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Despite advances in penile cancer management, the mechanisms behind tumour progression and spread remain elusive. Currently, clinically node-negative patients are stratified into risk groups based solely on primary tumour features, as current imaging lacks sensitivity for detecting occult lymph node metastases and no validated predictive biomarkers are available yet.

However, the present risk stratification, where surgery is the cornerstone of both diagnostics and treatment, needs an overhaul. Despite its high sensitivity, the risk of false-negative results and associated morbidity cannot be disregarded when performing dynamic sentinel node biopsy (DSNB). Conversely, unconditional inguinal lymph node dissection (ILND) would mean overtreatment with the risk of severe adverse effects on quality of life. Additionally, an improved understanding of the possible risks of second cancers related to persistent HPV infection can help decrease subsequent morbidity and mortality. Rapid progress in molecular biology offers hope for more precise initial risk stratification of cancer patients. Identifying novel biomarkers for aggressive penile cancer is of utmost importance to enable individually tailored therapy, improve survival, and minimise overtreatment. This thesis is based on four papers addressing these challenges.

Paper I examines the risk of second HPV-associated cancers (oral, oropharyngeal, and anal) in penile cancer patients.

Paper II assesses long-term morbidity following ILND with a focus on infectious and thromboembolic events.

Paper III explores the value of a panel of 14 soluble immune checkpoint proteins for predicting lymph node metastases.

Paper IV evaluates the sensitivity and complication rates of DSNB performed at a tertiary national referral centre.

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DOMINIK GLOMBIK Penile cancer: Diagnosis, prognosis, and treatment

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