Rationale and definition of the lateral extension of the inguinal lymphadenectomy for vulvar cancer derived from an embryological and anatomical study.

Recurrent Squamous Cell Carcinoma of the Vulva

Clinicopathologic Determinants Identifying Low Risk Patients

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BACKGROUND. The identification of prognostic factors in the recurrence of vulvar squamous cell carcinoma is crucial for less invasive treatments.

METHODS. The authors studied 101 patients treated for primary invasive squamous cell carcinoma of the vulva. Selected pathologic variables were observed in a standardized manner during treatment, and their association with disease free survival was investigated using the Cox model. Independent prognostic factors were selected by a stepwise procedure. The absolute survival of patient groups determined on the basis of such factors was computed by the product limit method.

RESULTS. The median follow-up was 3.1 years (range, 56 days to 15.5 years). Recurrences developed in 33 patients. The independent recurrence predictors were as follows: International Federation of Gynecology and Obstetrics (FIGO) Stage IVA (vs. IB, II, or III) (risk ratio [RR]adjusted for other independent factors, 7.39), tumor multifocality (RR, 4.10), lymphovascular space involvement (LVSI) (RR, 2.96), the presence of associated vulvar intraepithelial neoplasia (VIN) Grade 2 or 3 (RR, 3.34), and the involvement of resection margins (RR, 4.88). By ignoring the FIGO stage and lymph node status, the independent predictors were then as follows: greatest tumor dimension < 2.5 cm, 2.5–4 cm (RR, 2.86), or > 4 cm (RR, 5.98); tumor multifocality (RR, 3.36); LVSI (RR, 4.19); the presence of VIN 2 or 3 (RR, 3.06); and the involvement of surgical margins (RR, 2.78). No recurrences were observed in 119 at-risk years among patients with unifocal tumors < 2.5 cm in greatest dimension, free surgical margins, no LVSI, and no associated VIN 2 or 3.

CONCLUSIONS. The presence of associated VIN 2 or 3 was revealed to be a previously unidentified independent prognostic factor for recurrence. Subjects at low risk of recurrence could be identified even without consideration of lymph node status. ***Cancer* 2000;88:1869–76.** *© 2000 American Cancer Society.*

KEYWORDS: vulvar neoplasm pathology, neoplasm recurrence, multivariate analysis, treatment outcome.

Over the last 2 decades, improvements in understanding the prognostic factors for vulvar squamous carcinoma have led to a reexamination of the application of total radical vulvectomy with bilateral inguinofemoral lymphadenectomy as the standard therapy for women affected by this disease.[1] Less invasive treatments with lower morbidity and fewer psychosexual consequences are appropriate nowadays for some groups of patients, even if concern about the increased risk of recurrence with conservative approaches suggests caution.[2]

In the relatively few studies on recurrent vulvar carcinoma, different methodologic approaches and statistical analyses were employed to investigate the role of clinicopathologic parameters in predicting disease free survival. A clear definition of the terms employed

in these studies was often omitted, hence accounting for the difficulty in comparing results.

In a previous study[3] we found that greatest tumor dimension and lymphovascular space involvement (LVSI) could actually predict the probability of lymph node metastases with reasonably good precision.

This study was designed to evaluate different clinicopathologic features as independent prognostic factors and to identify groups of women at low risk of recurrence, in particular considering prognostic factors not involving lymph node status.

MATERIALS AND METHODS

Study subjects were patients treated for vulvar malignancies at the Department of Gynecology and Obstetrics, University of Turin, Turin, Italy, from January 1, 1982, through December 31, 1996.

Eligibility criteria were as follows:

- Histologic diagnosis of epidermoid carcinoma (8 patients were excluded, 7 with verrucous carcinomas and 1 with an adenocarcinoma of the Bartholin gland);
- Diagnosis of primary vulvar carcinoma (6 patients with recurrent carcinoma were excluded);
- Depth of stromal invasion $>$ 1 mm, measured from the most superficial adjacent dermal papillae to the deepest point of invasion[4] (8 patients with International Federation of Gynecology and Obstetrics [FIGO] Stage IA[5] T1aN0M0 tumor confined to the vulva or vulva and perineum, 2 cm or less in greatest dimension, with stromal invasion no greater than 1 mm,[6] were excluded);
- No recurrence during the first month after surgery (2 patients with shorter disease free survival were excluded);
- No previous malignancy and no associated malignancy diagnosed at the time of the operation (no cases were excluded);
- Total and bilateral inguinofemoral lymphadenectomy (11 patients were excluded to ensure homogeneity and comparability: 5 not total, 6 not bilateral).

