Carcinoma of the vulva: critical analysis of survival and treatment of recurrences

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Summary: Prognostic variables in vulvar cancer include: stage, lymph nodal status, tumour diameter, vascular space invasion, depth of invasion. Treatment must in the cost/benefit balance, be adequate to these prognostic variables and surgery is today the cornerstone in vulvar cancer management. In early stages it is possible to control the disease with personalited radical non-mutilant operations limiting the high incidence of complications of the past, without endangering the 5-year survival rate.

The risk of relapses is related to some factors such as site of tumour growth, depth of tumoural infiltration, lymphnode involvement and vascular space involvement. Relapses appear earlier in the groin than in the primitive sites and cases with more than 3 effected nodes have a higher incidence of recurrences in any site. Survival in related to localization and time of relapses. The treatment of recurrence is personalised for different sites, almost always surgical, in local recurrences.

The problem of survival and of relapses in vulvar carcinoma is always present because the operative situations still remain unfavourable.

High indicence of advanced stages and tumoral aggressiveness factors both play an important role.

In our case series in the last 30 years incidence of advanced cases has decreased but not much, with little statistical significance from 63.2% in the 60ies to 54.9 in the 80ies. This contrasts, for example, with a notable reduction of advanced stages in cervical carcinoma. Maybe this is due to slight engagement of gynaecologists in careful examination of the vulva at every visit and on every occasion of screening for genital neoplasias.

Consequently the precise evaluation of the stage for prognosis and treatment is important. We follow the postsurgical FIGO staging on the basis of our Surgical Pathological Staging ([1]).

As we know stage remains the most important prognostic factor, based on the evaluation of the tumour diameter as well as of possible diffusion to surrounding tissues and lymphnodal involvement.

Other prognostic elements are the depth of stromal infiltration, the thickness of the lesion and the site itself, median or lateral.

It must also be remembered that dimension and thickness of the tumour are directly correlated with the incidence of lymphnodal metastases.

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Lecture at the Vth International Symposium on Gynaecological Oncology, Surgery and Urology, Venice, 5th-8th April 1992.

Reprint from Europ. J. Gynaec. Onc.
XIII, 6, 1992

Table 1. – *Vulvar cancer: correlation between clinical and pathological findings of inguinal nodes.*

Author	N 0 nº (%Pos)	N 1 nº (%Pos)	N 2-3 nº (%Pos)
Rutledge 1970 (2)	40 (13)	28 (11)	42 (74)
Morley 1976 (3)	120 (19)	43 (16)	83 (66)
Morris 1977 (4)	27 (15)	27 (26)	16 (69)
Boyce 1985 (5)	42 (17)	19 (32)	18 (92)

As is well known lymph node involvement is the main prognostic factor (number of affected nodes, mono or bilateral diffusion) and it conditions integrated therapies (Tab. 1).

Clinical evaluation of lymphnodal status is not reliable: from literature 15-20% of inguinal lymphnodes clinically negative proved instead positive at following pathological examination. On the other hand 30% of clinically positive inguinal lymphnodes proved negative at successive pathological examination ([2, 3, 4, 5]).

The incidence of lymphnodal involvement, even in early stages (tumours less than 2 cm.), is very high ([1]) and consequently inguino-femoral lymphadenectomy is always mandatory, except in microcarcinoma (as defined by ISSVD: infiltration depth less than 1 mm) ([6]).

In fact, as is well known, only neoplastic infiltration less than 1 mm is without risk of lymphnodal involvement, which is described in superficial invasive cancers more than 1 mm ([7, 8, 9, 10, 11, 12]) (tab. 2).

Some pathological variables appear to be correlated with lymphnodal spread but *tumour aggressiveness factors* can have a prognistic value only in early stages.

We did not find any correlation between *grade* and survival rate or lymphnodal involvement, while others reported a correlation with lymphnodal metastases.

