Gynecologic Oncology 140 (2016) 415–419

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Repeat sentinel lymph node procedure in patients with recurrent vulvar squamous cell carcinoma is feasible

Helena C. van Doorn [a,*], Heleen J. van Beekhuizen [a], Katja N. Gaarenstroom [b], Jacobus van der Velden [c], Ate G.J. van der Zee [d], Maaike H.M. Oonk [d], Johanna A. de Hullu [e]

[a] Department of Obstetrics and Gynecology, Erasmus MC Cancer Institute, PO Box 2040, 3000CA Rotterdam, The Netherlands
[b] Department of Gynecology, Leiden University Medical Center, 2333ZA Leiden, The Netherlands
[c] Department of Obstetrics and Gynecology, Academic Medical Center, Meibergdreef 9, 1105AZ Amsterdam, The Netherlands
[d] Department of Obstetrics and Gynecology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9700RB Groningen, The Netherlands
[e] Department of Obstetrics & Gynecology, Radboud University Medical Center Nijmegen, P.O. Box 9101, 6500HB Nijmegen, The Netherlands

HIGHLIGHTS

- In recurrent vulvar cancer an inguino femoral lymphadenectomy is recommended.
- The repeat Sentinel Lymph Node (SLN) procedure is technically demanding.
- Repeat SLN procedure is feasible, but not yet a safe alternative.

ARTICLE INFO

Article history:
Received 20 October 2015
Received in revised form 8 January 2016
Accepted 11 January 2016
Available online 12 January 2016

Keywords:
Vulvar cancer
Sentinel node procedure
Recurrence
Patients' preference

ABSTRACT

Objective. Standard treatment of primary T1 squamous cell carcinoma (SCC) of the vulva <4 cm consists of wide local excision (WLE) and sentinel lymph node (SLN) procedure of the groin(s). In case of a local recurrence WLE and inguino femoral lymphadenectomy (IFL) is generally recommended. In this study we assessed the feasibility of repeat SLN procedure in patients with recurrent vulvar SCC who were not able or willing to undergo IFL.

Methods. A retrospective study was performed in consecutive patients with recurrent vulvar SCC who underwent a repeat SLN procedure between 2006 and 2014. We present the clinical and pathological outcomes. The study conforms to the STROBE guidelines.

Results. A total number of 27 patients aged 35–87 years at first diagnosis of SCC of the vulva were identified. Median follow-up after 2nd surgery was 27.4 (range 2–96) months. In 78% of patients and in 84% of the groins the repeat SLN procedure was successful. No structured questionnaires were used to describe details on the repeat SLN procedures but in general the gynecologic oncologists experienced repeat SLN procedures more challenging compared to primary procedures. There were no groin recurrences documented.

Conclusions. Our findings suggest that it is feasible to perform a repeat SLN procedure in recurrent vulvar SCC, but the procedure appears technically more challenging compared to primary setting, resulting in a lower SLN identification rate.

1. Introduction

The treatment for vulvar cancer has changed over the last decades. Currently the standard treatment for unifocal squamous cell carcinoma (SCC) of the vulva <4 cm diameter without suspicious inguinofemoral lymph nodes at imaging consists of wide local excision and sentinel lymph node (SLN) procedure of the inguinofemoral lymph nodes [1–4]. The advantages of SLN procedure over an inguinofemoral lymphadenectomy (IFL) are obvious: the short and long term sequels such as wound healing problems, lymphocyst formation, recurrent erysipelas and lymph edema are much less common after SLN procedure [3]. Groin recurrences after negative SLN biopsies in primary vulvar SCC patients were reported in 2–3% of the patients [1,3,8]. Unfortunately, a groin recurrence after negative SLN was shown to have a very high mortality rate; therefore very strict criteria with respect to tumor characteristics, preoperative and pathological assessment and surgical technique should be met to guarantee the safety of the SLN procedure and to

* Corresponding author at: Room DHA135, Department of Obstetrics and Gynecology, Erasmus MC Cancer Institute, PO Box 2040, 3000CA Rotterdam, The Netherlands.
E-mail addresses: h.vandoorn@erasmusmc.nl (H.C. van Doorn), h.vanbeekhuizen@erasmusmc.nl (H.J. van Beekhuizen), k.n.gaarenstroom@lumc.nl (K.N. Gaarenstroom), j.vandervelden@amc.nl (J. van der Velden), a.g.j.van.der.zee@umcg.nl (A.G.J. van der Zee), m.h.m.oonk@umcg.nl (M.H.M. Oonk), joanne.dehullu@radboudumc.nl (J.A. de Hullu).

http://dx.doi.org/10.1016/j.ygyno.2016.01.013
0090-8258/

decrease the number of false negative results and the risk of groin recurrence. Local recurrences of SCC of the vulva are reported in 20–30% [9]. Many of these recurrences might be second primary tumors in a background of lichen sclerosis and vulvar intraepithelial neoplasia (VIN) rather than a real recurrence [10]. In patients with recurrent vulvar SCC, IFL is considered standard treatment for patients who previously did not undergo an IFL [11]. Since many of these patients are elderly and frail an alternative treatment other than IFL may be justified to avoid or reduce long term morbidity in this particular group of patients.

The main reasons not to perform a repeat SLN procedure in patients with a local recurrence of vulvar SCC is the assumption that the lymph flow might be altered because of previous surgery or radiotherapy. However, data about the accuracy and safety of repeat SLN procedures are lacking [11].

