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CLINICAL ARTICLE

Invasive vulvar carcinoma and the question of the surgical margin

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ABSTRACT

Objective: To assess the discrepancy between width of surgical margin measured with the naked eye/ruler by a surgeon before removing an invasive vulvar carcinoma, and width of margin measured under microscope by pathologist after fixation of the resected lesion with formalin. Potential relationships between discrepancy and disease recurrence were also investigated. *Methods:* This prospective study was conducted with resected lesions from 86 women who underwent surgery for primary/recurrent invasive vulvar carcinoma. After the surgeon removed the lesions surrounded by 1–2-cm margins, the pathologist determined margin width at the 4 cardinal points of 86 lesions (for a total of 344 margin assessments), first macroscopically and then under the microscope. *Results:* A safety margin of 0.8 cm on microscopic view was achieved in 83% of cases (112 of 135) when the macroscopic measurement was 1 cm, in 91% of cases (58 of 64) when it was 1.5 cm, and 98% of cases (105 of 107) when it was 2 cm. *Conclusion:* There was a small discrepancy between the surgeon's intent and the microscopic margin measurement, mostly related to tissue shrinkage. A 1-cm surgical margin corresponded to a 0.8-cm margin in microscopic view (the "safe margin") in most cases.

1. Introduction

Vulvar cancer accounts for 3% to 5% of all genital cancers affecting women [1]. Over the decades, its surgical management has evolved from radical vulvectomy in all cases to individualized approaches aiming at removing less than the entire vulva, when possible. These are referred to as modified radical vulvectomy, hemivulvectomy, and wide local excision, and the interventions can be performed with or without flap reconstruction.

Tumor size, thickness, keratinization, depth of invasion, and growth pattern, lymphovascular space invasion, and width of the surgical margin are all considered potential predictors of tumor recurrence after surgery. Among these variables, the width of the margin is the only one that can be "tailored" at the time of surgery. The proper width of the surgical margin, however, remains a matter of debate among gynecologic surgeons [2–7].

Formalin fixation and paraffin embedding of surgical samples are thought to cause resected tissues to shrink by approximately 20%, and most authors consider that the safety margin should be no less than 8 mm on microscopic view to ensure prevention of local recurrence. It is therefore generally recommended that surgeons allow a margin of 1 cm around the resected lesion [5,7]. However, de Hullu et al. [8] found that a surgical margin of 1 cm resulted in a microscopic margin less than 8 mm in 50% of cases, and suggested that the rates of local recurrence were high because of 1-cm surgical margins. These authors recommend a surgical margin of 2 cm.

We conducted this study to assess the discrepancy between the width of the surgical margin as measured with the naked eye and a ruler by the surgeon removing invasive vulvar carcinomas, and the width of the margin as measured under the microscope by the pathologist after the resected lesion has been fixed with formalin. We also looked for a relationship between discrepancy and disease recurrence and discuss treatment and prognosis.

2. Materials and methods

In a prospective study conducted from December 1, 1998, to March 31, 2007, 86 women with an operable primary or recurrent invasive vulvar carcinoma were treated at Sapienza University and Campus Biomedico in Rome, Italy. The study protocol was reviewed and approved by the local ethics committee.

Besides having an invasive carcinoma of the vulva, the inclusion criteria were WHO performance status less than 2, good nutritional status, no contraindications to surgery, expected strict adherence to follow-up, and signed informed consent. The women with dysplasia, intraepithelial neoplasia, or microinvasive carcinoma of the vulva were excluded. The preoperative evaluation included a general physical examination, blood tests, an electrocardiogram, and a chest radiograph as well as a complete gynecologic evaluation that included vulvoscopy, colposcopy, an ultrasound examination of the pelvis, and a computed tomographic scan of the abdomen and pelvis. During the first 3 postoperative days, the patients were prophylactically treated with subcutaneous low-molecular-weight heparin and early

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mobilization (to prevent deep-vein thrombosis) and with antibiotics (to prevent wound infection). Moreover, they underwent urinary drainage with catheterization and daily suction until complete wound healing. The follow-up consisted of physical and gynecologic examinations, the latter including vulvoscopy and colposcopy, 1 month after surgery, then every 3 months for the first 2 years, and then every 6 months for another 3 years. A computed tomographic scan of the abdomen and pelvis was also performed once a year. Disease recurrence was surgically treated when indicated.

The patients underwent radical vulvectomy, hemivulvectomy, modified partial vulvectomy, or wide local excision depending on disease site and extension. If a lesion was located far from the urethra, clitoris, or anus, the intent of the surgeon was to excise the lesion plus 1 to 2 cm of healthy vulvar tissue around the lesion so that the margin width would be at least 0.8 cm (the "safe" width) on microscopic view. After measuring the lesion with a ruler, the surgeon traced using an ink line the outer edge of the surrounding healthy tissue to be resected together with the lesion. Inguinofemoral lymphadenectomy was also performed unilaterally or bilaterally, as needed.

