Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Prognostic value of lymph node ratio and number of positive inguinal nodes in patients with vulvar cancer

Stephan Polterauer [a,b,*], Richard Schwameis [a], Christoph Grimm [a], Ronalds Macuks [c], Sara Iacoponi [d], Kamil Zalewski [e,f], Ignacio Zapardiel [d], VULCAN Study Collaborative Group

[a] Department of General Gynaecology and Gynaecological Oncology, Gynecologic Cancer Unit - Comprehensive Cancer Center, Medical University of Vienna, Vienna, 1090, Austria
[b] Karl Landsteiner Institute for General Gynecology and Experimental Gynecologic Oncology, Vienna, 1090, Austria
[c] Latvian Oncology Center of Riga - Eastern Clinical University Hospital, Riga, Latvia
[d] Gynecologic Oncology Unit, La Paz University Hospital - IdiPAZ, Madrid, Spain
[e] Department of Gynecologic Oncology, Holycross Cancer Center, Kielce, Poland
[f] Department of Molecular and Translational Oncology, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland

HIGHLIGHTS

- High LNR is associated with unfavorable survival in patients with vulvar cancer.
- High LNR shows reduced overall survival independent of number of positive nodes.
- In patients with a LNR > 20% adjuvant radiation improved overall survival significantly.
- LNR allows more accurate prognostic stratification than number of positive nodes.

ARTICLE INFO

Article history:
Received 5 May 2017
Received in revised form 24 July 2017
Accepted 30 July 2017
Available online xxxx

Keywords:
Lymph node metastases
Lymph node ratio
Prognosis
Recurrence
Vulvar cancer

ABSTRACT

Objective. To estimate the prognostic significance of lymph node ratio and number of positive nodes in vulvar cancer patients.

Methods. This international multicenter retrospective study included patients diagnosed with vulvar cancer treated with inguinal lymphadenectomy. Lymph node ratio (LNR) is the ratio of the number of positive lymph nodes (LN) to the number of removed LN. Patients were stratified into risk groups according to LNR. LNR was correlated with clinical-pathological parameters. Survival analyses were performed.

Results. This analysis included 745 patients. In total, 292 (39.2%) patients had positive inguinal LN. The mean (SD) number of resected and positive LN was 14.1 (7.6) and 3.0 (2.9), respectively. High LNR was associated with larger tumor size and higher tumor grade. Patients with LNRs 0% (N0), >0 < 20%, and >20% had 5-year overall survival (OS) rates of 90.9%, 70.7%, and 61.8%, respectively ($P < 0.001$). LNR was associated with both local and distant recurrence-free survival ($P < 0.001$). Patients with 0, 1, 2, 3 or >3 positive lymph nodes had 5-year OS rates of 90.9%, 70.8%, 67.8%, 70.8% and 63.4% respectively ($P < 0.001$). In multivariate analysis, LNR ($P = 0.01$) and FIGO stage ($P < 0.001$), were associated with OS, whereas the number of positive nodes ($P = 0.8$), age ($P = 0.2$), and tumor grade ($P = 0.7$), were not. In high-risk patients, adjuvant radiotherapy was associated with improved survival.

Conclusions. LNR provides useful prognostic information in vulvar cancer patients with inguinal LN resection in vulvar cancer. LNR allows for more accurate prognostic stratification of patients than number of positive nodes. LNR seems useful to select appropriate candidates for adjuvant radiation.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Vulvar cancer is the fourth most common gynecologic cancer and comprises for only approximately 5 to 6% of malignancies of the female genital tract [1]. Over the last decades, incidence has risen by 20% and the median age at diagnosis decreased [2,3]. Inguinal lymph node involvement is the most significant prognostic factor for survival in patients with vulvar cancer [4]. Reported five-year survival ranges from 70 to 93% for patients with negative nodes, to 25 to 41% for those with positive nodes [5,6]. In node positive disease outcome can vary widely depending on the extent of lymph node involvement. However, the number of positive lymph nodes can be influenced by the extent of

* Corresponding author at: Department of Obstetrics and Gynecology, Medical University Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria.
E-mail address: stephan.polterauer@meduniwien.ac.at (S. Polterauer).

http://dx.doi.org/10.1016/j.ygyno.2017.07.142
0090-8258/© 2017 Elsevier Inc. All rights reserved.

Please cite this article as: S. Polterauer, et al., Prognostic value of lymph node ratio and number of positive inguinal nodes in patients with vulvar cancer, Gynecol Oncol (2017), http://dx.doi.org/10.1016/j.ygyno.2017.07.142

surgical staging. Adjuvant radiotherapy after surgical excision of the primary tumor and inguino-femoral lymphadenectomy was shown to improve prognosis in patients with lymph node involvement [7]. Various parameters influence the decision if adjuvant radiotherapy is administered [8].

Several recent studies have focused on the clinical relevance of lymph node ratio (LNR) in assessing prognosis in different solid tumors malignancies, such as endometrial, cervical and ovarian cancer [9–11]. LNR is defined as the ratio of the number of metastatic LNs to the total number of removed LNs. This parameter incorporates not only the burden of nodal disease and cancer spread but also the extent and quality of surgical staging. Therefore, LNRs are most meaningful when standardized comprehensive lymphadenectomy templates are utilized routinely in surgical practice. The purpose of this large cohort study was to investigate the value of LNR as well as number of positive nodes for estimating outcome in patients with vulvar cancer who had groin lymph nodes removed.

