Patterns and frequency of recurrences of squamous cell carcinoma of the vulva

Woolderink, Jorien; de Bock, Gertruida H; de Hullu, Joanne A.; Davy, Margaret J.; van der Zee, Ate; Mourits, Marian J.E.

Published in:
Gynecologic Oncology

DOI:
10.1016/j.ygyno.2006.03.010

Publication date:
2006

Available online at www.sciencedirect.com
ScienceDirect
Gynecologic Oncology 103 (2006) 293–299
Gynecologic Oncology
www.elsevier.com/locate/ygyno

Patterns and frequency of recurrences of squamous cell carcinoma of the vulva

Jorien M. Woolderink [a], Geertruida H. de Bock [b], Joanne A. de Hullu [c], Margaret J. Davy [d], Ate G.J. van der Zee [a], Marian J.E. Mourits [a,*]

[a] *Department of Gynaecological Oncology CMC V, University Medical Center Groningen, University of Groningen, 4th floor, PO Box 30.001, 9700 RB Groningen, The Netherlands*
[b] *Department of Epidemiology and Bio-informatics, University Medical Center Groningen, University of Groningen, The Netherlands*
[c] *Department of Gynecologic Oncology, University Medical Center St. Radboud, Nijmegen, The Netherlands*
[d] *Department of Gynecologic Oncology, Royal Adelaide Hospital, Adelaide, Australia*

Received 7 December 2005
Available online 2 May 2006

Abstract

Objective. To analyze patterns and frequency of recurrences of squamous cell carcinoma (SCC) of the vulva after wide local excision (WLE) and superficial inguinal lymphadenectomy with separate incisions and to identify prognostic factors for the development of recurrences.

Methods. Between January 1985 and December 1999, all 125 consecutive patients with primary SCC of the vulva, treated with WLE and superficial inguinal lymphadenectomy, were retrospectively analyzed. Recurrences were registered by localization as: local, skin bridge, groin or distant.

Results. A local recurrence was diagnosed in 29 (23%) patients, 11 (9%) developed a groin and 4 (3%) a distant recurrence. No skin bridge recurrences were identified. The 5 years local relapse-free survival was 70%. After a first local recurrence, 72% of these patients developed a second local recurrence. Adjusted for other predictors, older age (>74 years) is an independent risk factor for local recurrences (HR: 2.38; 95%-C.I.: 1.08–5.23) and stage III/IV cancer for developing groin/distant recurrences (HR: 3.03; 95%-C.I.: 1.0–9.18).

Conclusion. WLE and superficial inguinal lymphadenectomy with separate incisions result in a high groin recurrence rate in this study; superficial lymphadenectomy should be replaced by deep inguinofemoral lymphadenectomy. After a local recurrence, 72% of the patients developed a second local recurrence. These patients are at high risk and need a close follow-up.

Keywords: Vulvar carcinoma; Local recurrences; Groin recurrence; Skin bridge recurrences; Progression-free survival; Local relapse-free survival

Background

Vulvar cancer is a rare malignancy, representing about 4% of the malignancies of the female genital tract [1]. The incidence is 2.1 per 100,000 women in South Australia [2]. In the early 1950s, Stanley Way introduced the radical vulvectomy with "en bloc" bilateral inguinofemoral lymphadenectomy as standard treatment for all operative vulvar cancers [3 4]. This strategy resulted in excellent survival rates up to 90% 5-year survival for patients without lymph node metastases (stages I and II) and an overall survival rate of about 70% [1,4]. However, the complication rate was high because of the extension of the operation. Major early complications were infections and wound breakdown [5]. The major late postoperative complication was chronic leg edema. Other complications were erysipelas, urinary stress incontinence and significant disturbances of sexual function and body image [1].

Since 1985, major modifications have been introduced to the standard surgical treatment to reduce morbidity without compromising the prognosis. These modifications are: wide local excision instead of radical vulvectomy, no lymph node dissection in case of a micro-invasive tumor (invasion <1 mm), unilateral lymph node dissection in case of a lateral

* Corresponding author. Fax: +31 50 3611806.
E-mail address: m.j.e.mourits@og.umcg.nl (M.J.E. Mourits).

0090-8258/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.ygyno.2006.03.010

tumor (a unilateral lesion with the medial margin >1 cm from the midline, provided that the contralateral side of the vulva is histological-free from a second primary tumor) [6] and either superficial or deep inguinal lymphadenectomy by separate incisions in stead of en bloc inguinofemoral lymph node excision. In 1985, this new treatment, WLE and superficial lymph node dissection, has been introduced in South Australia.

