

HPV Infection is Common and Highly Prognosed in Early-Stage Cervical Cancers

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Introduction

Cervical cancer is the world's fourth leading cause of cancer incidence and mortality in women. According to a secondary analysis of GLOBOCAN 2020 data, cervical cancer was responsible for an estimated 109,741 (18.17%) cases and 59,060 (17.28%) deaths in women in China. Cervical squamous cell carcinoma (CSCC) is the most common histological type of cervical cancer, accounting for more than 70% of all cases in the United States and more than 90% in China. Epidemiological studies have clearly demonstrated that persistent HPV infection is the primary cause of more than 91% of cervical cancer cases. HPVs were generally classified into two subgroups based on their pathogenic potential: high-risk and carcinogenic HPV types (HR-HPV) and HPV types with a low risk of cancer (LR-HPV). HR-HPV types were further classified into two species based on genomic nucleotide similarity: alpha-7 (HPV18, 39, 45, 59, 68, and 70) and alpha-9, which account for more than 80% of all cervical cancer cases. Although it is widely accepted that HPV16 and 18 are the most common prevalent genotypes worldwide, accounting for 70% of all cervical cancers, the prevalence of the other HR-HPV genotypes varies by country and geographical region. HPV45, 31 and 33 are more common in Western countries, whereas HPV58 and 52 are more common in Asian populations, including Chinese. There are currently three effective HPV vaccines available. The bivalent vaccine (HPV16/18), quadrivalent vaccine (HPV16/18/6/11) and nonavalent vaccine (HPV16/18/6/11/31/33/45/52/58) are all available on the global market. It is of considerable importance to understand the geographic-specific patterns of HPV to correctly select prophylactic vaccines and cervical cancer prevention because of this knowledge [1].

Description

Though most cervical cancers are thought to be caused by HR-HPV infections, the prognostic correlation of HPV infections with patient survival remains variable in different data settings from different studies. Furthermore, the prevalence of HPV infection varies by geographic region. In our study, we extracted medical record data from 1425 patients with early-stage CSCC who underwent radical surgery in Hangzhou, China, and described the prevalent distribution and subtype patterns of HPV infections, explored the associated clinicopathological parameters with HPV infections, and analysed the potential predictive biomarkers of 5-year survival factors such as HPV infection and other clinicopathological factors. We discovered that the overall HPV infection rate was 84.3%, with 13 HR-HPV and 8 LR-HPV genotypes. The distribution of HPV infection was proportional in patients across different age and FIGO stages [2].

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The pattern of single infections was much more than the multiple infections, HPV16, 58, 18 and 52 were the dominant top four sub-genotypes with infection rates of 65.1%, 8.7%, 7.7%, and 4.5%, respectively SCC-Ag levels and LVSI were statistically associated with HPV status DSI, LVSI, and lymph node metastasis were all independent prognostic factors. Overall, the HPV positivity rate of 84.3% in our population with early-stage cervical cancer is lower than previously reported studies with rates of 95.1% or 90.9%, which may be due to geographic variation, as our data also suggests significant local variation in the prevalent distribution features. Furthermore, the disparity may have contributed to the different methods of specimen sampling used for HPV genotyping in various studies. In our study, we used samples of exfoliated cervical cells collected with a disposable cytology brush, whereas other studies used formalin-fixed paraffin-embedded tissue specimens.

As a result, the relatively high rate of non-HPV positivity described in our study and its relationship with patient prognosis requires confirmation by additional epidemiological studies. Data and experimental studies are both available. For the sub-genotype, HPV16, 58, 18, and 52 were the dominant top four sub-genotypes in our selected population with early-stage CSCC, which was basically consistent with the data from our previous study indicating that a 9-valent vaccine (Gardasil 9, Merck) would be recommended. As previously reported, the pattern of multiple infection was very common in cervical cancers but our data showed that single infections outnumbered multiple infections by a large margin. Another important topic addressed in this study is whether there is a link between HPV status and clinical parameters. Of the factors examined, 2 analysis revealed that SCC-Ag levels and LVSI had a statistically significant relationship with HPV status. More importantly, based on previous research the prognostic role of HR-HPV infection in SCC remains debatable [3].

According to some studies, patients with HPV-positive ICC have a better prognosis than those with HPV-negative ICC, especially for head and neck squamous carcinomas. The possible mechanisms were summarised as follows: HPV-positive tumours are more radio- and/or chemosensitive and HPV-positive tumours have less genetic heterogeneity. It has been reported that far fewer mutations were found in HPV-positive tumours than in negative ones, particularly in genes such as TP53, CDKN2A, PTEN, PIK3CA, FBXW7, HRAS, and NOTCH1, which are involved in various critical cellular signalling pathways such as EGFR, PI3K-AKT and mTOR. Patients with HPV-positive infection are usually younger and have better epidemiological, performance status, and other clinical and histopathological characteristics. In the case of cervical cancer, however, various studies have shown that HPV infection may predict either worse or better clinical outcomes, or even have no prognostic value [4].

For example, HPV16 positivity was associated with pelvic node metastases and LVSI and HPV-18 was associated with an increased risk of death and disease recurrence. However, HPV31 and HPV58 subtypes were found to be associated with a better survival outcome. Other studies have found no link between HPV infection and clinical outcomes. The results of our study revealed that the 5-year survival rates in patients with different HR-HPV infection status, patterns, and subtypes were comparable, even after PSM was subjected to reduce selection bias, showing that HR-HPV infection status had no predictive value for 5-year OS in patients with early-stage CSCC. However, because information on recurrence and metastasis for these patients in our cohorts was incomplete, we did not conduct a confirmation analysis of the relationship between HPV infection and progression-free survival (PFS). As a result, more research is needed to establish and determine the prognostic value of HR-HPV infection [5].

Conclusion

In conclusion, our study adds to the growing body of literature on the prevalence of HPV in early-stage CSCC patients, and HR-HPV infections were not associated with 5-year OS, except for FIGO stage, LVSI, and lymph node metastasis.

Acknowledgement

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Conflict of Interest

None.

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