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Clinical significance and prognostic value of femoral lymph node metastasis in FIGO stage III vulvar carcinoma

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Abstract

Objectives: To determine the clinical significance and prognostic value of femoral lymph node metastasis (FLNM) in patients with International Federation of Gynecology and Obstetrics (FIGO) stage III vulvar carcinoma.

Methods: The medical records of patients with vulvar carcinoma who underwent inguinofemoral lymphadenectomy between 1990 and 2013 were retrospectively reviewed.

Results: Of 66 patients with stage III vulvar carcinoma, 42 had superficial lymph node metastasis (SLNM) only and 24 had FLNM. Significantly higher rates of extracapsular invasion (P = 0.008), multiple nodal metastasis (P = 0.042), and advanced FIGO substage (P = 0.026) as well as a larger tumor diameter (≥4 cm, P = 0.023) and greater depth of invasion (≥5 mm, P = 0.020) were observed among patients with FLNM compared to those with SLNM only. After a median follow-up of 46 months (range, 6–172 months), 35 patients experienced relapse and 30 died from disease. The 5-year cancer-specific survival (CSS) rates were 70.1% and 30.8% for patients with SLNM only and FLNM, respectively (P = 0.001). In multivariate analysis, only FLNM was found to be an independent risk factor for reduced recurrence-free survival (RFS) and CSS among patients with stage III vulvar cancer (hazard ratio [HR] = 2.277, P = 0.037 for RFS; HR = 2.360, P = 0.042 for CSS). When the FLNM cases were considered together as stage IIIC, significant differences emerged in the RFS (P = 0.002) and CSS (P = 0.004) among the re-divided FIGO substages.

Conclusions: FLNM represented an unfavorable status of node metastasis with a worse prognosis compared to that of SLNM alone, and this should be considered in a future FIGO staging system for vulvar cancer.

Keywords: Vulvar cancer; FIGO; Lymph node; Femoral; Inguinal; Metastasis

Introduction

In vulvar cancer, lymph node metastasis (LNM) is the most important pathway by which the cancer spreads.[1] LNM occurs in 20–30% of apparent early-stage vulvar cancer cases and is associated with significantly diminished prognosis.[2] The standard surgical approach for vulvar cancer treatment involves radical excision of the primary tumor and inguinal lymphadenectomy (IL). The extensive boundary of lymphadenectomy is not just essential for staging but also a measure of the therapeutic effect.[3] On the other hand, recurrent diseases emerge more frequently in the inguinal region than at the vulva.[4] While vulvar recurrence can be salvaged by further operation, groin recurrence usually leads to a fatal outcome due to lack of an effective therapy.[5] Thus, the primary management of vulvar cancer demands more extensive evaluation of the inguinal lymph nodes.

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The number, diameter, and extranodal invasion of nodal metastases are reported to be important factors that influence survival.[6,7] The International Federation of Gynecology and Obstetrics (FIGO) has made revisions corresponding to these evidences in the latest staging system (2009) for vulvar cancer.[8] According to the current staging system, patients with LNM should be assigned a substage according to the number of involved nodes, diameter of the metastatic lesion, and presence of extranodal invasion. However, a large cohort analysis revealed that the new staging standards are underpowered to discriminate the prognosis of substages of stage III vulvar cancer.[9] Therefore, the current classification of node metastasis requires further investigation in order to more precisely describe the extent of disease.

Femoral lymph nodes, which are located in the fossa ovalis medial to the femoral vein, are commonly recognized as deep inguinal lymph nodes that collect lymph drainage from the superficial groin and drain into the pelvic region.[10] Theoretically, femoral lymph node metastasis (FLNM) should occur only when superficial groin nodes are positive. In the Gynecologic Oncology Group (GOG) 74 study,[11] patients were treated by modified vulvectomy and superficial IL in which the femoral nodes were not dissected. Yet, there was an unexpectedly high rate of groin relapse, implying a non-negligible role of femoral nodes in surgical assessment. Unfortunately, data on the clinical characteristics of FLNM in vulvar cancer are scarce, and the prognostic value of FLNM remains largely unknown.

In this retrospective study, we analyzed the outcomes of IL in patients with vulvar carcinoma in order to determine the clinical significance and prognostic value of FLNM in patients with FIGO stage III vulvar cancer.

Patients and methods

Patient characteristics

The medical records of 369 patients with vulvar carcinoma treated at Sun Yat-sen University Cancer Center (SYSUCC) between January 1990 and December 2013 were retrospectively reviewed with institutional review board approval. Patients who had confirmed lymph node metastasis after surgery involving both superficial and deep IL were enrolled in this study. Cases were excluded if only superficial nodes were dissected, neoadjuvant radiochemotherapy was applied, fixed or bulky nodes were present, an ulcer in the groin was present, vulvar sarcoma or melanoma was identified, the disease was at T4-stage (FIGO 2009), pelvic or distant metastasis was suspected or confirmed, or the follow-up data was not available. The final study population included 66 patients with a median age of 58 years (range, 24–75 years). All patients were diagnosed with carcinoma of the vulva by biopsy or wedge resection of the primary tumor. The histological type was squamous cell carcinoma in 60 patients and adenocarcinoma in 6 patients. The preoperative evaluation consisted of gynecologic examination, inguinal palpation, serum squamous cell carcinoma antigen (SCC-Ag), and imageological examination of the chest, abdomen, and pelvis. None of the patients presented pelvic or distant disease before treatment.

Surgical procedure

In our series, patients were treated by modified radical vulvectomy and unilateral or bilateral IL. Modified radical vulvectomy refers to the wide excision of the primary vulvar tumor with the normal margin of at least 2 cm and deep excision to the urogenital diaphragm. A uniform surgical extent was adopted for IL, which was similar to that described by Micheletti et al.[12] The dissection of superficial nodes involved a triangular region with boundaries superiorly along the inguinal ligament, laterally along the sartorius muscle, and medially along the adductor longus muscle. After removal of superficial nodes, the femoral canal was carefully inspected and the femoral nodes medial to the femoral vein were identified and dissected. The saphenous vein and fascia lata were preserved in this procedure. All operations were performed by senior gynecologic oncologists.

Adjuvant treatment and follow-up

Adjuvant radiotherapies were planned in all cases with more than one metastatic nodes or extracapsular invasion. Radiotherapy consisted of external beam radiation to the groin and pelvic regions. Pelvic external beam radiation was planned only when Cloquet's node (the uppermost femoral node) was involved. All radiotherapy was performed using linear accelerators or a Co^{60} teletherapy machine with a median dose of 56 Gy (range: 50–70 Gy) in 20–28 fractions. When all required treatments were finished, patients were advised to follow-up every 3 months during the first 2 years and twice per year thereafter.

Data collection and statistics

Data on surgical outcomes and survival were obtained from medical charts, outpatient clinic records, and the SYSUCC follow-up office. All pathological slides of lymph nodes were re-reviewed by two pathologists (P. Sun and X.K. Zhang) in order to assign a new FIGO (2009) stage for each patient. Cancer-specific (CSS) was calculated as the time from initial diagnosis to the cancer-related death or last follow-up, and recurrence-free survival (RFS) was calculated as the time from initial diagnosis to the emergence of relapse or last follow-up. The relationship between LNM and clinicopathological factors was investigated using Chi-square or Fisher's exact tests. Survival curves were plotted according to the Kaplan–Meier method and compared by the log-rank test. Multivariate survival

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