The new standard treatment, consisting of wide local excision with uni- or bilateral lymph node dissection by separate incisions, has never been investigated as far as we know in randomized studies, although several studies evaluated the new technique retrospectively [7–9].

A potential disadvantage of separate incisions is the possible occurrence of skin bridge recurrences. The mechanism of lymphatic spread in vulvar cancer is by embolization rather than by permeation. Therefore, the possibility of leaving tumor emboli in efferent lymphatics in the tissue bridge between the vulvar and the groin resections must be considered [5]. The typical occurrence of a skin bridge recurrence shortly after primary therapy in a patient with nodal metastasis suggests that this may represent retrograde permeation of emboli in lymphatic channels in patients with nodal metastases [10]. However, skin bridge recurrences have also been described in patients with negative lymph nodes [10]. Skin bridge recurrences are nearly always fatal [8,11].

The most common site of recurrence for vulvar cancer is the vulvar region [12]. It also may be a second primary tumor (tumor de novo) especially in patients with premalignant vulvar disease. Groin recurrences develop mostly earlier than vulvar recurrences or second primaries, and the prognosis is much worse compared to patients with a recurrence on the vulva [5,8,13]. While local recurrences may be controlled with a new wide local excision and/or radiotherapy, groin recurrences are usually fatal [13].

The objective of this study was: to analyze patterns and frequency of recurrences of squamous cell carcinoma of the vulva after wide local excision and superficial inguinal lymphadenectomy with separate groin incisions and to identify prognostic factors for the development of recurrences.

Patients and methods

Between January 1985 and December 1999, all consecutive 182 patients with primary vulva cancer, without a previous history of vulvar cancer, were treated by the same surgeon (M.J.D) and were analyzed for this study: 78 at the Royal Adelaide Hospital, 54 at the Queen Elizabeth Hospital, 43 at the Attunga Medical Centre in Adelaide and 7 interstate patients from Darwin. Of 182 patients, five medical records were destroyed and 17 patients had vulvar cancer with non-squamous cell carcinoma (adenocarcinomas (2), basal cell carcinomas (5), melanoma (2), sarcoma (1) and 7 other tumors). A total of 160 patients had primary squamous cell carcinoma. Six of 160 patients received chemoradiation because of very extensive vulvar cancer, and 29 patients did not have a lymph node dissection because of extensive vulvar cancer or poor general condition. A total number of 125 patients were analyzed in the present study.

All patients were staged with the surgical and pathological staging system for vulvar cancer of the International Federation of Gynecology and Obstetrics (FIGO 1996) [14]. All patients were treated with wide local excision 1 cm macroscopically around the tumor, without lymph node dissection in case of a micro-invasive tumor (invasion <1 mm). In case of a lateral tumor with invasion of >1 mm, patients were treated by wide local excision with unilateral inguinal lymph node dissection and by wide local excision with bilateral inguinal lymphadenectomy in case of a midline tumor. All inguinal lymphadenectomies were performed with separate groin incisions. Radiotherapy (45–50 Gy) was given to all patients with positive inguinal lymph nodes, unless there was only one intranodal lymph node metastasis in combination with well differentiated vulvar cancer. Patients received regular follow-up, every 3 months during the first 2 years, every 6 months for the subsequent 3 years and then once every 12 months. When a recurrence was diagnosed, the localization of the recurrence was registered as local, skin bridge, groin or distant. Local recurrences were treated with wide local excision, whereas recurrences in the groin were treated with surgery and radiotherapy.

Demographics, medical history, histopathological and clinical data were obtained from medical records. If not available in medical records, these data were obtained from the cancer registries of the Royal Adelaide Hospital and the Queen Elizabeth Hospital. Histopathology reports were retrospectively analyzed for diameter, depth of invasion, tumor grade, presence of lymph vascular space involvement or perineural invasion, uni- or multifocality of the tumor, presence of lichen sclerosis, vulvar intraepithelial neoplasia (VIN) and histopathologic features such as koilocytosis suspicious for human papilloma virus (HPV) infection around the tumor, localization of the tumor and free surgical margins of carcinoma and dysplasia. No central histopathological revisions were made.

Statistical methods

Endpoints for this study were: local recurrences, skin bridge recurrences, groin recurrences and distant recurrences. The progression-free survival was defined as the time from the date of primary treatment to the date of diagnosis of first recurrence, the end of life or last date of follow-up. All clinical and histopathological factors included in this study (for an overview, see Table 4) were related to any recurrence risk. Univariate Cox regression analyses were performed for each prognostic factor separately, considering local recurrences and other recurrences. Hazard ratios (HR) and 95% confidence intervals (95%-C.I.) were estimated. Multivariate Cox regression analyses were performed including all factors with a hazard ratio in the univariate model exceeding the value of 1.3. With these variables, a model was constructed by using a stepwise procedure. To test the assumption of proportional hazards, an interaction term of a prognostic variable and a time-dependent covariate was added [15]. A significant effect of that interaction term denotes the presence of a time-dependent effect and thus a violation of the proportional hazards assumption. P values less than 0.05 were considered to be statistically significant. All analyses were performed with program SPSS version 12.01.

