Lymph node status (Core)

Lymph node involvement in vulval cancer is one of the most important adverse prognostic parameters,¹ and the appropriate management and pathological assessment of regional (inguinofemoral) lymph nodes is considered the most important factor in reducing mortality from early vulval cancer.² Regional nodal assessment is therefore typically indicated in all carcinomas (with the exception of basal cell carcinomas) that are greater than International Federation of Gynecology and Obstetrics (FIGO) Stage IA (pT1A) on clinicopathological assessment, i.e., those that exceed 20 millimetres (mm) in maximum size, those with greater than 1 mm depth of invasion and those of any size that involve adjacent structures (lower third of urethra, lower third of vagina or anus).^{3,4} Clinically suspicious/palpable inguinal nodes should be biopsied. Tumours that are <40 mm in size and \geq 20 mm from the midline are usually managed by an ipsilateral inguinofemoral lymphadenectomy. Bilateral inguinofemoral lymphadenectomy is typically undertaken in tumours larger than 40 mm, those that cross or are located within 20 mm of the midline, or those that clinically or radiologically are felt to have positive ipsilateral lymph nodes.⁵ Significant changes in surgical practice in the last decades, both in terms of vulvar excision and nodal assessment have led to publication of algorithms to help direct surgical procedure.

When lymphadenectomy is performed, one or more sections of all identified nodes should be submitted for histological examination, including sections containing perinodal fat to confirm the presence or absence of extracapsular extension, especially if grossly suspected. For nodes which are grossly involved by tumour, representative sampling is acceptable whereas nodes which are not suspicious should be submitted in their entirety after sectioning at 2 mm intervals perpendicular to the long axis of the node. Ultrastaging does not need to be performed for lymphadenectomies (see discussion on sentinel lymph node biopsy (SLNB) below)).

Lymph node status is a powerful indicator of local recurrence and survival. The site, size and nature of nodal metastasis all influence prognosis and are integral to tumour stage. Involvement of regional lymph nodes represents Stage III, and this is further subdivided according to the number of involved nodes, the maximum size of the deposit and the presence or absence of extracapsular spread. It has been shown in multivariate analysis that extracapsular lymph node spread is an independent prognostic factor for earlier recurrence and overall survival.⁶ The presence of fixed or ulcerated inguinofemoral lymph nodes as determined by clinical examination, or of involvement of nonregional, including pelvic, lymph nodes, upstages the carcinoma to Stage IVA or IVB respectively. The anatomic location and number of lymph nodes dissected, the number containing tumour and the size of the largest tumour deposit should be accurately documented in the pathology report. In recent years, owing to the high morbidity of groin dissection, SLNB has become the standard of care in some vulval cancers.⁷⁻⁹ SLNB can be performed for unifocal lesions which are confined to the vulva and less than 40 mm in size, with no prior vulval or groin surgery or radiation, and in the absence of clinically palpable or radiologically suspicious nodes. The evaluation of sentinel lymph nodes should follow an established locally agreed protocol. It should be documented whether or not an ultrastaging procedure has been carried out and whether nodal metastases have been detected on routine histological examination (without ultrastaging) or by ultrastaging, including cytokeratin immunohistochemistry. Sentinel (and non-sentinel) nodal involvement should be recorded as presence of isolated tumour cells (ITC), micrometastases (MIC) or macrometastases (MAC). An ideal ultrastaging protocol used should detect almost all MIC (0.2-2 mm). The anatomic location and number of lymph nodes dissected, the number containing tumour, the size of the largest tumour deposit and the presence or absence of extracapsular spread should be accurately documented in the pathology report. According to TNM8,¹⁰ nodal involvement should be recorded as the presence ITC (<0.2 mm), MIC (0.2-2 mm) or MAC (>2 mm). MAC are regarded as pN1, MIC as pN1 (mi) and ITCs are pN0 (i+); ITCs do not upstage a carcinoma. The possibility of performing radiologicallyguided fine needle aspiration cytology (FNAC) of suspicious lymph nodes should be considered. A positive result enables the surgeon to immediately perform a bilateral inguinofemoral lymphadenectomy, thus avoiding an unnecessary SLNB.

References

- 1 Chen J and Ln H (2020). A review of prognostic factors in squamous cell carcinoma of the vulva: Evidence from the last decade. *Semin Diagn Pathol*(38(1):37-49).
- 2 Rogers LJ and Cuello MA (2018). Cancer of the vulva. *Int J Gynaecol Obstet* 143 Suppl 2:4-13.
- 3 Koh WJ, Greer BE, Abu-Rustum NR, Campos SM, Cho KR, Chon HS, Chu C, Cohn D, Crispens MA, Dizon DS, Dorigo O, Eifel PJ, Fisher CM, Frederick P, Gaffney DK, Han E, Higgins S, Huh WK, Lurain JR, 3rd, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Fader AN, Remmenga SW, Reynolds RK, Tillmanns T, Ueda S, Valea FA, Wyse E, Yashar CM, McMillian N and Scavone J (2017). Vulvar Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 15(1):92-120.
- 4 Dellinger TH, Hakim AA, Lee SJ, Wakabayashi MT, Morgan RJ and Han ES (2017). Surgical Management of Vulvar Cancer. *J Natl Compr Canc Netw* 15(1):121-128.
- 5 Stehman FB and Look KY (2006). Carcinoma of the vulva. *Obstet Gynecol* 107(3):719-733.
- 6 Ferrari F, Forte S, Ardighieri L, Bonetti E, Fernando B, Sartori E and Odicino F (2019). Multivariate analysis of prognostic factors in primary squamous cell vulvar cancer: The role of perineural invasion in recurrence and survival. *Eur J Surg Oncol* 45(11):2115-2119.
- 7 Coleman RL, Ali S, Levenback CF, Gold MA, Fowler JM, Judson PL, Bell MC, De Geest K, Spirtos NM, Potkul RK, Leitao MM, Jr., Bakkum-Gamez JN, Rossi EC, Lentz SS, Burke JJ, 2nd, Van Le L and Trimble CL (2013). Is bilateral lymphadenectomy for midline squamous carcinoma of the vulva always necessary? An analysis from Gynecologic Oncology Group (GOG) 173. *Gynecol Oncol* 128(2):155-159.
- Van der Zee AG, Oonk MH, De Hullu JA, Ansink AC, Vergote I, Verheijen RH, Maggioni A,
 Gaarenstroom KN, Baldwin PJ, Van Dorst EB, Van der Velden J, Hermans RH, van der Putten
 H, Drouin P, Schneider A and Sluiter WJ (2008). Sentinel node dissection is safe in the
 treatment of early-stage vulvar cancer. J Clin Oncol 26(6):884-889.
- 9 Fotopoulou C, Ind T, Baldwin P, Crawford R, Devaja O, Dobbs S, Frost J, Gajjar K, Ganesan R, Kaushik S, Morrison J, Nobbenhuis M, Ratnavelu N, Rolland P, Singh N, Taylor A, Sundar S and Nordin A (2019). Sentinel lymph node consensus document of the British Gynaecological Cancer Society for endometrial, vulvar, and cervical cancers. *Int J Gynecol Cancer* 29(9):1348-1350.
- 10 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). Union for International Cancer Control. TNM Classification of Malignant Tumours, 8th Edition, Wiley, USA.