Among the 136 patients treated during the relevant period, 101 were eligible and entered the study. This series included 50 patients who were studied previously with respect to predictive factors for lymph node metastases.[3]

All the women gave informed written consent to therapeutic procedures and the analysis of clinicopathologic data related to their malignancy in accordance with local institutional guidelines and the Treaty of Helsinki.

Stages were defined according to the 1994 FIGO staging system[5] and the American Joint Committee on Cancer (AJCC) TNM classification.[6]

Patients were treated with a total deep vulvectomy or a partial deep vulvectomy with the deep fascia of the urogenital diaphragm as the depth limit of the resection.[7] An attempt was made to obtain 1.5 cm of macroscopically free surgical margins. Almost all operations prior to 1989 consisted of a vulvectomy and lymphadenectomy using a single en bloc incision. Subsequently, there was an increase in the use of three separate skin incisions: one over each groin, the third being the vulvectomy incision. This technique was not used on patients with clinically suspicious inguinal lymph nodes or with sufficiently extensive primary lesions that implied a risk of inadequate margins.

A total bilateral inguinofemoral lymphadenectomy with the preservation of the fascia femoralis included the superficial inguinal lymph nodes, the superficial femoral lymph nodes, and the deep inguinal or deep femoral lymph nodes. Surgery was performed as a single procedure on all patients.

Radiotherapy was given to all patients with 3 or more positive inguinal lymph nodes, with irradiation of the groin and the pelvis varying from 45 to 55 grays over a period of 4–5 weeks. No patients other than those just described were submitted to radiotherapy before a recurrence appeared. No chemotherapy was provided to any patient included in this series.

Patients received regular follow-up. Checkups were scheduled every 3 months during the first 2 years, every 6 months for the subsequent 3 years, and then once every 12 months. An appointment for the next checkup was made during each checkup. Checkups were also carried out at patient request. Women who did not show up at a scheduled checkup were reminded by telephone. Whenever it was not possible to find a woman, an effort was made to contact her relatives. Most patients exhibiting severe illness, even when different from recurrence, were referred to our unit or we were asked for a consultation. We could therefore assess cancer recurrence directly, if present, just before death, even in patients dying from causes other than vulvar carcinoma. In a few cases where this was not possible, the doctors in charge of the women's care were contacted and the medical records consulted.

No distinction between recurrence and reoccurrence was made. If the first recurrence occurred in more than one site, the patient was assigned to a group on the basis of the most advanced level of disease involvement (vulva $<$ lymph nodes $<$ distant).

The recurrence free interval was computed as the time from the day of surgery (admission date) to the

discharge date, i.e., the moment of evidence of disease recurrence, or the end of the follow-up period. In operational terms, the discharge date was taken to be the date of the last checkup for women with no evidence of recurrence. The study ended on June 2, 1997. Where checks were performed after that date, only the period until June 2, 1997, was considered for the follow-up. For women who died without recurrence, the discharge date was defined as the date of death. We could not assess whether recurrence was present in only one patient who died. She was considered as having exited the study without recurrence at the date of her last checkup.

All surgical specimens were sectioned in the same standardized manner.[8] An average of 7 blocks of the primary lesion and 12 blocks of the inguinal lymph nodes were examined.

The predictive variables considered were FIGO stage,[5] pT classification[6], patient age, greatest tumor dimension, tumor focality, depth of stromal invasion,[4] number of metastatic lymph nodes, koilocytosis within the tumor tissue, tumor necrosis, pattern of tumor invasion, lymphovascular space involvement, perineural space involvement, vulvar intraepithelial neoplasia (VIN) Grade 2 or 3 in tissue adjacent to the invasive tumor,[4] nonneoplastic epithelial disorders and superficially invasive carcinoma adjacent to the invasive tumor,[4] status of resection margins (positive when tumoral cells were found within 3 mm of the resection perimeter), type of vulvar surgery (total deep vulvectomy or partial deep vulvectomy), type of skin incision (single or triple), and distal uretrectomy.