Results

Primary treatment and staging

The median age of 125 patients at the time of the primary diagnosis was 72 years (range 23–91 years). (See Table 1 for an overview of patient characteristics.) Lichen sclerosis was observed in 62 (50%) patients. VIN was observed in 89 (71%) of the patients. In 38 (30%) patients, lichen sclerosis and VIN were present. The median age of patients with lichen sclerosis was 72 years (range 31–90 years) and for patients with VIN 72 years (range 26–90 years) (data not in table). In 96 of 125 (77%) patients, bilateral lymph node dissection by

Table 1
Patients treated with wide local excision with or without lymph node dissection with separate groin incisions: characteristics of primary vulva cancer

Patients (n = 125)	
Median age	72 years (range 23–91)
Lichen sclerosis	
No	63 (50%)
Yes	62 (50%)
VIN	
No	36 (29%)
Yes	89 (71%)
Treatment groins	
No lymph node dissection	15 (12%)
Unilateral lymphadenectomy	14 (11%)
Bilateral lymphadenectomy	96 (77%)
Tumor-free margins	
Yes	109 (87%)
No	16 (13%)

separate incisions was performed while 14 (11%) patients underwent unilateral lymph node dissection. In 15 (12%) patients with stage IA carcinoma, no lymph node dissection was performed. In 109 (87%) patients, the margins were free of tumor after wide local excision and 16 (13%) patients had tumor positive margins, of which 6/16 (38%) received postoperative radiotherapy while 9/16 (62%) received a re-excision.

A total of 49 (39%) patients were diagnosed with a T1N0M0 tumor, 42 (33%) with a T2N0M0 tumor, 6 (5%) with a T1N1M0 tumor, 16 (13%) with a T2N1M0 tumor and 12 (10%) patients were diagnosed with a T2N2M0 tumor of the vulva (Table 2).

Recurrences

Recurrent disease was diagnosed in 44 (35%) patients (Table 3). Local recurrent disease was diagnosed in 29 (23%) patients and was treated with wide local excision in 27/29 patients and in 2/29 patients with a wide local excision followed by radiotherapy. A second local recurrence or second primary tumor developed in 21 (72%) of 29 patients. In this group, most patients had other epithelial abnormalities. Fifteen (71%) patients had lichen sclerosis, and 15 (71%) of the patients had VIN. There were no recurrences in the skin bridge. The upper confidence bound is (t0: n = 125: 95%-C.I.r: 0.03; t5 n = 43: 95%-C.I.r: 0.09. The median interval from first to second recurrence was 10 months (range 2–32 months). Of these 21 patients, 15 were again treated with wide local excision, 1 patient was treated with radiotherapy and in 5 patients the treatment was unknown. In 12 (57%) of the 21 patients with a second local recurrence, three or more local recurrences were diagnosed. The site of the local recurrence was not analyzed. Local recurrences can be a recurrence at the same site as well as a second primary tumor (tumor de novo) on the contralateral site of the vulva, especially in patients with premalignant vulvar disease which was common in this study.

Table 2
TNM and FIGO classification of primary vulva cancer (n = 125)

TNM	No. (%)	FIGO	No. (%)
T1N0M0	49 (39%)	IA	15 (12%)
T1N1M0	6 (5%)	IB	34 (27%)
		II	42 (34%)
T2N0M0	42 (33%)	III	22 (18%)
T2N1M0	16 (13%)	IVA	12 (9%)
T2N2M0	12 (10%)		

Table 3
Characteristics of follow-up and recurrences in 125 patients with primary vulvar cancer

Patients (n = 125)	
First recurrences	
Local	29 (23%)
Skin bridge	0 (0%)
Groin	11 (9%)
Distant	4 (3%)
Second local recurrence after first local recurrence (n = 29)	
Yes	21 (72%)
No	8 (28%)
Third local recurrence after second local recurrence (n = 21)	
Yes	12 (57%)
No	9 (43%)
Overall median follow-up	42 (range 1–184 months)
Median interval primary therapy to recurrence in months	22 (range 3–141 months)
Median interval to first local recurrence	40 (range 3–141 months)
Median interval to first groin recurrence	11 (range 4–42 months)
Overall relapse-free survival at 5 years	58%
Local relapse-free survival at 5 years	70%