Besides, grade is a very personal evaluation for each pathologist with a consequent different incidence of grades in each case series (Tab. 3).

Vascular space invasion is statistically correlated (also in our case series) with survival rate and lymphnodal involvement.

Concerning *tumour site* same case series reported higher lymphnodal spread in midline localized tumours while we found only a higher incidence of central relapses, maybe because of the difficulties in reaching radicality in midline tumours.

In conclusion survival greatly depends on stage, on lymphnodal involvement and on vascular space invasion.

Treatment must be adequate in the cost-benefit balance and surgery is today the cornerstone in vulvar cancer management.

Radiotherapy alone has lost every role in primary local treatment of vulvar cancer; the frequent radionecrosis is dangerous, painful and often compromises the possibility of surgery itself ([13, 14, 15, 16]).

Neodjuvant chemotherapy in advanced cases is applied now in order to reduce the intraoperative diffusion of neoplastic

Table 2. – *"Superficial invasive" vulvar cancer. Lymphnodes metastases and recurrences.*

Author	No. cases	Lymph-adenect.	L. N. pos	Recurr.
Wharton 1974 (8)	25	10	0	2
Parker 1975 (9)	58	37	3	5
Magrina 1979 (10)	96	71	8	10
Wilkinson 1982 (11)	30	27	2	1
Kneale 1983 (12)	92	61	6	18
Totale	313	217	24 (11%)	36 (16.5%)

Table 3. – *Vulvar cancer, pathological variables and lymph-nodal Spread.*

	Boyce (5) (1985) 84 cases	Shimm (17) (1986) 98 cases	Seldis (18) (1987) 272 cases	Onnis (1992) 181 cases
Diameter	s.	s.	s.	s.
Midline location	s.	–	s.	n.s.
Vascular space pos.	s.	–	s.	s.
Grading	n.s.	s.	–	n.s.
Depth of invasion	s.	s.	s.	s.
Stromal reaction	n.s.	–	–	n.s.

n.s. = not statistically significant.
s. = statistically significant correlation.

cells and better define and limit tumoral invasion.

The results in reducing the tumoral volume are sometimes tremendous but we still do not know if survival will be really improved or not.

Survival must be evaluated on the basis of post surgical FIGO staging and of surgical management, which must always be radical, with systemic bilateral inguinocrural lymphadenectomy and, in target cases, pelvic lymphadenectomy too.

In our clinical experience *operability* was always high, even 30 years ago. Now it is close to 100% ([1]).

Radicality in operated cases has greatly improved in the last decade and now, in cases limited to the vulva (postsurgical FIGO I and II) it is almost as high as 100% ([1]) (Tab. 4).

In early stages 5-year survival rates in our case series are as good as in other case series, on the contrary in advanced cases and particularly in Post Surgical FIGO Stage II the survival in our case series is unsatisfactory and often worse than others'.

Incorrect mortality rates on very old patients may account for the low 5-year survival rate. We will check our cases evaluating an adjusted mortality too.

In our case series the incidence of very old patients (over 70 years old) in FIGO Stage II is very high (45.3%) compared to the incidence in FIGO Stage I (25.4%).

Also the type of surgery must be adequate to stage and to tumour aggressiveness factors. In modern oncology the respect for quality of life is mandatory and, when survival is ensured, the best quality of life must be looked for.

Most of all, the cost-benefit balance must be carefully evaluated.

Overtreatment does not change prognosis but often only quality of life, and in vulvar cancer as well as in breast cancer mutilations are very heavy,

In early cases mutilations may be limited but surgery must always be radical and enlarged with regional lymphadenectomy.