2. Methods

2.1. Patients

After receiving Institutional Review Board (IRB) approval, an international multicenter retrospective study of patients diagnosed with vulvar cancer was performed (VULCAN study). As published previously the study targeted 2453 vulvar cancer patients from 100 different centers, of which 1727 vulvar cancer cases (70.4%) were registered in an encrypted online database [12]. Data of patients treated between January 2001 and December 2005, including all histotypes, were collected. Participation in the study was offered to all oncological European centers via email calling and using the European Network of Young Gynecologist Oncologist (ENYGO) as well. Inclusion criteria were IRB approval from each collaborating center, pathological diagnosis of invasive carcinoma of the vulva, and primary treatment performed at the participating center.

2.2. Clinical management

Disease staging was based on the FIGO 2009 classification system [13]. Uniform criteria for surgical procedure nomenclature, pathologic variables, and sites of recurrence were used. Patients were treated according to international guidelines and treating clinician's decisions. In general ipsilateral lymph node dissection was performed for lateral lesions without clinically suspicious groins. Bilateral lymph node dissection was performed for midline lesions or when positive lymph nodes were suspected/found. However, due to the retrospective design of the study clinical management was not uniform based and decision was based upon clinical situation by the treating physician. All surgical specimens were fixed in formalin and embedded in paraffin prior to examination. Patient follow-up was carried out every three months for the first year, every 6 months until the fifth year and after that annually discharging the patient after 10 years. Data collection was performed via a web-based encrypted database.

2.3. Statistical analysis

Values are given as mean (standard deviation (SD)). One-Way ANOVA and Chi-squared tests were used to compare LNR and clinicopathological parameters. Patients were stratified into three risk groups according to LNR (0 vs. >0–20% vs. >20%) as published previously in the report from Gynecologic Oncolgy Group (GOG) protocol #37 [14]. LND was correlated with age (years, continuous variable), tumor size (mm, continuous variable), and histological grade (G1 vs. G2 vs. G3).

Univariate survival probabilities were calculated by the product limit method of Kaplan and Meier. Differences between groups were tested using the log-rank test. Multivariate Cox proportional hazard models for disease-free and overall survival were performed. A subgroup analysis was performed in the high-risk group and investigated the effect of adjuvant radiation on survival. The results were analyzed for the endpoint of disease-free and overall survival. Survival times of patients disease-free or still alive or dead as a result of other causes were censored with the last follow-up date. *P*-values of <0.05 were considered statistically significant. Statistical analysis was performed by use of the commercially available statistical software SPSS 24.0 for MAC (SPSS 24.0, IBM Inc., Armonk, NY).

3. Results

After excluding patients due to incomplete data entry, 1727 patients treated for vulvar cancer between January 2001 and December 2005 were registered for analyses. Information on the number of resected and positive nodes for calculation of LNR was available in 745 patients who had at least one node removed. Table 1 shows patients' characteristics of the cohort. The mean (SD) number of resected and positive lymph nodes was 14.1 (7.6) and 3.0 (2.9), respectively. The median (range) number of resected and positive lymph nodes was 13.0 (1–56) and 4.0 (1—22), respectively. Fig. 4 shows distribution of number of removed nodes. A total of 292 (39.2%) patients were found to have positive inguinal nodes. Patients were stratified into risk groups according to LNR values 0% (n = 453, 60.8%), >0–20% (n = 174, 23.4%) and >20% (n = 118, 15.8%), as previously described [14]. Clinico-

Table 1
Patients' characteristics.

Parameter	N (%) or mean (SD)
Total number of patients enrolled	745
Age at diagnosis (years)	69.9 (10.9)
Histological type	
Squamous cell carcinoma	700 (94.0%)
Melanoma	20 (2.7%)
Bartholin gland adenocarcinoma	6 (0.8%)
Paget disease	2 (0.3%)
Other	17 (2.3%)
Tumor stage	
FIGO I	372 (49.9%)
FIGO II	72 (9.7%)
FIGO III	272 (36.5%)
FIGO IV	29 (3.9%)
Histological grade	
G1	234 (31.4%)
G2	236 (31.7%)
G3	94 (12.6%)
Unknown	181 (24.3%)
Tumor size (mm)	34 (20.7)
Lymph nodes (LN)	
N0	453 (60.8%)
N1	292 (39.2%)
Resected LNs	14.1 (7.6)
Unilateral LN dissection	145 (19.5%)
Bilateral LN dissection	562 (75.4%)
Positive LNs[a]	1.2 (2.3)
Adjuvant teletherapy	215 (28.9%)
Recurrence status	
Patients with recurrent disease	313 (42.0%)
Local recurrence	226 (30.3%)
Distant recurrence	111 (14.9%)
Mean observation time (months)	47.7 (36.5)
Status at last observation	
Alive with no evidence of disease	421 (56.5%)
Alive with disease	208 (27.9%)
Tumor related death	116 (15.6%)

SD = standard deviation, FIGO = International Federation of Gynecologists and Obstetricians.
[a] Only node positive patients.

Please cite this article as: S. Polterauer, et al., Prognostic value of lymph node ratio and number of positive inguinal nodes in patients with vulvar cancer, Gynecol Oncol (2017), http://dx.doi.org/10.1016/j.ygyno.2017.07.142

Download English Version:

https://daneshyari.com/en/article/5695272

Download Persian Version:

https://daneshyari.com/article/5695272

Daneshyari.com