Groin recurrences were diagnosed in 11/125 (9%) patients. In six (5%) patients with negative lymph nodes at primary treatment, a groin recurrence was diagnosed. In four of six patients, bilateral groin dissection was performed, one of six underwent unilateral groin dissections while one of six patients did not have lymph node dissection because of stage IA vulvar cancer. Of 11 patients with groin recurrences, three received radiotherapy, two patients received surgery and radiotherapy, two patients received chemotherapy and the treatment of four patients was unknown. Of 11 patients with a groin recurrence, 10 died of vulvar cancer while 1 patient died of intercurrent disease. The number of removed lymph nodes was analyzed. In patients without a groin recurrence, the mean number of removed lymph nodes was 16 (range 3–35). In patients who developed a groin recurrence after negative lymph nodes, the mean number of removed lymph nodes was 13 (range 3–19). This difference is not significant (t = 1,74: df = 90: P = 0.09). Distant recurrences were diagnosed in four patients. All patients with distant recurrences were treated with chemotherapy. They all died of vulvar cancer.

The overall median follow-up time was 42 months (range 1–184 months). In 12 (10%) patients, the follow-up was less than 6 months, 2/12 (17%) died of vulvar cancer within 6 months, 3/12 (25%) died of intercurrent disease and 7/12 (58%) were lost to follow-up. The median interval from initial therapy to first recurrence was 22 months (range 3–141 months). Patients with tumors that recurred in the vulva had a longer median interval to recurrence of 40 months (range 3–141 months), compared to

these with recurrences to the groin with an interval of 11 months (range 4–42 months) (Fig. 1).

The local relapse-free survival was 70% at 5 years; the overall relapse-free survival was 58% at 5 years.

Clinical and histopathological characteristics related to any recurrence

Multifocality of the primary tumor was more often present in patients with local recurrences (Table 4). In 41% of the patients who developed a local recurrence, a multifocal disease was diagnosed instead of 25% of the patients without a recurrence. Lichen sclerosis was more often present in patients who developed local or groin recurrences. A total of 42% of the patients without a recurrence had lichen sclerosis whether 66% (local) and 64% (groin) of the patients who developed a recurrence had lichen sclerosis.

Univariately, age >74 years was the main risk factor for developing local recurrences (HR: 1.93; 95%-C.I.: 0.92–4.07, see Table 5). Univariately, differentiation grade, multifocality, lichen sclerosis and VIN around the tumor were not significant for developing a local recurrence (respectively HR: 2.10; 95%-C.I.: 0.86–5.12; HR: 1.27; 95%-C.I.: 0.37–4.34; HR: 1.76; 95%-C.I.: 0.84–3.71; HR: 1.55; 95%-C.I.: 0.72–3.34; HR: 1.40; 95%-C.I.: 0.56–3.45, see Table 5), however, these factors showed a trend and were used in multivariate analysis. Multivariately, age >74 years was the only independent prognostic factor for local recurrences (HR: 2.38; 95%-C.I.: 1.08–5.23, see Table 6).

A risk factor for groin or distant recurrences in univariate analysis was positive lymph nodes (HR: 3.12; 95%-C.I.: 1.05–9.29, see Table 5). Multifocality, lymph vascular space involvement, perineural invasion and FIGO stage (respectively HR: 1.26; 95%-C.I.: 0.40–3.97; HR: 2.08; 95%-C.I.: 0.47–9.24; HR: 3.33; 95%-C.I.: 0.94–11.85; HR: 2.59; 95%-C.I.: 0.94–7.16, see Table 5) showed a trend and were also analyzed in multivariate analysis. Multivariately, stage III/IV was the only independent prognostic risk factor for groin or distant recurrences (HR: 3.03; 95%C.I.: 1.0–9.18). Because positive lymph nodes were a linearly dependent covariate with stage, positive lymph nodes was not included in the multivariate analysis. In the Cox regression model, there was no violation of the assumption of proportional hazards regarding the two outcomes and any prognostic factor (data not shown).

Discussion and conclusions

In this retrospective analysis of vulvar cancer patients, none developed a skin bridge recurrence after wide local excision and superficial inguinal lymphadenectomy with separate groin incisions. Although skin bridge recurrences mostly develop in patients with positive lymph nodes [16], other studies reported patients with negative nodes who developed a recurrent tumor in the skin bridge as well [8,10–12,17]. Our data are in accordance with others who also did not find any skin bridge recurrence after modifications in the treatment of patients with vulvar cancer [18–20]. Ansink et al. [7] reported a low frequency (<1%) of skin bridge recurrences based on pooling of limited data, suggesting that the use of separate incisions in patients without suspicious inguinal lymph nodes at palpation is supposed to be safe.