On the basis of these considerations, following the concept of quality of life (no « quality without life » but also « no life without quality »; both are valid), we have been performing for about 20 years, in early stages, an enlarged radical non mutilant vulvectomy ([1]). Further advantages

Table 4. – *Five-years survival in the different stages.*

Case series	No.	STAGE I	II	III	IV
Iversen T. (19) (1980	424	93	75	50	–
Podraz K.C. (20) (1982)	224	90	1	68	20
Boyce J. (5) (1984)	84	100	83	53	0
Shimm D.S. (17) (1986)	98	87	67	48	0
Hacker N.F. (21) (1986)	113	98	90	60	0
Cavanagh D. (22) (1986)	154	84	61	28	5/10
Onnis A. (1992)	181	95	64	45	0

Table 5. – *Incidence of recurrences in vulvar cancer.*

Stage	Podraz (20) 1982	Boyce (5) 1985	Shimm (17) 1985	Onnis 1992
I	0%	12%	14%	19%
II	25%	26%	17%	10.2%
III	55%	60%	34%	36.3%
IV	66%	–	71%	11%

of this technique are the low incidence of anatomo-functional complications, the possibility of a normal sexual life and the positive psychological aspect which is stimulating for the young patient.

This technique is a modification of Way's vulvectomy only in the preservation of the skin, because it is almost the same in the removal of deep subcutaneous lymph-adipose surrounding tumoural tissues and regional lymphnodal chains ([23, 24, 25]).

The enlarged removal of surrounding tissues at the border of vagina and urethra, and sometimes a colpectomy of the lower third, are necessary in order to avoid midline relapses.

In our opinion this is the real limit, in many cases, of enlarged surgery which often cannot be exceeded without compromising urinary or rectal continence. In fact the incidence of recurrences in central sites is significantly high and it does not change with enlargement of inguino crural skin demolitions together with the vulva.

In our case series there was no difference in survival rate between cases treated with classic Way's vulvectomy and cases treated with non-mutilant operation ([1]).

Table 6. – *Vulvar cancer risk of relapses.*

	p	Odds ratio
Site of tumour growth		
Median vs lateral	0.004 s.	4.8
Tumour infiltration		
Profound vs superficial	0.003 s.	4.6
Lymph-nodes		
Positive vs negative	0.01 s.	3.5
Vascular spaces		
Positive vs negative	0.01 s.	3.4
Stromal rection		
Intense vs absent/mild	0.2 n.s.	1.6
Tumour grade		
G3 vs G1-G2	0.4 n.s.	1.4

The incidence of relapses is equally without significant statistical differences between the two types of operations.

We believe that, more often than surgical technique, stage and aggressiveness factors influence the patient's destiny and the incidence of relapses (Tab. 5).

The risk of relapses is related to some factors such as site of tumour growth, depth of tumoral infiltration, lymphnode involvement and vascular space invasion (Tab. 6).

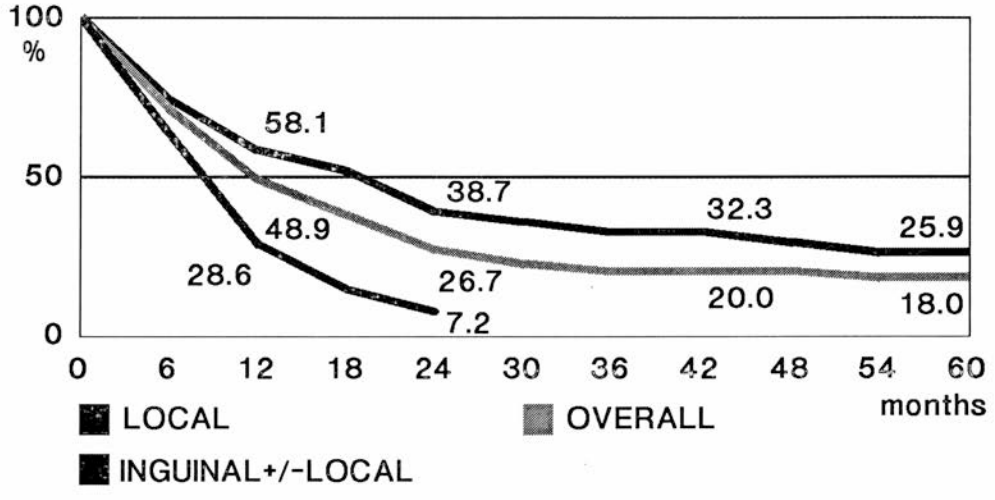

Fig. 1. — Vulvar cancer. Survival and site of relapses.

