Histological tumour type (Core)

All vaginal carcinomas should be typed according to the most recent edition of the World Health Organization (WHO) Classification of Tumours of Female Genital Tumours, 5th edition, 2020 (Table 1).[1] The International Collaboration on Cancer Reporting (ICCR) dataset includes 5th edition Corrigenda, June 2021.[2] While squamous cell carcinoma (SCC) is by far the most common carcinoma to arise in the vagina, these neoplasms are uncommon and thus care should be taken to rule out secondary involvement from adjacent sites, especially the cervix and vulva. Although there are no 'hard and fast' rules, a diagnosis of a cervical SCC in the past five years is usually taken as evidence for exclusion of a primary vaginal SCC. Aligning with SCC of the vulva and cervix, SCC of the vagina is divided in the 2020 WHO Classification[1] into human papillomavirus (HPV)-associated and HPV-independent types. HPV-associated SCC are secondary to persistent infection by oncogenic high-risk HPV (most commonly type 16) and are associated with smoking, immunosuppression and often multifocal disease including HPV-associated lesions in other areas of the lower female genital tract (vulva, cervix) and anal/perianal regions.[3,4] Similar to the vulva, primary vaginal HPV-associated SCC are more likely to be non-keratinizing, basaloid and warty, while HPV-independent SCC are more likely to be keratinizing. The presence of an adjacent high grade squamous intraepithelial lesion (HSIL) may be useful in suggesting an HPV-associated lesion. However, as in the vulva, in practice, ancillary testing is necessary to determine the HPV status given the overlap in morphology in some cases (see **ANCILLARY STUDIES**).[4,5] When HPV status cannot be confidently determined or resources are not available to undertake ancillary testing, a morphological diagnosis of SCC, not otherwise specified (NOS) is acceptable, although this is not recommended. Although because of the rarity of these neoplasms within the vagina, evidence is much more limited compared to the vulva, HPV-independent SCC have worse disease-free and overall survival compared to HPV-associated SCC, independent of age and stage.[6]

Grading of vaginal SCC is not recommended and is not included as a core or non-core item in this dataset. Grading has not been shown to correlate with clinical outcome. In fact, as with vulval SCC, there is a paradox in that HPV-independent SCC, which tend to be keratinising and often well-differentiated have a worse prognosis than HPV-associated SCC, which are typically non-keratinising, basaloid and poorly differentiated. In addition, no validated grading system exists for primary vaginal SCC.

Primary adenocarcinomas of the vagina are extremely rare and of various morphological types, including HPV-associated, endometrioid, clear cell, mucinous (gastric-type or intestinal-type) and mesonephric; adenocarcinoma of periurethral Skene gland origin may also occur and present as a primary vaginal neoplasm.[7-11] The specific histologic type should be specified in the report. These categories of adenocarcinoma are broadly similar to those described in the cervix and before diagnosing a primary vaginal adenocarcinoma, a metastasis from elsewhere should always be excluded. The most likely alternative site of primary depends on the morphological type. For example, before diagnosing an HPV-associated adenocarcinoma or a gastric-type adenocarcinoma, a primary in the cervix should be excluded and before diagnosing an intestinal-type adenocarcinoma, a large intestinal primary should be ruled out. Some primary vaginal adenocarcinomas, for example those of gastric, HPV-associated and clear cell type may be associated with and arise from vaginal adenosis via 'atypical adenosis' which is usually sporadic but which may be secondary to in-utero exposure to diethylstilbestrol.

Carcinosarcomas, adenosquamous carcinomas and adenoid basal carcinomas are extremely rare as primary neoplasms in the vagina and before diagnosing a primary vaginal carcinosarcoma or adenosquamous carcinoma, a metastasis from another site in the female genital tract should be excluded. Neuroendocrine neoplasia is classified according to the 2020 WHO Classification[1]

(neuroendocrine tumour, small cell neuroendocrine carcinoma, large cell neuroendocrine carcinoma, mixed neuroendocrine-non-neuroendocrine carcinoma); again these are extremely rare primary vaginal neoplasms.

Table 1: World Health Organization classification of malignant epithelial tumours of the vagina.[1]

Descriptor	ICD-O codes[a]
Squamous cell carcinoma, HPV-associated	8085/3
Squamous cell carcinoma, HPV-independent	8086/3
Squamous cell carcinoma NOS	8070/3
Adenocarcinoma NOS	8140/3
Adenocarcinoma, HPV-associated	8483/3
Endometrioid adenocarcinoma NOS	8380/3
Clear cell adenocarcinoma NOS	8310/3
Mucinous carcinoma, gastric type	8482/3
Mucinous adenocarcinoma	8480/3
Mesonephric adenocarcinoma	9110/3
Carcinosarcoma NOS	8980/3
Carcinoma of Skene, Cowper, and Littré glands	8140/3
Adenosquamous carcinoma	8560/3
Adenoid basal carcinoma	8098/3

[a] These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).[12] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Incorporates all relevant changes from the 5th Edition Corrigenda June 2021.

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