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Demographic, Clinical, and Treatment Trends Among Women Diagnosed with Vulvar Cancer in the U.S.

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Abstract

Objective—Describe the treatment and survival patterns among a population-based sample of vulvar cancer patients diagnosed in the U.S. in 1999.

Methods—Cases were identified for the National Cancer Institute's Patterns of Care Study (POC) using Surveillance, Epidemiology, and End Results Program (SEER). A stratified random sample of non-Hispanic white, non-Hispanic black, and Hispanic women age 20 and older was selected from cases reported by eleven SEER registries. Analyses of the association between vulvar cancer and key demographic, clinical, and hospital characteristics by stage were performed. Cox proportional hazards was used to estimate the odds of death due to cancer. All estimates were weighted, and analyses were conducted with SUDAAN.

Results—90% of cases were diagnosed with *in situ* or early stage invasive disease. Older patients were more likely to present at advanced stages. 25% of women with Stage III–IV vulvar cancer received chemotherapy plus radiation. We noted widespread use of radical local excision among women with Stage I/II cancer, but 46%–54% with invasive disease underwent a radical or total vulvectomy. Factors associated with cancer death were limited to age and stage. Women 75 years and older were at higher risk compared to women aged 20–49 and the risk of death increased with advancing stage.

Conclusions—Vulvar cancer is diagnosed at early stages. Late stage disease is associated with a significant increase in mortality. Radical surgery was still commonly performed in 1999. Radiation was more common in women diagnosed at late stage, while the use of chemoradiation remained limited.

Keywords

Vulva; vulvar; cancer; patterns of care; treatment

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Article Précis

Describe treatment and survival among a population-based sample of women in the US diagnosed in 1999 with vulvar cancer and treated in the community.

Introduction

Although cancer of the vulva accounted for less than 3% of all female-related cancers diagnosed from 1999–2003 [1], it is estimated that in 2007 as many as 3,490 women will be diagnosed with vulvar cancer and 880 will die from the disease [2]. The 5-year relative survival rate from vulvar cancer is quite good; greater than 78% [3], however, the lack of change in age-adjusted incidence and mortality for the last 10 years [1–5] suggests that we have far to go in making significant progress in the areas of cancer control, prevention, and treatment.

Epidemiological evidence to date suggests that there are two etiologic paths at work in vulva carcinogenesis [6–7]. The first type is often seen in women over the age of 50 and is associated with non-neoplastic epithelial disorders (VNED) such as chronic inflammation or lichen sclerosis [6]. Additionally, VNED-related vulvar cancer does not typically present with cervical neoplasia or condylomas. The second type is often seen in women under the age of 50 and is associated with human papillomavirus (HPV) infection [6–7]. Unlike vulvar cancers that are VNED in origin, the HPV type is associated with precursor lesions, namely vulvar intraepithelial neoplasia (VIN), and a history of condylomata. Other risk factors among this age group include current tobacco use, the presence of genital warts, and a high number of sexual partners [6]. These factors, however, are closely linked to the risk of HPV infection, and their link to vulvar cancer may be through HPV infection.

Surgical treatment for the disease is varied. Historically, vulvar cancer has been treated by radical vulvectomy with bilateral dissection of the inguinal groin nodes. More recently, radical local excision, with inguinal lymph node dissection based on depth of invasion has become more widely used [6,8–10]. Adjuvant chemoradiation is commonly recommended as primary therapy for women with large tumors, as well as for patients who undergo primary surgery and are found to have close or positive margins or with metastatic disease in inguinal lymph nodes [9–11].

The primary objective of this study is to describe the treatment and 5-year survival patterns among a population-based sample of vulvar cancer patients diagnosed in 1999 who were identified for the National Cancer Institute's (NCI) Patterns of Care Study using the Surveillance, Epidemiology and End-Results (SEER) Program,.

Materials and Methods

SEER collects detailed data on all cancer cases diagnosed within defined geographic regions in the United States. At the time of this study, SEER-funded registries represented approximately 14% of the total U.S. population. In addition to data on tumor characteristics, demographics and therapy, SEER registries maintain an active follow-up of the cases for vital status. Data for SEER registries are primarily collected from hospitals, surgical centers, and radiation facilities. Because much of the adjuvant therapy is provided in an outpatient setting, the NCI annually conducts Patterns of Care (POC) studies to supplement the treatment data for selected cancer sites. Patients diagnosed in 1999 with vulvar cancer were identified through the SEER program for inclusion in this POC study.

All non-Hispanic white, non-Hispanic black, and Hispanic women age 20 and older diagnosed with vulvar cancer in 1999 were eligible for inclusion in the study. *In situ* and invasive vulvar cancers were further selected by histology (M8050–M8094). We excluded women with a previous diagnosis of cancer (other than non-melanoma skin), a simultaneous diagnosis of cancer of a second site, or who were diagnosed at autopsy or identified solely via death certificate; leaving a total of 523 cases.

