

Inguinal Sentinel Lymph Node Dissection vs. Complete Inguinal Lymph Node Dissection in Patients with Vulvar Cancer

LUKAS A. HEFLER, CHRISTOPH GRIMM, LUCIA SIX, VERONIKA SEEBAKER, STEPHAN POLTERAUER,
ELMAR JOURA, CLEMENS TEMPFER, GERHARD SLIUTZ and ALEXANDER REINTHALLER

Department of Obstetrics and Gynecology, Medical University of Vienna, Austria

Abstract. *Background:* The aim of this retrospective study was to ascertain the postoperative morbidity in patients with vulvar cancer undergoing sentinel lymph node vs. complete inguinal lymph node dissection. *Patients and Methods:* In total 29 and 46 patients with vulvar cancer, were treated by the technique of inguinal sentinel lymph node dissection or complete inguinal lymph node dissection, respectively. *Results:* Inguinal sentinel lymph node dissection was associated with a shorter operation time, a reduced rate of inguinal seromas, wound breakdown and wound infection, fewer days of inguinal drainage, and reduced postoperative lymphatic secretion. *Conclusion:* Evidence of reduced peri- and postoperative morbidity with the sentinel lymph node technique for inguinal lymph node dissection in patients with vulvar cancer was demonstrated.

Vulvar cancer is the fourth most common gynecological cancer comprising five percent of malignancies of the female genital tract. The goal of surgery in early stage disease is to cure the disease with the least postoperative and long-term morbidity possible (1, 2). Surgical staging by wide local excision and separate incisions for inguinofemoral lymphadenectomy (1) is standard in the treatment of vulvar cancer. Despite the good prognosis with overall survival rates of 70-80%, a high postoperative morbidity including seromas, wound breakdown, wound infection, and lymphatic secretion has been described in patients undergoing complete inguinofemoral lymphadenectomy (1).

The sentinel lymph node dissection technique has therefore been introduced. The studies published to date have focused on establishing the feasibility of the sentinel node detection, the diagnostic accuracy and the choice of

tracer (3-8). Preliminary data have been published with respect to the oncological safety of this technique (9). However, reports critical of this technique have also been published (10-12). Although lower morbidity with the sentinel technique seems probable, no study has ascertained the postoperative morbidity in patients with vulvar cancer undergoing inguinal sentinel lymph node dissection vs. complete inguinal lymph node dissection.

Patients and Methods

The clinical data were collected retrospectively from files at the Medical University of Vienna, Department of Obstetrics and Gynecology. Seventy-five consecutive patients with invasive squamous cell vulvar cancer treated between August 1995 and January 2006 were included in the study. Patients with vulvar cancer with an invasion depth of no more than 1 mm, vulvar melanoma, adenocarcinoma, basal cell cancer and verrucous carcinoma were excluded.

From 1995 to 2000, only complete inguinal lymph node dissections were performed. In 1998, the sentinel lymph node technique was introduced. From 1998 to 2000, the sentinel lymph node technique was always followed by a complete inguinal lymph node dissection. From 2001 up to the present, all patients were offered the sentinel lymph node technique without being followed by a complete lymph node dissection. After preoperative counselling, 29 and 19 patients opted for the sentinel lymph node technique and complete inguinal lymph node dissection, respectively. In the cases with a tumor at least 2 cm from the midline, only the unilateral groin was dissected. In the cases of lymph node metastases, postoperative radiotherapy was applied according to standardized treatment protocols. Staging and grading was performed according to the current International Union Against Cancer (UICC) classification.

The technique of sentinel lymph node dissection was as described earlier (6). Routine histopathological examination of the sentinel and all other lymph nodes was performed using hematoxylin-eosin staining and serial sections with standard techniques. In brief, the nodes were first cut in 2- to 3-mm intervals and then each block was cut in 400- μ m intervals. In the case of negative sentinel nodes, additional immunohistochemical cytokeratin examination was performed, as described previously (6). All the patients were followed up at three month intervals, including inspection, vagino-rectal and groin palpation, and in some cases serum tumor marker evaluation.

Correspondence to: Lukas A. Hefler, MD, Department of Obstetrics and Gynecology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria. Tel: +43 1 40400 2962, Fax: +43 1 40400 2911, e-mail: lukas.hefler@meduniwien.ac.at

Key Words: Vulvar cancer, sentinel, postoperative morbidity, prognosis.

