

A second Pap smear during colposcopy: is it really worth it?

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Summary

The aim of this study was to determine whether the clinical value of a second Pap smear during colposcopy outweighed its cost-effectiveness and reliability parameters. We studied retrospectively 569 cases focusing on A) The initial Pap smear, B) The smear performed during colposcopy, C) The colposcopic findings, and D) The histopathological reports of the cases where biopsy sampling was performed.

In 380 patients (67%), the second Pap smear corresponded to the first one. In 13% of the patients, the cytological lesions were worse (particularly in 2% of the patients staging increased from HPV-associated reactive cellular changes to CIN II, or from CIN I to CIN III), and in 20% slighter than the initial.

In 79% of the cases revealing more serious lesions in the second smear, the histological result of the biopsy corresponded to that of the initial smear.

Conclusively, only 2% seem to benefit from a second repeat Pap smear during referral colposcopy.

Key words: HPV; SIL; Pap smear; Colposcopy; Smoking; Condom use.

Introduction

The incidence of HPV-related female lower genital tract infection has unquestionably reached pandemic dimensions, being worldwide one of the commonest sexually transmitted infections (STIs) in young women. Given the correlation, through preinvasive lesions with female genital tract malignancies, the effort is to ameliorate reliable screening of premalignant changes.

The implemented methods on cervical screening are mainly cytopathology (Papanicolaou smear), colposcopy (alone or combined with directed punch biopsy and the corresponding histological interpretation), HPV DNA testing (hybrid capture test), cervicography and intracervical sonography.

Despite consensus guidelines [1] the management of cervical cytologic abnormalities still remains an era of conflict concerning the clinical and financial cost, as well as aspects of patient anxiety and satisfaction.

The American Society for Colposcopy and Cervical Pathology (ASCCP)-Sponsored Consensus Conference in 2001 concluded that women with ASC-US should have two consecutive cytology tests, immediate colposcopy, or DNA testing for high-risk types of HPV, whereas women with ASC-H, LGSIL or HGSIL, or atypical glandular cells should be referred for immediate colposcopic evaluation [1].

Tuon *et al.* [2] believe that cytopathology is a high specificity examination, while colposcopy from selected patients has high sensitivity. The association of colpo-

scopical and cytological findings on selected patients can significantly increase the diagnostic accuracy.

When a Pap smear is considered inadequate, in order to reduce morbidity associated with colposcopy, it may be acceptable to repeat the smear after six months rather than arranging immediate recall [3].

Normal colposcopic findings have an excellent negative predictive value for HPV-positive women with normal cytology, as cited by Paraskevaidis *et al.* [4], who recommend that these patients may be safely screened cytologically on a three-yearly basis.

Due to the proven oncogenic potential of HPV serotypes 6, 11, and especially 16, and the fact that the risk of having premalignant and malignant cervical diseases upon HPV infection is much higher in younger age, Tanaka *et al.* [5] recommend that HPV -testing should be applied in every young woman with an abnormal Papanicolaou smear test. Guido *et al.* [6] point out that the most efficient test for identifying women with CIN grade II or III after colposcopy might be an HPV test alone at 12 months.

Paraskevaidis *et al.* [7] question HPV testing, citing that it does not appear to add significantly to cytology in terms of positive predictive value or detection rate, if extended cytologic indications for colposcopy are used.

The initial Pap smear is of great importance. An adequate and conclusive cervical smear should include squamous cells, metaplastic cells from the transitional zone, and endocervical cells. The presence of metaplastic cells from the transitional zone is highly significant, since most preinvasive and malignant cervical lesions commence from this site [8].

The ideal time to obtain the smear is shortly before ovulation [9], when the clarity of the smear is optimal, and cellular segregation is distinct.

Materials and Methods

Under the former outline, given that Pap smear and colposcopy are complementary examinations, and that usually women are referred for colposcopy either for an HPV or a CIN lesion, the aim of this study was to determine whether the policy of repeating a Pap smear during colposcopy had a certain clinical benefit that justifies it.

The study was retrospective, and regarded the evaluation of 569 women in relation to:

1. The initial Pap smear
2. The Pap smear obtained during colposcopy
3. The colposcopic findings
4. The histopathological reports when directed punch biopsy was performed.

The median age of the patients included in the study was 30.6 years old (range: 17-43 years old).

Informed consent was obtained from all women after the nature of the procedures had been fully explained.

Advice concerning condom use and discontinuation of smoking was provided to all patients.

In 340 patients, a low grade squamous intraepithelial lesion (LGSIL) was confirmed in the initial smear, consisting of (using the older terms) HPV-associated reactive cellular changes (mild koilocytosis, mild dyskeratosis, hyperchromatic nuclei, bimultinucleation, and cleared cytoplasm) or CIN I.