Statistical Methods

The main study outcome was disease free survival. It was computed for the entire group by the Kaplan–Meier method.[9] Determinants of disease free survival were studied by using the Cox proportional hazards model.[9] Subjects with missing values for any of the variables were considered part of a separate category. For each variable P values were computed on the basis of Wald χ^2. If a variable could assume more than two values, then a likelihood ratio (LR) χ^2 was also computed for the overall effect.[10] Variables were considered in both the univariate analysis and after adjustment for the FIGO stage. This is an established prognostic factor and was found to be the most important predictor of disease free survival in our study.

Independent prognostic factors were selected by a stepwise procedure. In order to evaluate whether it was possible to select a low risk group without considering groin lymph node status, the same procedure was repeated with the FIGO stage and the number of involved lymph nodes excluded. Study women were grouped into subpopulations on the basis of selected variables, and absolute disease free survival was computed for each subpopulation by the Kaplan–Meier method.

RESULTS

The 101 patients were followed for a median of 3.1 years (range, 56 days to 15.5 years). Among study patients, 63% either had a recurrence or were followed for at least 5 years, and 76% were followed for at least 3 years. Among the 68 women in whom no recurrence was documented, 8 died of intercurrent causes, 41 had their last checkup within 6 months of the end of the study, and 13 more had their last checkup within 12 months. All women in the latter group were followed for at least 3 years. The remaining 6 women had their last checkup more than 18 months before the end of the study and were considered lost to follow-up. However, 4 of them were followed for at least 3 years.

Of 101 patients, 33 developed recurrences. One patient had a lymph node recurrence 2 months after the initial therapy. All the remaining patients had recurrence 3–127 months following surgery (median, 9.13 months).

Recurrence was vulvar in 18 patients, nodal in 11, and distant in 4. Multiple failure sites were noted in seven patients (vulvar and nodal recurrence in six, vulvar and distant in one). Fifteen of the 18 vulvar recurrences were on the same side of the primary neoplasm. With respect to distant recurrences (two bone and two lung metastases), all four patients had LVSI in their primary tumor, suggesting hematogenous spread.

Disease free survival probability at 1, 2, 3, and 5 years in the overall study population was 79.7%, 76.1%, 70.8%, and 66.2%, respectively (Fig. 1).

In univariate analysis (Table 1), FIGO stage, pT classification, greatest tumor dimension, multifocality, depth of stromal invasion, number of metastatic lymph nodes, presence of koilocytosis, LVSI, and the presence of associated VIN 2 or 3 were statistically associated with shorter disease free survival ($P < 0.05$). The presence of tumor necrosis and the involvement of surgical resection margins reached borderline significance.

After adjustment for the FIGO stage (Table 1), only tumor multifocality, the presence of koilocytosis, LVSI, and the presence of associated VIN 2 or 3 maintained independent effects. On the other hand, tumor necrosis and the involvement of surgical margins turned out to be significantly associated with shorter disease free survival, and neural invasion reached borderline significance.

