

# 30 years of preventive studies of uterine cervical cancer 1982–2012

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## Summary

The studies for the prevention of uterine cervical cancer in Panama City began in a private institute, impelled by the high incidence of cancer. The preventive programs were initiated with the support of the Obstetrics and Gynecology Institute of the University of Padua in Italy. In these studies, we applied the methodological diagnostics of this Institute with certain modifications adapted to our needs. The diagnosis, treatment, and follow-up were carried out under the protocol of the University of Padua. We achieved a diagnosis of oncogenic risk (OR) in 6,411 patients which corresponded to 5,498 cases of human papillomavirus (HPV), 1,150 cases of dysplasia, 210 cases of cancer, and 794 cases of OR. From 2011, polymerase chain reaction (PCR) was also applied with the aim to improve the accuracy of the diagnosis. With this method the prevalence of pathologies were HPV infections both in healthy patients or in patients cured from HPV. Patients were treated by means of local destructive treatments (LDT), basically with cryotherapy and cauterization. We can consider these results as successful prevention and suggest to extend a preventive program to all the population.

*Key words:* Oncogenic risk prevention; Cervical cancer: Treatment evolution.

## Introduction

On a global level, cervical cancer is the second most common and fifth deadliest cancer in women [1, 2]. It occurs in approximately 16 per 100,000 women per year and accounts for nine per 100,000 deaths annually [3]. Approximately 80% of cervical cancers occur in developing countries [4]. In 2008, it was estimated that there were 473,000 cases of cervical cancer [5] and in 2010 225,000 deaths worldwide [6].

Cancer screening using the Papanicolaou (Pap) test smear can identify precancerous and potentially precancerous changes in cervical cells and tissue. Treatment of high-grade changes can prevent the development of cancer in many cases. In developed countries, the widespread use of cervical screening programs has dramatically reduced the incidence of invasive cervical cancer [7].

Infection with some types of human papillomavirus (HPV) is the greatest risk factor for cervical cancer, followed by smoking [8]. Although not all of the causes of cervical cancer are known, several other contributing factors have been implicated [9]. HPV infection appears to be a necessary factor in about 90% for the development of cervical cancer [10].

The global variability of treatment of cervical cancer is mostly due to large variances in disease burden in developed and developing nations, access to skilled surgeons in radical pelvic surgery, and the evolution of fertility-sparing options in developed countries. Because cervical cancers

are radiosensitive, radiation may be used in all stages where surgical options do not exist.

## Materials and Methods

In the present study, six provinces of the Republic of Panama, were covered which included medical tours, whose studies were published in a recent article and where the value of routine colposcopy was highlighted [11]. This value was reflected in recruitment of patients with OR which reached about 53%, defined as a result of health control, while the OR was confirmed in those patients referred for suspected uterine cervical cancer [12].

Between 1982 and 2012, we examined 12,679 women, applied 26,889 colposcopies, 26,251 colpocytologies, and 5,868 directed biopsies were applied to them. The Colpo-Pap methodology was applied, that is taking a Pap smear sample through a colposcopic approach. Through a direct line of vision of the lesion via colposcopy, a biopsy was taken (Table 1).

The diagnosis was clinical, cytological, histological, and the patient was defined with OR as a simple HPV, pure dysplasia or associated with HPV, as well as cancers with or without HPV, and finally, pure OR, which meant that the lesion was without cytological and histological support.

The profile of patients evaluated corresponded to these parameters: two pregnancies, two births, no abortions, menarche between 13 and 15 years, the beginning of coitus between 15 and 20 years, two sexual partners throughout life, and almost all used the family planning method. The age range was from eight to 90 years [13].

Treatment was applied adequately to different pathologies and consisted in cryotherapy, and/or associated to cauterization, electro-

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Table 1. — *Types of diagnosed pathologies in 30 years of studies.*

Type of pathology	Quantity	Percentage
Pure HPV	4257	66.4%
HPV associated to dysplasia	1096	17.1%
HPV not associated to dysplasia	54	0.8%
HPV associated to cancer	145	2.3%
HPV not associated to cancer	65	1.0%
Simple OR	794	12.4%
Total	6411	100%

coagulation, and surgery where it was required. The patients treated conservatively were checked every three months, until the viral lesions disappeared, and then every six months or a year.

We achieved an initial diagnosis, that is to say, recruitment, whose value is of utmost importance when it comes to preventing cervical cancer, but also the conclusion or evolutionary diagnosis. Both diagnoses are important because they sustain the findings, and in the end, they are a true representation of Panama's reality.