All patients selected for the study had their clinical and demographic information re-abstracted from the hospital, surgical center and/or radiation facility. Surgical procedures were abstracted from the patient's operative report in the hospital chart, and defined as either no surgery, incisional biopsy, excisional biopsy, wide or radical local, radical or total vulvectomy, and unknown if surgery performed. Wide or radical local excision includes a wide incision around the tumor with dissection to the deep perineal fascia, and radical vulvectomy refers to the butterfly or longhorn surgical approach removing the entire vulva [12]. Each patient's treating physician was contacted to verify adjuvant therapy information and provide a referral to any other health care professional who might have provided therapy. In most cases the patient's medical oncologist or radiation oncologist was contacted. If the patient was not known to have been referred to either a medical oncologist or radiation oncologist the surgeon was contacted. One abstractor from each of the participating registries (the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, Seattle, San Jose/Monterey and Los Angeles County and the states of Connecticut, Iowa, New Mexico, Utah and Hawaii) attended a central training session to ensure the consistency of data abstraction and coding among registries.

All data on comorbidities at the time of most definitive therapy, usually surgery, were recorded from the hospital record. These abstracted comorbidities were submitted to one central location and were coded by a single Registered Health Information Technologist. Data on comorbid conditions were summarized using the Charlson Comorbidity Score [13]. Lymph node dissection data were collected from the medical record and included the total of all regional lymph nodes removed. Lymph node data were summarized as a categorical variable of "regional lymph nodes"; these include superficial inguinal, deep inguinal and external iliac and removal of regional lymph nodes would include some or all of these.

Analyses of the association between vulvar cancer and clinical or non-clinical variables were performed. All estimates were weighted to reflect the population from which the sample was drawn. The sample weights, calculated as the inverse of the sampling proportion for *in situ*/ invasive and each racial/ethnic group, were used to obtain estimates that are representative of all eligible vulvar cancer patients in the study areas. We used the statistical software SUDAAN for all analyses [14]. The SUDAAN software allows for the use of sample weights and adjusts the standard errors appropriately

The statistical significance tests for associations were assessed using the Wald-type F statistics. All p-values were two-sided and the test results, including hazard ratios, were considered to be statistically significant if their associated p-values were less than or equal to 0.05.

Cox proportional hazards was used to estimate the odds of death due to any cancer by the end of follow up, December 31, 2004. Any cancer was chosen as the end point since coding of death certificates can be problematic and vulvar cancer might be coded to another gynecologic site. The final multivariate Cox model included age at diagnosis (20–49, 50–74, 75+), race/ ethnicity (non-Hispanic white, Black/Hispanic), International Federation of Gynecology and Obstetrics FIGO stage (0, I/II, III, IV, unstaged), Charlson score (0, 1, 2+), and presence of a residency training program at the diagnosing/treating hospital (yes, no/unknown).

Results

Weighted distributions of demographic and health system characteristics by FIGO stage are presented in Table 1. Overall, nearly 62% of women were diagnosed with *in situ* disease (FIGO Stage 0). Women aged 20–49 were more often diagnosed with *in situ* (57.3%) disease than women aged 50 and over (42.8%). Women in the older age group had more unstaged disease (68.3%) than younger women. Except for women with unstaged disease, more than half of all women were treated at hospitals with residency training programs. About 25% of *in situ*

patients, 41% of Stage I/II, 46% of Stage III and 34% of Stage IV patients were treated at larger hospitals with more than 400 beds.

When we examined the clinical characteristics of women diagnosed with vulvar cancer in 1999 (Table 2), we found that a larger percentage of women diagnosed at later stages (III/IV), who were also older, had two or more comorbid conditions and died by December 31, 2004 compared to women with Stage I and II disease. Fewer than 2% of women with Stage 0 vulvar cancer had lymph nodes examined. More women diagnosed with Stage I/II or III vulvar cancer had at least 10 lymph nodes examined, 34% and 33% respectively, compared to only 23% of women with Stage IV disease. Women with late stage disease were also more likely to have tumors with poor differentiation compared to women diagnosed at earlier stages.

When examining the distribution of diagnosis and treatment procedures by stage (Table 3), we found that women with Stage III or IV disease were more likely to undergo a CT scan, 49% and 67%, respectively. These women were more likely to have only an incisional biopsy or no definitive surgery, (32% and 46%, respectively) compared to women diagnosed with Stage 0 (6%) or I/II disease (3.7%). Women diagnosed with Stage 0 disease, however, were more likely to undergo a wide local excision, radical local excision, or a partial vulvectomy (42.7%), while women with Stage I/II, III, or IV disease were more likely to undergo a radical or total vulvectomy (47%, 45%, and 54% respectively).