FIGO Stage IVA (vs. IB, II, or III), tumor multifo-

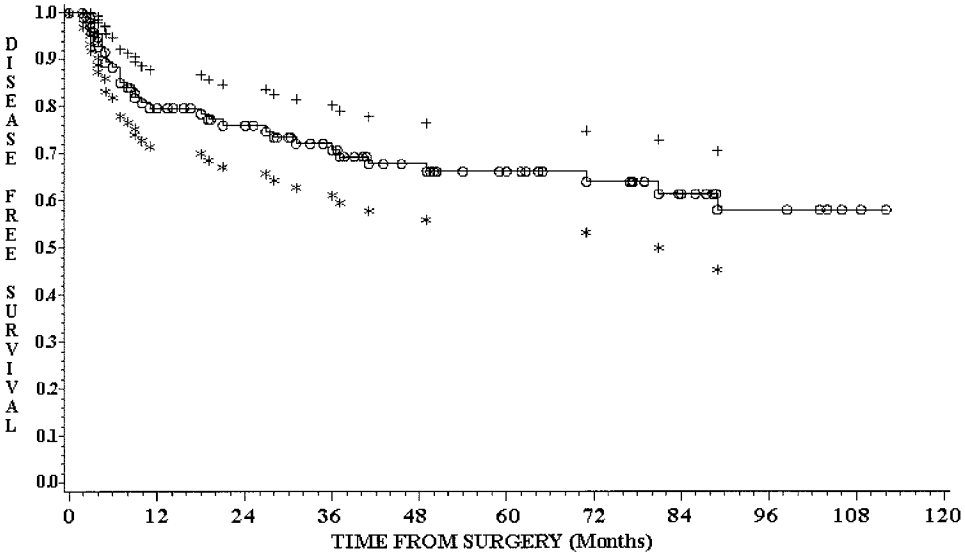

FIGURE 1. Disease free survival (with 95% CI) is shown for the entire study population.

cality, LVSI, the presence of VIN 2 or 3, and the involvement of resection margins were independent predictors of recurrence as based on stepwise model selection (Table 2). When a stepwise procedure was repeated while FIGO stage and lymph node status was ignored (Table 3), then greatest tumor dimension (< 2.5 cm, 2.5–4 cm, and > 4 cm), tumor multifocality, LVSI, the presence of associated VIN 2 or 3, and the involvement of surgical margins were selected as independent predictors.

When considering the type of vulvar surgery, the 88 patients treated by total deep vulvectomy showed no reduction in the risk of recurrence after adjustment for FIGO stage and the other independent prognostic factors. The same was observed in the 10 subjects who underwent distal urethrectomy. On the other hand, after adjustment for all independent risk factors, the 69 patients who had a single en bloc incision had a significantly lower relapse rate than the 32 patients who had a triple skin incision. This was true both after adjustment for variables in Table 2 (RR = 0.35, $P = 0.032$) and after adjustment for variables in Table 3 (RR = 0.37, $P = 0.032$). Adjustment for surgical technique variables only slightly changed the effect of the other clinicopathologic variables.

The group of patients with unifocal tumors of greatest dimension < 2.5 cm, no LVSI, no associated VIN 2 or 3, and no involvement of surgical margins (Group 1) comprised 16 patients and was followed for an average of 7.5 years. No recurrence was observed among them. Survival was, however, still high (Fig. 2) if greatest tumor dimension was still < 2.5 cm and there was no LVSI, even if the remaining criteria relapsed: 3 of these 16 subjects recurred (Group 2). On the other hand, 5-year disease free survival was 52% among women with greatest tumor dimension between 2.5 and 4 cm or LVSI: 22 of these 56 subjects had recurrence (Group 3), and 1-year disease free survival was only 42% among patients with greatest tumor dimension > 4 cm: 8 of these 13 subjects had recurrence (Group 4). Disease free survival was as low as 28.9% after 1 year in FIGO Stage IVA patients.

In Groups 1 and 2, lymph node involvement was present in 2 women and 1 woman, respectively, without capsular involvement in any of these cases.

DISCUSSION

This study was based on a series of patients in which a number of pathologic variables was measured systematically at treatment by the same pathologist (G.B.). In addition, the surgical technique was standardized and nonsurgical treatments were homogeneous. The duration of follow-up was long and the number of patients lost to follow-up very limited. Although the number of patients was not very large in absolute terms, it represents one of the largest series of this rare cancer currently studied at a single institution.

Only patients achieving free status were included in order to avoid confusion between residual and recurrent cancer. On the other hand, we did not discern recurrence from reoccurrence because the interval between a primitive carcinoma and the posttreatment appearance of a second vulvar invasive carcinoma is defined ambiguously in the literature.