In 229 women a high grade squamous intraepithelial lesion (HGSIL) was diagnosed in the initial smear - equivalent to the older terms CIN II or CIN III.

Results

In 380 patients (67%) the Pap smear obtained during colposcopy corresponded to the results of the initial smear. Two hundred and eighty-eight cases (76%) were LGSIL and 99 cases (24%) were HGSIL. (Summary statistics: total chi-square: 122.324, $p = .0001$).

In 177 patients (31%) the new smear differed at one point from the initial one (Table 1). In 63 patients (11% of total) the new smear was worse than the initial one (CIN I from HPV associated changes, CIN II from CIN I, or CIN III from CIN II), and in 114 patients (20% of total) it was better than the initial smear (HPV associated changes from CIN I, CIN I from CIN II, CIN II from CIN III). Of these 177 patients, in 47 patients (27%) the initial diagnosis was LGSIL, and in 130 patients (73%) it was HGSIL.

Finally (Table 1), in 12 patients (2%) the new smear differed at two points from the initial one (CIN II from HPV, CIN III from CIN I, or HPV from CIN II or CIN I from CIN III).

It is worth mentioning that a significant number of patients (70 out of 114 patients) with improved cytologic

findings during colposcopy complied with the advice to quit smoking ($p > 0.05$), while 79 followed similar advice concerning condom use ($p > 0.05$).

It must be cited here, that in 79% of the patients showing progressive lesions in the second Pap smear, the histopathologic report from the directed punch biopsy corresponded to the cytologic report of the initial smear.

Discussion

Considering the cytologic results, it proved that in 88% of the cases where the former and the latter Pap smear had been obtained within one to four days of the estimated ovulation, the histopathologic diagnosis was identical. When interpreting a Pap smear, it should be taken into account that in smears obtained in the late secretory phase, the result might be unreliable and inconclusive [9].

Higher probability of concurrence in diagnosis was indicated when LGSIL was found in the initial smear and in cases where the smear was obtained shortly before ovulation. Consequently, if a selection was to be performed, in which women the repeat Pap smear could be omitted, these two subgroups might be chosen.

Our results largely concur with the data from other authors. Panos J.C. *et al.* [10] affirm that a second Pap smear at the time of colposcopy might result in significant changes in the management of only 2% of the patients and in more careful follow-up in 1%. They comment that Pap smears performed at colposcopic biopsy are less sensitive than those done prior to biopsy, and conclude that the clinical benefit of repeating the smear during colposcopy is marginal, provided patients receive adequate follow-up.

Similar are the results from Spitzer *et al.* [11], who point out that repeating the Pap smear at the time of an initial colposcopy would have changed the management in 2.7% of patients and indicated a conization in only 1.1% of patients. They estimate that it is doubtful if these data justify the cost and 'the potential detrimental effects' of the colposcopic examination.

The latter findings correlate with those of Zardawi and Rode [12], who found that the changes noted in the second Pap smear and in the punch biopsies in their group originally diagnosed as having high-grade disease were generally less advanced. Moreover, they found that there had been more advanced changes in the group originally diagnosed as having low-grade disease. They comment that removal of part of the abnormal epithelium during the first Pap smear and the desire of the colposcopist not to damage the surface epithelium prior to performing a cervical biopsy may account for some of these findings.

Simsir *et al.* [13] also question the policy of repeating the Pap smear at colposcopy, finding that 16% of the HGSIL and 28% of the LGSIL cases were diagnosed on second Pap smear only, given that the following biopsies were negative, underlying that an important sum of money could have been saved if the repeat smear had been omitted.

Table 1. — Correlation between the initial smear and the smear performed during colposcopy upon the diagnosis of SIL.

	LGSIL, n	LGSIL, %	HGSIL, n	HGSIL, %
1 st Cytologic exam	340	59.75	229	40.25
2 nd Cytologic exam equity	288	76	92	24
Difference at 1 point	47	27	130	73
Difference at 2 points	5	42	7	58

Similar are the points made by Korman [14], Massad and Cejtin [15], Smith and Nguyen [16], and Gerber *et al.* [17].

Another finding stated in our study is the statistically significant contribution of condom use and smoking discontinuation to the amelioration of cervical lesions, which has also been demonstrated in previous studies [18-23], despite the controversial data [24-26]. Regardless of the connection between these factors and cervical cancer, either through immunosuppression and/or direct carcinogenesis, it seems that simple behavioral modifications, might prove vital.

Conclusion

Given the limitation that the accuracy of the histopathological diagnosis is based on a well performed and representative cervical biopsy after a meticulous colposcopic interpretation, only 2% of the women with abnormal initial Pap smear would benefit from the repetition of the Pap smear during colposcopy. Discontinuation of smoking and condom use may have beneficial results in the regression of cervical lesions.

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