

Report of the NDA Grant 2021: HPV in invasive penile cancer and risk factors and treatment for Penile intraepithelial neoplasia

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Penile cancer and its precursor, penile intraepithelial neoplasia (PeIN), are rare malignancies. Data on risk factors, incidence, and treatment of PeIN is scarce. The prevalence of human papillomavirus (HPV) varies substantially between studies of penile cancer.

The aims of the research project were to explore the incidence, risk factors and treatment of PeIN; to analyse the prevalence of HPV and skin diseases in circumcised preputium; to investigate the prevalence of HPV in penile cancer compared to age-matched controls; and in HPV16-positive cases, to analyse viral activity.

Risk factors for PeIN, studied in a case-control study of 580 cases and 3436 controls, showed increased odds ratios for lichen sclerosus (LS), lichen planus (LP), genital warts, balanoposthitis, taking immunosuppressive drugs, penile surgical procedures and organ transplantation.

The incidence of PeIN retrieved from the Swedish National Penile Cancer Register over 20 years, revealed an increased standardized incidence rate of 2.37 from 2019 compared to year 2000. A comparison of given treatment for PeIN in the last five years, compared to the first five years of the period studied, showed surgery to be more common than laser treatment and, topical imiquimod and 5-FU to be more common than local destructive methods.

Analysis of symptomatic foreskin (N=351) showed HPV in 17.1% of cases, high-risk (HR) HPV types in 9.1% with HPV16 in only 2.3%. Histologically, LS, LP and lichenoid dermatitis were seen in 73.5% and PeIN in 2%, despite no clinical suspicion of malignancy.

In penile cancers (N=135) HR HPV types were detected in 38.5% of cases and HPV16 was present in 27.4%. Among age-matched cases and controls (N=105) HR HPV types were found in 35.6% (48/135) of tumours and in 4.8% (5/105) of controls ($p < 0.001$). Among tumours and controls, HPV16 was present in 27.4% (37/135) and 1% (1/105), respectively ($p < 0.001$). Viral activity (HPV16 mRNA) among HPV16-positive cases was more common in the tumour (86.5%) compared to adjacent to the tumour (21.7%) ($p < 0.001$).

In conclusion, the research project provides knowledge about risk factors, change in incidence, and treatment methods over 20 years for PeIN. For penile cancer, HR HPV types were significantly more common in penile cancer cases than in age-matched controls. The finding of active HPV16 in penile cancer suggests that HPV16 is an oncogenic driver of the disease.

I defended my doctoral thesis named Penile Intraepithelial Neoplasia and Penile Cancer – risk factors and treatment April 1st, 2022. The **Nordic Dermatology Association Research Grant 2021** was a great financial support in finishing my thesis. The grant was used to pay for the statistician helping with age standardizing the PeIN incidence and to pay my salary, so that I could have time for research and be off clinical work in the department of dermatology.