The FIGO staging classification is based on tumor size and adjacent spread, lymph node involvement, and the presence of any distant metastases.[5] It is known to be the most important prognostic criterion for vulvar carcinoma, as confirmed in studies with

TABLE 1
Relative Disease Free Survival after Surgery for Vulvar Carcinoma: Effect of Studied Potential Determinants in Univariate Analysis and after Adjustment for FIGO Stage Classification

	Univariate analysis			Adjusted for FIGO stage	
Parameter	Recurrences/ subjects	Risk ratio	Specific *P* value (Wald)	Risk ratio	Specific *P* value (Wald)
FIGO stage/AJCC TNM[a]	(LR $\chi^2_{3df} = 20.86$, $P < 0.0001$)				
IB/T1bN0M0	7/34	1			
II/T2N0M0	8/25	1.59	0.37		
III/T3N0M0, T1–3N1M0	5/18	1.61	0.42		
IVA/T1–3N2M0	13/24	8.03	< 0.0001		
pT classification	(LR $\chi^2_{2df} = 12.95$, $P < 0.005$)			(LR $\chi^2_{2df} = 2.87$, $P > 0.05$)	
1	9/41	1		1	
2	19/54	2.24	0.047	1.59	0.46
3	5/6	9.53	< 0.0001	3.63	0.11
Greatest tumor dimension (cm)	(LR $\chi^2_{3df} = 14.22$, $P < 0.005$)			(LR $\chi^2_{3df} = 2.44$, $P > 0.05$)	
≤ 1.5	8/34	1		1	
> 1.5–2.5	5/24	0.96	0.94	0.82	0.76
> 2.5–4	12/30	2.96	0.019	1.89	0.40
> 4	8/13	5.16	0.0011	1.89	0.45
Tumor focality					
Unifocal	19/79	1		1	
Multifocal	14/22	2.90	0.0027	2.79	0.0044
Depth of stromal invasion (mm)	(LR $\chi^2_{4df} = 11.13$, $P < 0.05$)			(LR $\chi^2_{4df} = 4.02$, $P > 0.05$)	
≤3	7/23	1		1	
> 3–5	4/22	0.76	0.76	0.70	0.59
> 5–9	8/21	1.69	0.31	0.96	0.94
> 9	9/17	4.01	0.006	1.90	0.27
Missing	5/18	0.89	0.84	0.69	0.54
No. of metastatic lymph nodes	(LR $\chi^2_{4df} = 17.18$, $P < 0.025$)			(LR $\chi^2_{4df} = 0.796$, $P > 0.05$)	
0	16/62	1		1	
1	2/8	0.92	0.88	0.55	0.62
2	4/9	3.79	0.0202	1.07	0.96
3–5	8/15	4.46	0.0002	0.95	0.97
> 5	3/7	8.10	0.0014	1.32	0.84
Koilocytosis					
Absent	25/88	1		1	
Present	8/13	2.96	0.0083	4.00	0.0017
Tumor necrosis					
Absent	25/87	1		1	
Present	8/14	2.19	0.055	2.34	0.042
LVSI					
Not evident	10/52	1		1	
Evident	23/49	3.99	0.0005	3.09	0.0095
Neural invasion					
Not evident	28/88	1		1	
Evident	5/13	2.15	0.12	2.72	0.054
Association of VIN 2 or 3					
Absent	19/74	1		1	
Present	14/27	2.30	0.019	3.37	0.0018
Surgical resection margins					
Negative	27/91	1		1	
Positive	6/10	2.44	0.052	4.09	0.0055

FIGO: International Federation of Gynecology and Obstetrics; AJCC: American Joint Committee on Cancer; LR: likelihood ratio; LVSI: lymphovascular space involvement; VIN: vulvar intraepithelial neoplasia.
[a] Definition of TNM:[6] T1b: tumor confined to the vulva or vulva and perineum, 2 cm or less in greatest dimension, with stromal invasion greater than 1 mm; T2: tumor confined to the vulva or vulva and perineum, more than 2 cm in greatest dimension; T3: tumor of any size with adjacent spread to the lower urethra and/or vagina or anus; N0: no regional lymph mode metastasis; N1: unilateral regional lymph node metastasis; N2: bilateral regional lymph node metastasis; M0: no distant metastasis.

TABLE 2
Relative Disease Free Survival after Surgery for Vulvar Carcinoma: Independent Determinants (Stepwise Model Selection)

Determinant	Risk ratio[a]	Specific *P* value (Wald)
FIGO stage		
IB, II, III	1	
IVA	7.39	0.0001
Tumor focality		
Unifocal	1	
Multifocal	4.10	0.0003
LVSI		
Not evident	1	
Evident	2.96	0.0089
Associated VIN 2 or 3		
Absent	1	
Present	3.34	0.0017
Surgical resection margins		
Negative	1	
Positive	4.88	0.0031

FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymphovascular space involvement; VIN: vulvar intraepithelial neoplasia.
[a] Each risk ratio is adjusted for the other variables in this table.