Prospective studies on the effect of previous vulvar surgery on the SLN procedure are not available, but retrospective analyses suggest a limited effect of the extent of previous vulvar surgery regarding the identification of the SLNs in primary vulvar SCCs [12,13]. Up till now previous surgery of the groin for other (benign) causes, like crossectomy in case of varicose vein ligation, or inguinal hernia repair have not been classified as contraindications to perform a SLN procedure. A possible advantage of the SLN procedure, also in recurrent disease, is that the SLN procedure might be helpful in the visualization of the lymph drainage and guide the surgeon in the removal of the lymph nodes at risk. This was described earlier in recurrent breast cancer [14]. Until now only case reports have been published regarding on repeat SLN procedure in recurrent vulvar SCC [15,16]. Whether a repeat SLN procedure is safe is still under debate [11].

The objective of this study is to investigate the feasibility of a repeat SLN procedure in patients with recurrent vulvar SCC who were not able or willing to undergo IFL as part of their treatment for recurrent disease.

2. Methods

2.1. Patients

This study is a retrospective cohort study, performed by a collaboration of five university hospitals in the Netherlands. All these hospitals have an oncology center with an expert team of gynecological oncologists experienced in the treatment of vulvar cancer and the SLN procedure. From each centers' database consecutive patients with recurrent vulvar SCC who underwent a repeat SLN procedure between 2006 and 2014 were identified. A retrospective chart review was performed, including the rationale of the treatment, surgical procedure, pathology results, and follow-up.

All patients underwent a local radical excision of the vulvar tumor and unilateral or bilateral SLN at initial surgery, followed by radiotherapy when indicated. Standard treatment for recurrent vulvar cancer would be uni- or bilateral IFL. However, in this patient group a repeat SLN procedure was considered in patients who were not appropriate candidates for IFL (bad general condition, fragility) or patients who refused IFL. All women were informed that IFL would be the standard treatment for their recurrent disease and all gave oral consent to the repeat SLN procedure as alternative and experimental treatment.

2.2. Imaging and surgical procedure

Preoperative imaging consisted of ultrasound or CT scanning of the groin, and in case of suspicious nodes ultrasound guided fine needle aspiration (FNA) of the lymph nodes was performed. In case of proven lymph node metastases at FNA, the SLN procedure was canceled.

Three to 24 h prior to surgery four injections with 99Tc nanocolloid with a total dose of 50–100 mBq were injected around the tumor. Dynamic and static films were obtained instantly and after 2 h, and the localizations of the SLNs were marked on the skin. In the operating room 1 to 2 ml of patent blue were injected intracutaneously around the tumor. Preferably the groins were operated first, followed by resection of the vulvar tumor. When the signal in the groin(s) node was very weak, or when the SLN(s) could not be localized, the sequence of surgery was reversed to reduce disturbance of background radiation and improve the chance to identify the SLNs. In case of an unsuccessful SLN identification, IFL was performed unless patients had refused this on forehand; then further treatment was individualized in agreement with the patient.

2.3. Histological assessment

All retrieved SLNs were examined by a routine hematoxylin/eosin protocol followed by ultra-staging: multiple sectioning and immunohistochemistry as described previously [3]. Patients with positive SLNs were again advised to undergo IFL and/or possibly subsequent radiotherapy of the groins and iliac nodes. Follow up was performed with 2 or 3 month checkups for 2 years, followed by 4 monthly visits the third year and 6 monthly visits thereafter.

2.4. Outcome and statistics

The primary outcome variable was the proportion of groins in which a SLN was identified during surgery for recurrent SCC. A SLN was defined as either a radioactive (hot) and/or blue node. Follow- up started at the day of groin(s) surgery and ended at last date of follow-up or death.

In The Netherlands retrospective research of patient charts is exempted from permission of the Medical Ethical Review Board. Statistical analyses to describe the study population were performed using Microsoft Excel (version 2010).

This study conforms to the STROBE guideline for cohort studies (Strengthening the Reporting of Observational Studies in Epidemiology) [17].

3. Results

In 27 patients a repeat SLN procedure was performed. The median age of the patients at the first SLN procedure was 65.3 years, (range 38–87.7 years) (Table 1), the median interval between the first and recurrent disease was 37 months, with a range of 10–146 months. The reasons to omit the (standard) IFL and to perform the alternative treatment with a repeat SLN procedure were frailty and severe co-morbidity in four patients, cognitive impairment in four, refusal of IFL (nine patients), small lesions (<20 mm) at the contralateral site (contralateral with respect to the initial site of the SLN procedure) (four patients), and in six patients the reasons could not be retrieved from the file.

Table 1
Tumor characteristics and outcome of surgical procedures (N = 27).

	Median, range
Age at first procedure (years)	63.7 (35.7–87.7)
First procedure	
Size tumor (mm)[a]	13 (4–31)
Infiltration depth (mm)[a]	3.5 (1.0–10)
Number of nodes right groin[b]	1 (1–6)
Number of nodes left groin[b]	1 (1–4)
Interval between 1st and 2nd SN procedure (months)	37 (10–146)
Second procedure	
Size tumor (mm)	13 (2–65)
Infiltration depth (mm)[c]	3.0 (1.1–10.0)
Number of nodes right groin[d]	1 (1–5)
Number of nodes left groin[e]	2 (1–4)
Follow-up (months)	27 (2–96)

[a] 3 missing: previous surgery at other clinic.
[b] $n = 19$ groins.
[c] 1 missing.
[d] $n = 21$ groins.
[e] $n = 16$ groins.