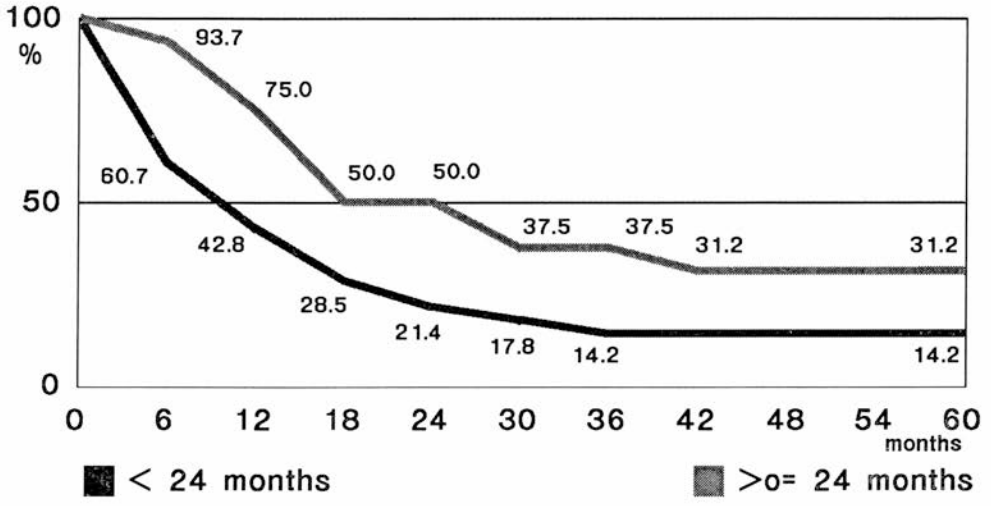

Fig. 2. — Vulvar cancer. Time of relapse and survival rate.

Relapses appear earlier in groin (after 10.4 months) than in primitive sites (33.9 months) and earlier in cases with positive nodes (18.1 months) than in cases with negative nodes (36.3 months).

The number of more than three involved lymphnodes appears to be related with a higher incidence of recurrences in any site ([6]). Survival is related to relapse localization; in our case series it is better in local recurrences than in inguinal recurrences (Fig. 1).

Also the time of relapse influences prognosis: it is worst in cases of early relapses (Fig. 2).

The treatment of recurrence is personalized for different sites, almost always surgical in local recurrences. In the last period the association of radiotherapy and of Fluoruracil can prove useful in some cases, particularly in order to avoid anorectal surgical demolition ([26, 27, 28]). In other cases surgery, even highly mutilant and with intestinal or urinary diversions may be indicated. In these cases, reconstruction by skin flap, miocutaneous translocations or mash skin graft can satisfactorily resolve the problem of a wide demolition (Tab. 7).

In inguinal and/or pelvic lymphnodal relapses radiotherapy and chemotherapy alone or associated with surgery allow some results but with an overall bad prognosis.

In conclusion we believe in a better future in vulvar cancer management only with much earlier diagnoses in order to improve preinvasive or very early invasive case incidence.

Only in this way will we be able to reduce the cost of therapies and to improve the quality of life without endangering survival.

Unfortunately still today vulvar cancer continues to be terrible for the patient's life and destiny.

Table 7. – *Vulvar cancer treatment of relapses* (57 cases).

Surgery	36	63.1%	73.7%
Surgery + chemotherapy	3	5.3%	
Surgery + radiotherapy	3	5.3%	
Chemotherapy	8	14.0%	
Palliative care	7	12.2%	

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