In our study, 29 patients developed one or more local recurrences. This is in accordance with the 15–35% as reported in literature with modified surgical treatment. Piura et al. and

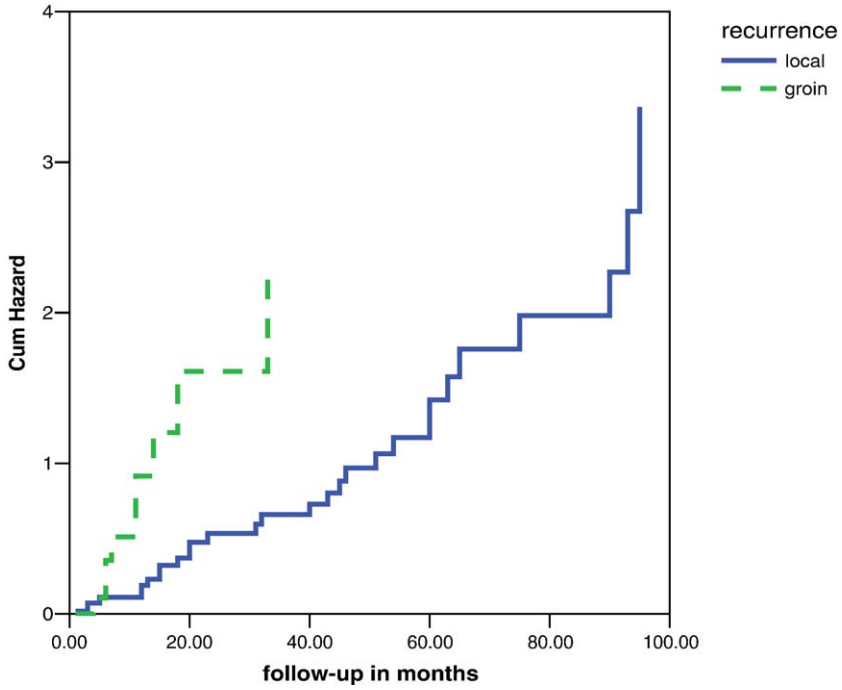

Fig. 1. Development of local and groin recurrences.

Table 4
Clinical and histopathological characteristics related to outcomes (n = 125)

Clinical and histopathological characteristics:	Without any recurrence (n = 81)	With a local recurrence (n = 29)	With a groin recurrence (n = 11)	With a distant recurrence (n = 4)
Age in years; median (range)	71.0; (23–91)	74.0; (27–88)	74.0; (42–90)	68.0; (53–76)
Localization of tumor				
Lateral	79%	83%	82%	50%
Clitoris	17%	14%	18%	50%
Perineum	3%	3%	–	–
Vulvovaginal.	1%	–	–	–
Maximum Ø of the tumor in mm; median (range)	25.0; (2–100)	20.0; (2–75)	25.0; (9–48)	42.5; (8–70)
Maximum invasion in depth in mm; median (range)[a]	4.0; (<1.0–>5.0)	3.0; (<1.0–>5.0)	6.0; (<1.0–>5.0)	6.0; (<1.0–>5.0)
Differentiation grade[b]				
Well	36%	25%	55%	–
Moderate	40%	61%	45%	75%
Poor	24%	14%	–	25%
Multifocality				
Present	25%	41%	27%	25%
Lymph vascular space involvement				
Present	6%	3%	9%	25%
Perineural invasion				
Present	5%	–	9%	25%
Lichen sclerosis				
Present	42%	66%	64%	25%
VIN/CIS around tumor				
Present	67%	79%	64%	50%
HPV				
Present	9%	7%	9%	–
Free margins				
Present	85%	90%	100%	75%
Free margins VIN				
Present	80%	66%	100%	100%
Stadium				
I/II	73%	76%	55%	50%
III/IV	27%	24%	45%	50%
Lymph nodes[c]				
Negative	71%	68%	56%	25%
Positive	29%	32%	44%	75%

[a] Only available in 98 patients.
[b] Only available in 123 patients, 80 without a recurrence, 28 with a local recurrence, 11 with a groin recurrence and 4 with a distant recurrence.
[c] Only available in 112 patients, 77 without a recurrence, 22 with a local recurrence, 9 with a groin recurrence, 4 with a distant recurrence (13 patients did not have lymph node dissection).