TABLE 3
Relative Disease Free Survival after Surgery for Vulvar Carcinoma: Independent Determinants when Ignoring FIGO Stage and Lymph Node Status (Stepwise Model Selection)

Determinant	Risk ratio[a]	Specific *P* value (Wald)
Greatest tumor dimension (cm)		
< 2.5	1	
2.5–4	2.86	0.0129
> 4	5.98	0.0003
Tumor focality		
Unifocal	1	
Multifocal	3.36	0.0021
LVSI		
Evident	1	
Not evident	4.19	0.0005
Associated VIN 2 or 3		
Absent	1	
Present	3.06	0.0027
Surgical resection margins		
Negative	1	
Positive	2.78	0.0420

LVSI: lymphovascular space involvement; VIN: vulvar intraepithelial neoplasia.
[a] Each risk ratio is adjusted for the other variables in this table.

multivariate statistical analysis. Identifying other independent prognostic factors is, however, relevant in order to understand better the natural history of vulvar carcinoma and to select subgroups of patients at low risk of recurrence and suitable for a less aggressive surgical approach. In our study, tumor multifocality, LVSI, associated VIN 2 or 3, and involvement of surgical margins were actually independent predictors of recurrence.

Multifocality of neoplastic lesion, occurring in about 25% of invasive carcinomas (22% in our series), was already reported as associated with local recurrences.[11] Our data did not support the evidence that in multifocal cancers surgical margins are positive more frequently than in unifocal cancers:[11] only 1 of 22 multifocal tumors had positive margins versus 9 of 79 unifocal tumors. In addition, multifocality maintains its effect even after adjustment for the involvement of surgical margins (Table 3). Therefore other mechanisms are involved.

The association of LVSI with an increase in frequency of lymph node involvement was first reported by Donaldson[12] and confirmed in a large series of the Gynecologic Oncology Group.[13] In our data, the presence of LVSI increased slightly (though statistically not significantly) from vulvar recurrences (12/18) to lymph node (8/11) and distant (4/4) recurrences.

To our knowledge, our study is the first to report adjacent VIN 2 or 3 as a significant independent predictor of reduced disease free survival in multivariate analysis. Among the 14 cases of recurrence associated with VIN 2 or 3, 7 were vulvar recurrences, 5 lymph node recurrences, and 2 distant recurrences. At variance is another recent study[14] that found better disease free and overall survival of cases associated with VIN 3 when compared (without adjustment for other factors) with cases associated with lichen sclerosus. We found koilocytosis to be a significant prognostic factor after adjustment for FIGO staging, but it did not show an independent effect in the final model. In our data, koilocytosis in invasive carcinoma was strongly associated with the presence of VIN 2 or 3 in adjacent lesions: indeed, koilocytosis was present in 10 of 27 cases with associated VIN 2 or 3 and in only 3 of 74 cases without VIN 2 or 3 (OR = 10.4, $P < 0.0001$). Therefore, it behaved mainly as an indicator of associated VIN 2 or 3 presence. The clinical significance of HPV infection in vulvar carcinoma has not been well established and results regarding its prognostic significance are conflicting.

The involvement of surgical resection margins is frequently reported in association with local relapses. The recurrence rate is higher when tumor free margins are less than 1 cm[11,15] without correlation with the type of vulvar surgery (modified wide radical vulvar excision vs. total radical vulvectomy).[16] In our series, neither patients treated with deep total vulvectomy nor those who underwent distal urethrectomy showed a significant reduction in the risk of recurrence after adjustment for the FIGO stage. On the other hand, we found an increased risk of relapse for triple incision,

