

Abstract 1842

HPV POSITIVE CERVICAL SQUAMOUS CELL CARCINOMAS: ASSOCIATION WITH EXPRESSION OF P16, P53 AND KI67.

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Introduction

Cervical cancer is the fourth most common malignancy in females. The majority of cervical carcinomas (CC) are associated with high-risk HPVs (hrHPV). Here, we investigated the association between hrHPV genotypes, virus load, p16, p53, and Ki-67 expression in hrHPV-positive CCs.

Methods

FFPE cervical tissues of 76 patients (median age 60 years) with primary cervical squamous cell carcinomas were assessed. Tumor grades were evaluated histologically, and expression of p16, p53, and Ki-67 immunohistochemically using Flex kits, Autostainer Link-instrument (Dako), and Eclipse 55i microscope (Nikon). DNA isolated from FFPE samples (Qiagen) was used for hrHPV DNA detection and semiquantification (Anyplex Seegene).

Results

All 76 cancer cases were positive for at least one hrHPV, mainly HPV16, followed by HPV33. Other genotypes were less prevalent (Table 1)

table 1.png

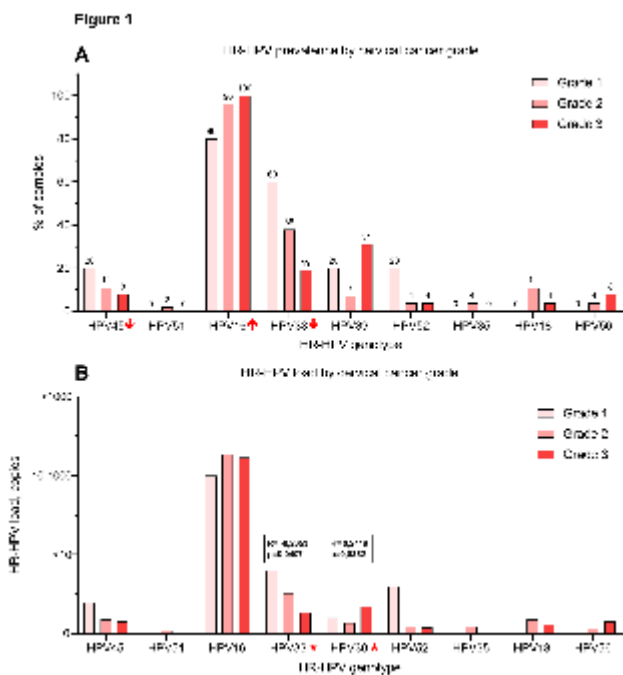
Table 1. HR HPV genotype prevalence in cervical cancer tissues by cancer grade.

	Total n=76	Grade 1 n=5	Grade 2 n=25	Grade 3 n=46
HPV68	0	0	0	0
HPV45	8 10.5%	1 20%	5 11.1%	2 7.7%
HPV58	0	0	0	0
HPV51	1 1.3	0	1 2.2%	0
HPV69	0	0	0	0
HPV16	73 96.1%	4 80%	43 95.6%	26 100%
HPV35	25 32.9%	3 60%	17 37.8%	5 19.2%
HPV39	13 15.8%	1 20%	3 6.7%	8 30.8%
HPV32	4 5.7%	1 20%	2 4.4%	1 3.8%
HPV35	2 2.6%	0	2 4.4%	0
HPV18	6 7.9%	0	5 11.1%	1 3.8%
HPV56	4 5.3%	0	2 4.4%	2 7.7%
HPV65	0	0	0	0
HPV31	0	0	0	0

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Prevalence of HPV16 increased, while HPV33 and HPV45 decreased with tumor grade (Figure 1A(F1A)). HPV33 load correlated negatively, while HPV39 - positively with tumor grade (F1B).

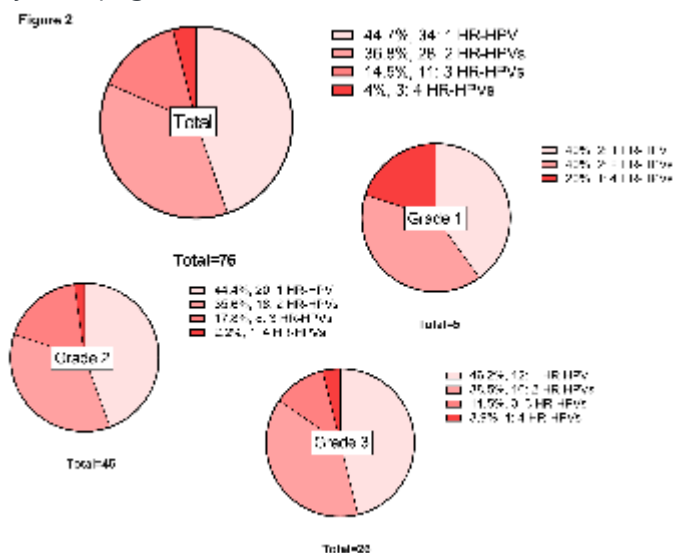
layout 1.png



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Many CC samples were positive for multiple hrHPVs (F2), without correlating with tumor grade.

layout 2.png



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74 CCs (97.4%) were p16(+). Median % of ki67-expressing cells was 43.5% (IQR: 25.3 – 70.0%). ki67-expressing cells positively correlated with HPV39 (R=0,2406, p=0,0362) and negatively with HPV18 load (R=-0,3079, p=0,0067), and tended to increase with increasing cancer grade (median: 52 vs 56 vs 65). Aberrant p53 expression was detected in six CC cases (7.9%), most often in Grade 3 (5/6) in patients older than 60 (4/6) and positively correlated with cancer grade (R=0,2936, p=0,0100), and HPV18 virus load (R=0,2783, p=0,0149).

Conclusions

p16 positivity acted as a surrogate marker of hrHPV(+) cancer, with 97% sensitivity. Percent of Ki67-positive cells was not informative in distinguishing tumor grades. Least informative was p53-staining. Of note, HPV33 and 39 correlated with tumor grade. Thus, immunostaining for p16 is sufficient to confirm an hrHPV(+) CC.

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