in 23 cases (65.7%), LGSIL in 8 cases (22.8%) and HGSIL in 4 cases (11.4%) (Table 3 and 4).

Pap smear	Negative: 70 (54.1%)	L-SIL: 35 (26.6%)	H-SIL: 25 (19.1%)
Biopsy (H-SIL) and Colposcopy unsatisfactory	Negative: 17 (60.7%)	L-SIL: 6 (21.4%)	H-SIL: 5 (17.8%)

Table 3: Follow 6 weeks after-treatment.

Pap smear	Negative: 80 (62.5%)	L-SIL: 30 (22.5%)	H-SIL: 20 (14.9%)
Cervical biopsy	Negative: 23 (65.7%)	L-SIL: 8 (22.8%)	H-SIL: 4 (11.4%)

Table 4: Follow a 1 year after-treatment.

Hysterectomy was performed on these 4 patients (3%), since they didn't want any more children.

The result of endocervical curettage was positive for SIL in 12 patients corresponding to 9% of all positive Pap smears and these patients were treated with loop conization.

The results of the colposcopy performed at one year after treatment were: typical images (ectopy and or new squamous columnar junction in 86% of the patients (66.1%), atypical reepithelization zone in 42 (32.3%) and cervical condyloma images in two cases (1.5%).

From the 123 women come for revision at five year, 85 cases were negative, 39 had a low grade SIL and three patient had a high grade SIL for this reason suffered an hysterectomy.

From the 123 women that come for revision at seven year after treatment, 88 had a negative result (71.5%) and 35(28.4%) had a low grade SIL, none had a high grade SIL.

In the figure is exposed the evolution before and after the treatment.

Discussion and Conclusion

Cervical HPV had an incidence of 9% in our unit, with Pap smear, colposcopy, cervical biopsy and endocervical curettage. This can be because we used all these methods on a systematic basis. Vidart, *et al.* found 12% [7,8].

Sexual promiscuity is the epidemiological factor most commonly suggested by other authors. In this study 24.9% of the women said that they had had more than one partner. It is difficult to evaluate this parameter because it is difficult to evaluate the partner's promiscuity [9,10].

The pill is another epidemiologic factor that De Brux states that 70% of patients diagnosed with HPV had used them sometime in their lives. In our study 50.8% of the patients had used them sometime in the 5 years prior to HPV diagnosis [10,11].

Grunebaum has stated that the number of pregnancies influences the HPV infection. In our study, 72% had at least one pregnancy in the 5 years prior to diagnosis [12].

The connection between cervical HPV and cancer is considered the most important factor in the genesis of the disease.

It was suggested by Zur Hausen in 1977 that there was a relationship between genital condylomas and severe dysplasias [1,15]. Clinical experience has shown that most women with infection caused by HPV 6 and or 11 do not suffer complications in the genital tract, but have a high risk of cervical neoplasia and HPV-related infections with oncogenic potential (HPV 16, 18, 31 and 33) in 90% of cervical cancer cases both squamous and adenocarcinomas [13].

The Pap smear shows the presence of koilocytes, pathognomonic and its association with dyskerocytes, binucleation and hyperkeratosis.

The main purpose of treatment should be the removal of all condylomatous tissues and anomalous colposcopic zones and the relief of signs and symptoms, not the eradication of HPV.

Currently cervical HPV is treated regardless of the typing some authors think there is no reason to type HPV because they think that even if you type the virus there is no guarantee that another type of virus will not appear at a later date [13,14].

The best treatment is that which is applied after a prompt diagnosis and with follow-up until total healing or possible remission is achieved [12,13].

We consider like Bryson that the high grade SIL treatment with cryosurgery may be effective if a good selection is done and a rigorous selection protocol is made.

In our study the high grade lesion treated with cryosurgery had an exocervical localization, was a little lesion and always with a negative endocervical curettage. We consider that with the endocervical affectation this treatment is not indicate.

We consider too, that with easy treatment like the cryosurgery good results are obtained in large follow up until seven years in contrast of others like laser vaporization more expensive.

Aptima HPV shows a significantly higher sensitivity for cervical CIN2+ lesions than cytology alone. Unexpectedly, AHPV-positive women under 35 had the highest incidence of CIN2+ lesions, particularly when they are HPV16/18/45-positive. Considering HPV primary screening before the recommended age of 35 is warranted [16].

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