## Results

Diagnosis led to 6,411 women with OR. HPV reached 87% with 5,498 cases in total; pure HPV cases were 4,257, those associated with dysplasia were 1,096 cases, and 145 cases associated with cancer. The OR cases corresponded to 50.5% of total women attended in the past 30 years of this study; a considerably elevated number, but the percentage of the reported annual OR corresponded to an average of 44%, and almost exclusive to new patients which entered the study (Table 1).

The preventive cancer study's analytical diagnosis was achieved. The cytology contributed a risk diagnosis of 50%; most representative of the false negative was inflammatory alterations.

Concerning colposcopy, it reached a 79% OR, while the most frequent pathological pictures were atypical re-epithelization zone (ARZ) in 47%, leukoplakia in 22%, and HPV in 13%.

The directed biopsy with the colposcopic approach indicated 94% OR and false negatives were only 6%. While performing the analysis, we observed that by integrating the three diagnostic methodologies, we reduced false negatives to a mere 1%, confirming that concordance of the three methods is not the most common. Facing this discordance we worked with the most severe diagnosis.

We guided the majority of these patients, to local conservative treatments, such as cryotherapy, cauterization, caustic or chemical, and we emphasized the importance of successive controls, in order to assess their evolution, thus repeating, adding or adjusting the recommended treatments. The applied treatments were 3,780, distributed in 2,305 cryotherapies, 549 cauterizations, 702 mixed, and others in 224. Surgical treatments such as hysterectomy

Table 2. — *Applied conservative treatments according to presented pathology in 30 years of study (3,780 attentions).*

Type of treatment	Pure OR	Pure HPV	Dysplasia	Cancer	Total
Cryotherapy	229	1509	542	20	2300
Cauterization	178	305	66	0	549
Mixed	57	625	20	0	702
Others	11	60	73	80	224
Total	475	2499	701	100	3775

Table 3. — *Evolution of attended patients in 2011 with 210 cases, in 2012 with 200 cases, and with a follow-up of 30 years of study.*

Type of pathology	Quantity	Percentage
Healing	369	90%
Improvement	13	3%
Recurrence	8	2%
Persistence	12	3%
Progression	8	2%
Invasive cancer	0	0%
Total	410	100%

were few. We suspended cervical conizations in the early 1990s (Table 2) [14].

The evolution of the patients, which we carried out controls of every six months or every year, indicates that in total and in follow-up controls, that there were 210 cases in the year 2011, and 200 cases in 2012. Thus, we have the following results: healing reached 90%; improvement 3%; persistence 3%; recurrence 2%, and progression 2% (Table 3) [15].

In the most conservative aspect, and in the annual evolution, based on patient controls, it is shown that the values remain identical; though the patients have had different degrees of pathology, including cancer treated conservatively [16-18].

These clinical evaluations of lesions considered as OR eradication, contrast with findings of molecular biology studies, which began in December 2011 and also covered OR cured patients (patients with OR recently diagnosed and healthy ones). We managed to diagnose 90% of them with high-risk HPV. Within the same group, the most frequent subtypes were 31, 18, 35, and 16, while only ten cases were negatives [19-21].

HPV's behavior, pathophysiology, numerical incidence, and oncogenic potential have been analyzed by many researchers. The many doubts regarding the genesis of cancer and its chronic action (innate or acquired response) has become clear and has led to the use of vaccines in a prophylactic or therapeutic sense [22-24].

In January 2012, we included the PCR studies in samples of fibroids or myomas due to high incidence and above all, rapid development. These samples were obtained in the myomectomies, or in the hysterectomies performed during

that year, and which results, surprisingly, reached a 100% of HPV. Among them, the most frequently subtypes found were 16 and 18.

## Discussion

Panama is a small country with a high incidence of cancer. If we evaluated the actual precursor of cancer lesions incidence, we would have to consider that in the 30 years of study, we are failing to minimize this great illness, and above all, the death of many women because of late presentation, above all due to the bureaucracy in healthcare institutions, physicians, and ultimately, themselves.

Despite diagnosing 6,411 OR cases, evolutionary diagnosis is very important, because with it, we validate the application of conservative therapeutic measures. Thus our results are justified since invasive cancer had zero progression in the controlled patients up to 30 years, and in the last five years of studies, we had no cases of cancer at the time of concluding them. With these successes, there is nothing more to add.

## Conclusions

The inspection of the different aspects of the HPV affected women's profile, such as the planning methods, sexual experiences, the discipline in their own health management, good response to the recommendations of treatments, and care-taking, as well as compliance with medical appointments, and calmly receiving the PCR results, compared with the clinical pictures, healing was performed.

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