The surgical specimens were then oriented, placed on a cork support, and sent to a pathologist without being fixed with formalin. At the laboratory, the perimeter of the lesion was traced with blue ink and the distance between the perimeter and the outer edge of the sample was measured a first time by the pathologist at the 4 cardinal points, each margin surrounding the lesion thus receiving 4 measurements (86 studied lesions and 4 measurements per lesion providing 344 measurements). These measurements will be referred to as measurements on macroscopic view. The samples were fixed with formalin and the vulva and the neoplastic lesion were measured after 24 hours of fixation. The specimens were then embedded in paraffin and cut with microtome; the sections obtained were collected on slides for staining. Histopathologic study entailed determining the size, thickness, type, and grade of the lesion; the depth of invasion; and the presence or absence of lymphovascular cell invasion. When this part of the study was completed, the pathologist performed radial sections in the margins at the level of the 4 cardinal points and then measured the 4 margin widths for the second time. The resected margin samples were then stained with hematoxylin-eosin and evaluated for the presence of tumor cells. After 24 hours, the pathologist measured once more the distance between the perimeter of the ink-marked lesion and the outer edge of the sample at the level of the 4 cardinal points, this time under the microscope while looking for tumor cells within the margin. These measurements will be referred to as measurements on microscopic view.

To assess the occurrence and extent of tissue shrinkage better, we also measured vulva and lesion immediately after their removal and 24 hours after fixation in formalin in our last group of 9 patients. Analyses were carried out using the Fisher exact test.

3. Results

From December 1, 1998, to March 31, 2007, 86 women with invasive vulvar cancer, whether primary (n = 64 [74.4%]) or recurrent (n = 22 [25.6%]), underwent surgery at Sapienza University and Campus Biomedico in Rome, Italy. The characteristics of the patients are shown in Table 1. The median age was 69 years (range, 41–88 years). Most lesions were moderately or poorly differentiated squamous cell carcinomas, with a mean size of 3.7 ± 1.5 cm. The lesions were located in the anterior (n = 34), median (n = 45), or posterior (n = 7) part of the vulva. Twenty one women had multiple lesions.

Forty two (49%), 33 (38%), and 11 (13%) patients, respectively, underwent radical vulvectomy, hemivulvectomy, and wide local excision. Ten (6.4%) of the 64 patients with primary disease and 9 (0.4%) of those with recurrent disease received reconstructive surgery by means of a V-Y flap.

Table 1
Characteristics of the patients.[a]

Characteristic	Primary disease (n = 64)	Recurrent disease (n = 26)
Median age (range), y	70 (41–88)	68 (59–82)
Site of lesion		
Clitoris	5 (8)	4 (19)
Fourchette or anus	4 (6)	2 (9)
Labia majora	28 (44)	11 (52)
Labia minora	14 (22)	6 (29)
Paraurethral	13 (20)	6 (29)
More than 1 site	13 (20)	8 (38)
Type of surgery		
Radical vulvectomy	37 (58)	5 (23)
Hemivulvectomy	27 (42)	6 (27)
Wide local excision	0 (0)	11 (50)
Reconstructive flap	10 (16)	9 (43)
Inguinofemoral lymphadenectomy		
Ipsilateral	11 (17)	5 (23)
Bilateral	39 (61)	3 (14)
Lesion grade		
1	9 (14)	4 (19)
2	38 (59)	13 (59)
3	17 (27)	5 (24)
Positive lymph nodes	14 (22)	5 (24)

[a] Values are given as number (percentage) unless otherwise indicated.

The macroscopic values of the 344 margin measurements—256 from primary lesions and 88 from recurrent lesions—were checked against the values of the measurements on microscopic view. The measurements were categorized as being 0.5 cm, 1 cm, 1.5 cm, and 2 cm.

Of the 344 margin measurements taken on macroscopic view, 31 were categorized as being 0.5 cm, 114 as being 1 cm, 50 as being 1.5 cm, and 61 as being 2 cm among the primary lesions, and 7 as being 0.5 cm, 21 as being 1 cm, 14 as being 1.5 cm, and 46 as being 2 cm among the recurrent lesions (Table 2).

Of the 38 margins measurements of 0.5 cm, 29 (76%) were from lesions in the anterior part of the vulva close to the urethra, 7 (18%) from lesions in the posterior part of the vulva close to the anus, and 2 (5%) from lesions in the median part of the vulva. The 7 remaining lesions (18%) were from surgical specimens containing more than 1 lesion. There was a higher percentage of lesions with 1 macroscopic measurement greater than 1 cm in the median part of the vulva than in the anterior or posterior parts.

Tumor cells were found in one of the 4 resected parts of the margin for 6 (7%) of the 86 patients (in other words, 6 (2%) of the 344 resected margins parts were positive for disease). Of the 6 patients with tumor cells in the margin, 3 had primary and 3 had recurrent disease. In 5 cases, the macroscopic measurement (i.e. before fixation in formalin) was 0.5 cm and in the sixth case it was 1 cm (Table 3).

As expected, only in a small minority of cases (4 [10%] of 38) did margin widths of 0.5 cm, as measured on macroscopic view, achieve the safe width of 0.8 cm on microscopic view (Table 3).

As measured on microscopic view, 279 (81%) of the 344 margin widths were 0.8 cm or wider and the rate of margins at least 0.8 in width reached 90% (275 of 306) when margin width of 0.5 cm on macroscopic view were excluded.

Table 2
Margin width on macroscopic view according to form of disease.

Form of disease (No. of measurements)	Margin width, cm			
	0.5	1	1.5	2
Primary (256)	31 (12)	114 (44)	50 (20)	61 (24)
Recurrent (88)	7 (8)	21 (23)	14 (16)	47 (53)
Total (344)	38 (11)	135 (39)	64 (19)	107 (31)

[a] Values are given as number (percentage).