Table I. Clinical and outcome parameters in patients with vulvar cancer treated by inguinal sentinel lymph node dissection vs. complete inguinal lymph node dissection.

	Sentinel lymph node dissection	Complete inguinal lymph node dissection	P-value
Number of patients	29	46	
Patients' age at surgery	67.7 (14.0)	64.1 (15.9)	0.4
Tumor stage			
pT1	23	25	0.07
pT2	6	19	
pT3	-	2	
Lymph node status			0.4
pN0	21	31	
pN1	9	15	
Histological grade			0.4
G1	7	18	
G2	19	24	
G3	3	4	
Unilateral lymphadenectomy	12 (41.3%)	6 (13%)	0.01
Removed lymph nodes	4.4 (3.6)	11.8 (6)	<0.001
Operation time (min)	85.5 (28.7)	120.7 (52.0)	0.002
Length of hospital stay (days)	12.6 (6.1)	22.9 (11.35)	<0.001
Time of follow-up	35.8 (122.1)	35.3 (35.1)	0.9
Number of recurrences/deaths	5 (17.2%)/3 (10.3%)	16 (34.8%)/15 (32.6%)	0.2/0.06

Values are given either as numbers or as means (standard deviation).

Table II. Clinical and outcome parameters in groins of patients with vulvar cancer treated by inguinal sentinel lymph node dissection versus complete inguinal lymph node dissection.

	Sentinel lymph node dissection	Complete inguinal lymph node dissection	P-value
Number of dissected groins	46	85	
Removed lymph nodes	2.5 (2.2)	6.3 (3.5)	<0.001
Days of inguinal drainage	3.3 (1.5)	6.9 (4.6)	<0.001
Lymphatic secretion (mL)	131.1 (159.7)	480.7 (664.8)	0.001
Number of inguinal postoperative morbidity*	4/46 (8.7%)	27/85 (31.8%)	0.006
Number of primary groin recurrences	1	5	0.4

Values are given either as numbers or as means (standard deviation). *Includes inguinal seromas, abscesses, and wound breakdown.

Table III. Kaplan-Meier analysis and Cox regression model of prognostic covariates in patients with vulvar cancer.

	Disease-free survival		Overall survival	
	Univariate P	Multivariate P	Univariate P	Multivariate P ^c
Tumor stage	<0.001 ^a	0.2	<0.001 ^a	0.5
Lymph node involvement	<0.001 ^a	0.004	<0.001 ^a	0.001
Histological grade	0.001 ^a	0.6	0.02 ^a	0.5
Age at diagnosis	0.007 ^b	0.01	0.009 ^b	0.006
Sentinel vs. complete lymph node dissection	0.9 ^a	0.49	0.3 ^a	0.03

^aLog-rank test; ^bunivariate Cox regression model; ^cmultivariate Cox regression model.

The statistics were performed patient-wise and groin-wise depending on the outcome parameter. The comparisons between unpaired groups were made using Student's *t*-tests and Chi-square tests where appropriate. The survival probabilities were calculated by the product limit method of Kaplan and Meier. The differences between groups were tested using the log-rank test. The results were analysed for the end point of disease-free and overall survival. The survival times of patients disease-free or still alive were censored with the last follow-up date. Univariate and multivariate Cox regression models for disease-free and overall survival were performed. *P*-values of <0.05 were considered statistically significant. The statistical software SPSS 11.0 for Windows (SPSS 11.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

The clinical and outcome parameters are shown in Table I. Histologically, all the tumors were squamous cell vulvar carcinomas and no correlation between the sentinel lymph node dissection technique and lymph node status, tumor classification, tumor grade or patients' age was ascertained (Table I). A total of 131 groins (complete inguinal lymph node dissection: n=85, sentinel lymph node technique: n=46) were dissected. The outcome parameters with respect to dissected groins are shown in Table II.

Based on the relatively short mean follow-up of 35.5 (SD 79.7) months, the data with respect to the prognostic potential of the investigated parameters must be seen as preliminary and are shown in Table III. In addition to tumor related deaths, two patients died of co-existent medical conditions (myocardial infarction, stroke) and 55 patients had no evidence of disease at the time of last observation. The lymph node status was the only prognostic parameter associated with disease-free and overall survival in both univariate and multivariate models.