Oonk et al. showed local recurrence rates of 16% in 376 patients and 21% in 238 patients, and Cavanagh et al. gave an overview of studies and reported recurrences in 15–40% of which 55–90% were local recurrences [21–23]. Wide local excision leaves part of the possible abnormal vulva in situ. These vulvar abnormalities can become a local recurrence or a second primary tumor. A certain amount of local recurrences are second primaries (tumor de novo) especially after a long interval. However, of 29 patients, 21 (72%) developed a second local recurrence after a median interval of 10 months and in 12 of 21 (57%) patients 3 or more local recurrences were diagnosed.

Table 5
Clinical and histopathological characteristics related to outcomes: univariate analysis (HR (95% confidence intervals)) (n = 125)

Clinical and histopathological characteristics	With a local recurrence (n = 29)[a]	With a groin or distant recurrence (n = 15)[a]
Age in years		
<75 years	1	1
>/=75 years	1.93 (0.92–4.07)[b]	1.57 (0.57–4.35
Localization of tumor		
Lateral	1	1
Clitoris, perineum, vagina	0.97 (037–2.56)	1.55 (0.49–4.87)
Maximum Ø of the tumor in mm	1.0 (0.98–1.02)	1.0 (0.98–1.03)
Maximum invasion depth in mm	0.98 (0.81–1.19)	1.31 (0.91–1.88)
Differentiation grade		
Well	1	1
Moderate	2.10 (0.86–5.12)[b]	1.15 (0.40–3.27)
Poor	1.27 (0.37–4.34)[b]	0.32 (0.04–2.62)
Multifocality		
No	1	1
Yes	1.76 (0.84–3.71)[b]	1.26 (0.40–3.97)[b]
Lymph vascular space involvement		
No	1	1
Yes	0.73 (0.10–5.35)	2.08 (0.47–9.24)[b]
Perineural invasion		
No	–	1
Yes		3.33 (0.94–11.85)[b]
Lichen sclerosis		
No	1	1
Yes	1.55 (0.72–3.34)[b]	1.52 (0.54–4.27)
VIN/CIS around the tumor		
No	1	1
Yes	1.40 (0.56–3.45)[b]	2.01 (0.57–7.16)
HPV		
No	1	1
Yes	0.72 (0.17–3.06)	0.76 (0.10–5.82)
Free margins		
Yes	1	1
No	1.28 (0.38–4.27)	0.61 (0.08–4.61)
Free margins VIN		
Yes	1	–
No	1.62 (0.75–3.52)	
Stage		
I/II	1	1
III/IV	1.10 (0.47–2.60)	2.59 (0.94–7.16)[b]
Lymph nodes		
Negative	1	1
Positive	1.38 (0.56–3.39)	3.12 (1.05–9.29)[c]

[a] Compared to patients without a recurrence (n = 81).
[b] These variables were used in multivariate analysis.
[c] Because positive lymph nodes were a linearly dependent covariate with stage, positive lymph nodes were not included in the multivariate analysis.

Table 6
Clinical and histopathological characteristics related to outcomes: multivariate analysis (HR (95% confidence intervals)) (n = 110 [a])

Clinical and histopathological characteristics	With a local recurrence (n = 29)
Age over 74 years	
No	1
Yes	2.38 (1.08–5.23)
Differentiation grade	
Well	1
Moderate	2.06 (0.83–5.06)
Poor	1.67 (0.46–6.07)
Multifocality	
No	1
Yes	1.76 (0.77–4.04)
Lichen sclerosis	
No	1
Yes	1.63 (0.71–3.73)
Free margins VIN	
Yes	1
No	1.44 (0.61–3.42)

[a] A comparison between patients without a recurrence and with a local recurrence.

These patients therefore are at high risk for developing a local recurrence, and a close follow-up is necessary in these patients. These local recurrences had no negative effect on the survival for none of the patients died of vulvar cancer. No pathology revision was performed in this study, and therefore histological margins could not be analyzed. de Hullu et al. [8] reported that surgical margins measuring 1 cm which was performed in this study resulted in histological margins measuring ≤8 mm in 50% of patients leading to a higher local recurrence rate.