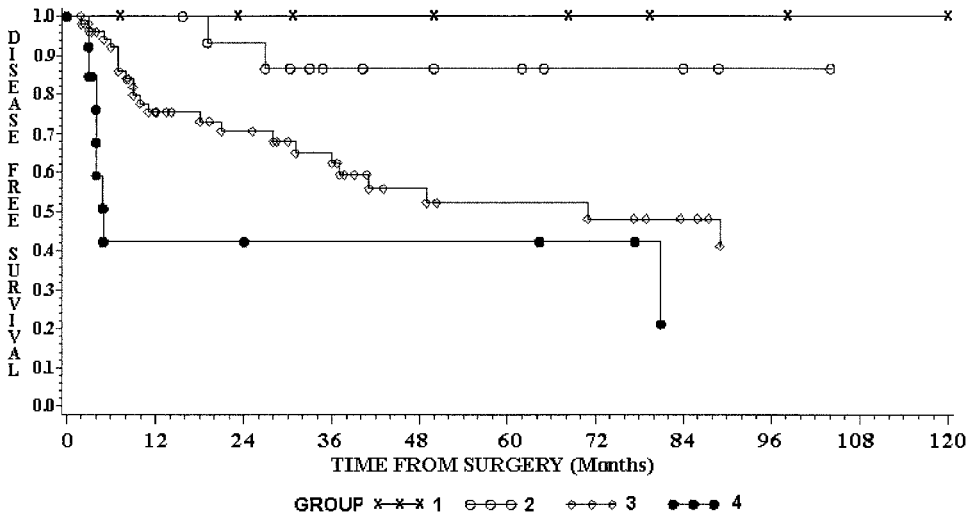

FIGURE 2. Disease free survival is shown for sub-populations of patients treated for vulvar carcinoma. Group 1: Patients with unifocal tumors of greatest dimension < 2.5 cm, no lymphovascular space involvement (LVSI), no associated vulvar intraepithelial neoplasia (VIN) 2 or 3, and no involvement of surgical margins. Group 2: Patients with greatest tumor dimension < 2.5 cm and no LVSI. Group 3: Patients with greatest tumor dimension between 2.5 and 4 cm or LVSI. Group 4: Patients with greatest tumor dimension > 4 cm.

after adjustment for the other independent prognostic factors. However, no relapse in this group occurred on the skin bridge preserved between the vulvar and groin incisions. In any case, this study was not designed to assess the effectiveness of different surgical techniques: a randomized trial would be more appropriate. Other observational studies have reported the risk of recurrence as not being altered by the type of incision,[17] with no drop in the overall cure rate for triple incision.[18] However, uncertainty remains regarding patients with positive inguinal lymph nodes treated with separate incisions.[17]

We considered tumor size and lymph node metastases in greater detail than FIGO staging does, but we found no independent effect after adjustment for the FIGO stage itself. Therefore, our study does not allow us to state that such further detail adds prognostic value.

We defined groups at different risks of relapse on the basis of our analysis. Our purpose, when computing their survival, was not to confirm a difference (as this was for the same subjects, it would have been tautological), but to obtain absolute risk estimates. Actually, these are interesting for patients and clinicians in the context of deciding the most appropriate treatment. Even when we used prognostic criteria that did not require lymphadenectomy to be verified, we identified a subpopulation of patients at an extremely low risk of recurrence (Group 1) and another at favorable prognosis (Group 2). This was in agreement with our previous finding that lymph node involvement could be predicted by tumor size and the presence of vascular invasion.[3] Such low risk subpopulations represent a nonnegligible proportion of vulvar carcinoma patients (in our series, about one subject out of three belonged to either group) and are therefore of substantial clinical interest.

Our findings could suggest the initial treatment of all patients by relatively conservative surgery. If, based on the results of such initial surgery, the woman is classified in a low risk group, then treatment could stop, whereas more radical intervention could follow in high risk subjects. The prediction of groin lymph node involvement by other pathologic criteria is, nevertheless, not completely precise. Indeed, more than 10% of cases in Group 1 had lymph node involvement. In such cases we cannot presume a favorable prognosis in the absence of a lymphadenectomy. Indeed, in previous studies in which an attempt to reduce the radicality in the surgical approach to the groin was made, an increased recurrence rate with subsequent high mortality rate was reported.[2,19]

Therefore, we still believe that total bilateral inguinofemoral lymphadenectomy is the standard approach to treating invasive vulvar carcinoma. However, given the a priori low risk of lymph node involvement and recurrence, patients belonging to Groups 1 and 2 could be candidates for a trial to evaluate more conservative inguinal surgery based on the recent results from sentinel lymph node lymphoscintigraphy technology.[20]

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