Discussion

In our study, we present a comparison of complete inguinal lymph node dissection vs. the sentinel lymph node technique in patients with operable vulvar cancer. Although some critical studies have been published (10-12), most reports have been in favor of the sentinel lymph node technique and in the present additional data with respect to a significant decrease of postoperative morbidity with this less invasive treatment were obtained. All the investigated outcome parameters were in favor of the sentinel technique. The patients undergoing inguinal sentinel lymph node dissection had a significantly shorter operation time and length of hospital stay, a significantly reduced rate of seromas, wound breakdown and wound infection, shorter inguinal drainage, and less postoperative lymphatic secretion.

Due to the retrospective design of our study, selection bias cannot be excluded. However, clinical and pathological parameters were evenly distributed between both the

groups. Therefore, it can be hypothesized that a randomized study would not yield significantly different results. In accordance with previously published data, no impaired outcome for patients treated with the sentinel technique only, was ascertained.

In conclusion, these data add evidence of reduced peri- and postoperative morbidity with the sentinel lymph node technique for inguinal lymph node dissection in patients with vulvar cancer.

Acknowledgements

Financial support was provided by the Ludwig Boltzmann Institute of Gynecology and Gynecologic Oncology, Vienna, Austria.

References

- 1 Hakim AA and Terada KY: Sentinel node dissection in vulvar cancer. *Curr Treat Options Oncol* 7: 85-91, 2006.
- 2 Dardarian TS, Gray HJ, Morgan MA, Rubin SC and Randall TC: Saphenous vein sparing during inguinal lymphadenectomy to reduce morbidity in patients with vulvar carcinoma. *Gynecol Oncol* 101: 140-142, 2006.
- 3 Wydra D, Sawicki S, Emerich J and Romanowicz G: Evaluation of sentinel node detection in vulvar cancer. *Nucl Med Rev Cent East Eur* 8: 128-301, 2005.
- 4 Selman TJ, Luesley DM, Acheson N, Khan KS and Mann CH: A systematic review of the accuracy of diagnostic tests for inguinal lymph node status in vulvar cancer. *Gynecol Oncol* 99: 206-214, 2005.
- 5 Dhar KK and Woolas RP: Lymphatic mapping and sentinel node biopsy in early vulvar cancer. *BJOG* 112: 696-702, 2005.
- 6 Sliutz G, Reinthaller A, Lantzsch T, Mende T, Sinzinger H, Kainz C and Koelbl H: Lymphatic mapping of sentinel nodes in early vulvar cancer. *Gynecol Oncol* 84: 449-452, 2002.
- 7 De Cicco C, Sideri M, Bartolomei M, Grana C, Cremonesi M, Fiorenza M, Maggioni A, Bocciolone L, Mangioni C, Colombo N and Paganelli G: Sentinel node biopsy in early vulvar cancer. *Br J Cancer* 82: 295-299, 2000.
- 8 de Hullu JA, Hollema H, Piers DA, Verheijen RH, van Diest PJ, Mourits MJ, Aalders JG and van der Zee AG: Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *J Clin Oncol* 18: 2811-2816, 2000.
- 9 Terada KY, Shimizu DM, Jiang CS and Wong JH: Outcomes for patients with T1 squamous cell cancer of the vulva undergoing sentinel node biopsy. *Gynecol Oncol* 102: 200-203, 2006.
- 10 Knopp S, Holm R, Trope C and Nesland JM: Occult lymph node metastases in early stage vulvar carcinoma patients. *Gynecol Oncol* 99: 383-387, 2005.
- 11 de Hullu JA, Oonk MH, Ansink AC, Hollema H, Jager PL and van der Zee AG: Pitfalls in the sentinel lymph node procedure in vulvar cancer. *Gynecol Oncol* 94: 10-15, 2004.
- 12 Frumovitz M, Ramirez PT, Tortolero-Luna G, Malpica A, Eifel P, Burke TW and Levenback C: Characteristics of recurrence in patients who underwent lymphatic mapping for vulvar cancer. *Gynecol Oncol* 92: 205-210, 2004.

Received August 2, 2007

Revised November 13, 2007

Accepted December 10, 2007