Eleven patients developed a groin recurrence after superficial inguinal lymph node dissection. Six (5%) patients with negative lymph nodes in primary treatment developed a groin recurrence. One patient did not have lymph node dissection because of stage IA vulvar cancer. In literature, unexpected groin relapses were found in 5–7% of patients with negative inguinofemoral lymph nodes after inguinofemoral lymphadenectomy by separate incisions [8,24,25], which appears to be a substantial increase in the number of groin recurrences compared with the en bloc approach [8,26]. Gordenier et al. [27] and Katz et al. [28] also found 9% and 16% groin recurrences. Kirby et al. [29] found a groin recurrence rate of 4.6% in 65 stage I/II vulvar cancers after inguinal lymphadenectomy. In these studies, however, only superficial inguinal lymph node dissection was performed as we did. Superficial inguinal lymph node dissection instead of deep inguinofemoral lymph node dissection may have increased the number of patients with lymph node recurrences also in our series as shown in literature [30] and should be replaced by inguinofemoral lymphadenectomy. Groin relapse in patients who had negative nodes at superficial inguinal lymphadenectomy in our series occurred in six patients, and it carried a very poor prognosis. Most patients with groin recurrence die of disease [31]. In our series, 10 of 11 patients with groin recurrences died of disease.

Patients over 74 years were at higher risk for developing a local recurrence than younger patients. In this group of patients, there was a trend towards more lichen sclerosis and of course lichen sclerosis was not completely removed by wide local excision. Although we do not have pathological information about the histological margins, it might be that older patients got less extensive treatment because of co-morbidity.

As expected, patients with FIGO stage III/IV showed a significant higher risk for developing a groin or distant recurrence in this study. All patients in this study with FIGO stage III/IV had positive lymph nodes. This is in accordance with others who also found positive lymph nodes as a predictive factor [21,32,33]. The primary route of spread in vulvar cancer is by lymphatic embolization to the regional inguinofemoral lymph nodes. Especially the number of positive lymph nodes and extra-nodal tumor growth are of great importance for the prognosis of the patient [31,34].

Conclusion: In this large study of vulvar cancer patients after introduction of modified surgical treatment, wide local excision and superficial inguinal lymphadenectomy with separate incisions lead to a local recurrence rate of 23%, a groin recurrence rate of 9% and no recurrences in the skin bridge. Superficial inguinal in stead of deep inguinofemoral lymphadenectomy may have increased the number of patients with lymph node recurrences also in our series and should be replaced by the latter. Of all patients with a local recurrence, 72% developed second or more local recurrences; this group of patients needs a close follow-up.

References

[1] Hacker NF. Vulvar cancer. In: Berek JS, Hacker NF, editors. Practical Gynecologic Oncology. 3rd ed. Baltimore: Williams and Wilkins; 2000. p. 553–96.
[2] Epidemiology of Cancer in South Australia 1977–1998 1st ed. South Australian Cancer Registry: Adelaide 1999.
[3] Way S. The anatomy of the lymphatic drainage of the vulva and its influence on the radical operation for carcinoma. Ann R Coll Surg Engl 1948;3:187–209.
[4] Way S. Carcinoma of the vulva. Am J Obstet Gynecol 1960;79: 692–7.
[5] Christophersen W, Herbert J, Buchsbaum MD, Voet R, Lifschitz S. Radical vulvectomy and bilateral groin lymphadenectomy utilizing separate groin incisions: report of a case with recurrence in the intervening skin bridge. Gynecol Oncol 1985;21:247–51.
[6] Burger MPM, Hollema H, Bouma J. The side of groin node metastases in unilateral vulvar carcinoma. Int J Gynecol Cancer 1996;6:318–2322.
[7] Ansink A, van der Velden J. Surgical interventions for early squamous cell carcinoma of the vulva (Cochrane review) In Cochrane Library, Issue 1, Oxford; Update Software 2002.
[8] de Hullu JA, Hollema H, Lolkema S, Boezen M, Boonstra H, Burger MP, et al. Vulvar carcinoma. De price of less radical surgery. Cancer 2002;95:2331–8.
[9] Arvas M, Köse F, Gezer A, Demirkiran F, Tulunay G, Kösebay D. Radical versus conservative surgery for vulvar carcinoma. Int J Gynecol Obstet 2005;88:127–33.
[10] Rose PG. Skin bridge recurrences in vulvar cancer: frequency and management. Int J Gynecol Cancer 1999;9:508–11.
[11] Rouzier R, Haddad B, Plantier F, Dubois P, Pelisse M, Paniel BJ. Local relapse in patients treated for squamous cell vulvar carcinoma: incidence and prognostic value. Obstet Gynecol 2002;100:1159–67.
[12] Hopkins MP, Reid GC, Morley GW. The surgical management of recurrent squamous cell carcinoma of the vulva. Obstet Gynecol 1990;75:1001–5.
[13] Tilmans AS, Sutton GP, Look KY, Stehman FB, Ehrlich CE, Hornback NB. Recurrent squamous carcinoma of the vulva. Am J Obstet Gynecol 1992;167:1383–9.

