

A cohort retrospective study of the high-risk HPV recurrence in Greek women after cervical lesion treatment through detection of viral E6/E7 mRNA expression



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Purpose: To detect and evaluate potential alterations in the post-operative status of E6/E7 HPV mRNA in women treated for Cervical Intraepithelial Lesions (CIN) and if so, to evaluate its potential use as a prognostic tool to identify patients with increased risk of treatment failure or recurrent disease.

Methods: Our study retrospectively analyzed 101 women with an abnormal Pap smear, or in some cases with histological reports or molecular analysis, suggesting colposcopic evaluation. Cytological samples were collected before colposcopy and histology (when necessary). After treatment, all women were scheduled for colposcopy in six months. The cytological material was analyzed with CLART-2 HPV-DNA test and HPV-PROOFER E6/E7 mRNA test.

Table 1. Cytological and colposcopic diagnosis before and after treatment

Cytological Diagnosis	Before Treatment	After Treatment
NILM	3 (3.0%)	59 (58.4%)
ASC-US	7 (6.9%)	25 (24.8%)
ASC-H	4 (4.0%)	0 (0.0%)
LSIL	33 (32.7%)	13 (12.9%)
HSIL	53 (52.5%)	4 (4.0%)
SCC	1 (1.0%)	0 (0.0%)
Total	101 (100%)	101 (100%)
Colposcopic al Diagnosis	Before Treatment	After Treatment
NEGATIVE	20 (19.8%)	87 (86.1%)
CIN1 /HPV/L SIL	43 (42.6%)	11 (10.9%)
CIN2/CIN3/ HSIL	37 (36.6%)	3 (3.0%)
SCC	1 (1.0%)	0 (0.0%)
Total	101 (100%)	101 (100%)

Table 2. Histological diagnosis of the excised lesion during treatment

Histology during treatment	N (%)
NEGATIVE	17 (16.8%)
CIN1 /HPV/ LSIL	15 (14.9%)
CIN2/CIN3/ HSIL	66 (65.3%)
SCC	3 (3.0%)
Total	101 (100%)

Table 3. HPV DNA test and HPV mRNA test before and after treatment

HPV DNA test	Before Treatment	After Treatment
-	8 (8.0%)	59 (58.4%)
+	93 (92.0%)	42 (41.6%)
HPV mRNA test	Before Treatment	After Treatment
-	22 (21.8%)	89 (88.1%)
+	79 (78.2%)	12 (11.9%)

Results: Concerning demographics, no significant correlations were found for smoking, condom use or vaccination status. It seems that the only statistically significant correlation with actual severity comes from mRNA-test after treatment. This probably shows that clinical cases with more severe CIN may have higher chances of unsuccessful treatment. At the first post-op visit, 83.5% of HPV mRNA-positive women had negative HPV mRNA-test while only 60.4% of HPV DNA-positive women became negative. There were 12 HPV-mRNA positive patients both before and after treatment, 3 of who had negative HPV DNA test, meaning that if based only on HPV-DNA results, they would have been managed wrongly as successfully treated patients. Our study shows that E6/E7 mRNA detection has particularly high specificity and positive likelihood ratio for the prediction of treatment failure in comparison with HPV DNA-testing.

Table 4. Spearman's rho statistical correlations

		Correlations				
		Cytology ¹	Colposcopy ¹	DNA test ¹	mRNA test ¹	Histology during treatment
Spearman's rho	Cytology ¹	1.000	0.539**	0.256**	0.258**	0.049
	Colposcopy ¹	0.539**	1.000	0.049	0.024	0.035
	DNA test ¹	0.256**	0.049	1.000	0.424**	0.092
	mRNA test ¹	0.258**	0.024	0.424**	1.000	0.261**
	Histology during treatment	0.049	0.035	0.092	0.261**	1.000

** Correlation is significant at the 0.01 level (2-tailed).

Table 5. Sensitivity, Specificity and Predictive values for test and HPV-DNA test and HPV-mRNA test after treatment

Threshold: CIN2+ confirmed with cytology, colposcopy or histology	HPV-DNA test	HPV-mRNA test
Sensitivity (SV)	94.44%	81.25%
Specificity (SP)	84.34%	98.82%
Positive Predictive Value (PPV)	56.67%	92.86%
Negative Predictive Value (NPV)	98.59%	96.55%