[14] Shepherd JH. FIGO definitions of cancer staging. Br J Obstet Gynaecol 1996;103:405–6.
[15] Klein JP, Moeschberger ML. Survival Analysis: Techniques for Censored and Truncated Data. 2nd ed. New York: Springer-Verlag; 2003.
[16] Hacker NF, Leuchter RS, Berek JS, Castaldo TW, Lagasse LD. Radical vulvectomy and bilateral inguinal lymphadenectomy through separate groin incisions. Obstet Gynecol 1981;58:574–9.
[17] Grimshaw RN, Murdoch JB, Monaghan JM. Radical vulvectomy and bilateral inguinal–femoral lymphadenectomy through separate incisions, experience with 100 cases. Int J Gynecol Cancer 1993;3:18–23.
[18] Helm CW, Hatch K, Austin JM, Partridge EE, Soong SJ, Elder JE, et al. A matched comparison of single and triple incision techniques for the surgical treatment of carcinoma of the vulva. Gynecol Oncol 1992;46: 150–6.
[19] Lin JY, DuBeshter B, Angel C, Dvoretsky PM. Morbidity and recurrence with modifications of radical vulvectomy and groin dissection. Gynecol Oncol 1992;47:80–6.
[20] Preti M, Guglielmo R, Ghiringhello B, Micheletti L. Recurrent squamous cell carcinoma of the vulva. Cancer 2000;88:1869–76.
[21] Piura B, Masotina A, Murdoch J, Lopes A, Morgan P, Monaghan J. Recurrent squamous cell carcinoma of the vulva: a study of 73 cases. Gynecol Oncol 1993;48:189–95.
[22] Cavanagh D, Hoffman MS. Controversies in the management of vulvar carcinoma. Br J Obstet Gynaecol 1996;103:293–300.
[23] Oonk MH, de Hullu JA, Hollema H, Mourits MJE, Pras E, Wymenga AN, et al. The value of routine follow-up in patients treated for carcinoma of the vulva. Cancer 2003;98:2624–9.
[24] Stehman FB, Bundy BN, Dvoretsky PM, Creasman WT. Early stage I carcinoma of the vulva treated with ipsilateral superficial inguinal lymphadenectomy and modified radical hemivulvectomy: a prospective study of the Gynecologic Oncology Group. Obstet Gynecol 1992;79: 490–7.
[25] Burke TW, Levenback C, Coleman RL, Morris M, Silva EG, Gerschenson DM. Surgical therapy of T1 and T2 vulvar carcinoma: further experience with radical wide excision and selective inguinal lymphadenectomy. Gynecol Oncol 1995;57:215–20.
[26] Burger MPM, Hollema H, Emanuels AG, Krans M, Pras E, Bouma J. The importance of the groin node status for the survival of T1 and T2 vulval carcinoma patients. Gynecol Oncol 1995;57:327–34.
[27] Gordenier ME, Malpica A, Burke TW, Bodurka DC, Wolf JK, Jhingran A, et al. Groin recurrence in patients with vulvar cancer with negative nodes on superficial inguinal lymphadenectomy. Gynecol Oncol 2003;90:625–8.
[28] Katz A, Eifel PJ, Jhingran A, Levenback CF. The role of radiation therapy in preventing regional recurrences of invasive squamous cell carcinoma of the vulva. Int J Radiat Oncol Biol Phys 2003;57:409–18.
[29] Kirby TO, Rocconi RP, Numnum TM, Kendrick JE, Wright J, Fowler W, et al. Outcomes of stage I/II vulvar cancer patients after negative superficial inguinal lymphadenectomy. Gynecol Oncol 2005;98: 309–12.
[30] Veldenvander J, Ansink AC. Re: outcomes of stage I/II vulvar cancer patients after negative superficial inguinal lymphadenectomy. Gynecol Oncol 2005;6 (electronic publication ahead of print).
[31] Hacker NF, Berek JS, Lagasse LD, Leuchter RS, Moore JG. Management of regional lymph nodes and their prognostic influence in vulvar cancer. Obstet Gynecol 1984;61:408–12.
[32] Podratz KC, Symmonds RE, Taylor WF. Carcinoma of the vulva: analysis of treatment failures. Am J Obstet Gynecol 1982;143:340–51.
[33] Shimm DS, Fuller AF, Orlow EL, Dosoretz DE, Aristizabal SA. Prognostic variables in the treatment of squamous cell carcinoma of the vulva. Gynecol Oncol 1986;24:343–58.
[34] Hoffman JS, Kumar NB, Morley GW. Prognostic significance of groin node metastases in squamous carcinoma of the vulva. Obstet Gynecol 1985;66:402–5.