Almost half of the women diagnosed with Stage III or IV disease were treated with external beam radiation, which stands in contrast to none for women with Stage 0 or only 13% for women with FIGO I/II disease. Radiation was administered after surgery in 25% of women diagnosed with Stage III with less than 3% receiving preoperative radiation and 33% of women diagnosed with Stage IV disease received post-operative radiation with none receiving preoperative radiation.

Chemotherapy was given to fewer than 6% of women diagnosed with FIGO I/II. However 35% and 23% of women with FIGO III and IV received chemotherapy respectively. Concurrent chemotherapy and radiation was administered in only about 13% of the FIGO stage III and IV patients. Of patients with Stage III disease who received chemotherapy as part of first-course treatment, 29% were administered 5-fluorouracil, 22% cisplatin and 6% carboplatin. Vulvar cancer patients with Stage IV disease received carboplatinum (10%), cisplatin (13%), 5-fluorouracil (23%), and taxanes (10%). Patients might have received more than one of these agents.

By December 2004, 11% of women diagnosed with vulvar cancer in 1999 died from cancer, 8% were recorded on the death certificate as vulvar cancer and 2% recorded as other cancers. Women aged 75 and older as well as women with invasive disease have the greatest risk of cancer death compared to women below the age of 50 and women with *in situ* disease, respectively (Table 4). While not statistically significant, the data suggest that the risk of dying from cancer increased with increasing age. The odds of death also increase progressively as stage at diagnosis increased. Women with unstaged vulvar cancer also have a significantly higher risk of death compared to women with *in situ* disease.

Discussion

Vulvar cancer grows slowly and tends to remain localized for a long period of time, evolving into invasive cancer within an 8-year period [9]. In our study, almost 90% were diagnosed with early stage (*in situ* or FIGO stage I/II) disease. Our data also indicated that older patients were more likely to present with more advanced disease, supporting previous reports of clinical and behavioral barriers that lead to delays in diagnosis [6,15–16]. According to Canavan and Cohen [6], VNED-related vulvar cancer among women aged 55 and older are less likely to present

with cervical neoplasia and a history of condyloma. These characteristics are typically associated with pre-invasive disease [16] and are a component of screening during routine gynecologic examinations, which older women are less likely to undergo. Additionally, older women are less likely to conduct home self-examinations of the vulva and often fail to seek treatment for VNED symptoms for as long as 16 months [6]. Physicians also have been reported to contribute to the delay in diagnosis by providing medical treatment for up to 12 months before obtaining a biopsy or consider referral [6]. It is important, therefore, that women understand the need for continued gynecologic examinations and the importance of timely evaluations of vulvar lesions.

As expected, women with advanced (FIGO Stage III–IV) disease in our study were more likely to undergo CT scans to evaluate for local or metastatic spread, following recommended clinical practice guidelines [8]. However, the use of radical or total vulvectomy did not differ substantially for women with invasive vulvar cancers, whether stage I/II or stage IV. This may be due, in part, to the individualized approach to treatment as described in the clinical practice guidelines [8] and other sources [15] or perhaps to the desire to avoid chemotherapy and/or radiation.

Primary chemoradiation has been shown to shrink vulvar cancers dramatically, thus permitting less extensive surgery [17–19] and for women with advanced illness (i.e., close/positive margins or metastatic disease in the lymph nodes), adjuvant chemoradiation is recommended. In our study, however, only about 13% of the patients diagnosed with FIGO Stages III or IV in 1999 received chemoradiation for their advanced stage disease while an additional 8–10% received non-concurrent chemotherapy plus radiation. While some studies have shown that oncologists are considered to be early adopters of new therapies when the evidence is clear [20–21], providers may have been hesitant to use less aggressive surgery without additional supporting evidence. Additionally, there may have been insufficient time between publication of the GOG clinical announcement in 1998 [17] and the current study to reflect changes in treatment practices. The Gynecologic Oncology Group is currently investigating the use of preoperative radiation and chemotherapy for advanced vulvar cancer [22]. However, it is interesting that even in 2004 one-third of patients with stage I/II vulvar cancer still receive total or radical vulvectomy [1].

Surgical recommendations are typically determined by FIGO stage at diagnosis and tumor size [23]. *In situ* (FIGO Stage 0) and IA (≤ 2 cm) may be treated by superficial partial vulvectomy, IB (stromal invasion >1.0) and II (> 2 cm) may be treated with partial vulvectomy and lymphadenectomy, and III (any size with adjacent spread) and IVA (tumor invasion to other organs) may be treated with radical (or *en bloc*) vulvectomy and lymphadenetomy. In a study conducted at the University of Mainz, Germany [24], more than half of the patients treated from 1973–2002 had undergone a radical vulvectomy, a third received hemivulvectomy, and the remaining 12% received exenteration and/or colpectomy. More extensive surgery often results in long-term complications, which may include chronic leg edema, dyspareunia, femoral hernia, genetal prolapse, and urinary stress incontinence for six or more weeks after surgery [6–7,24]. Quality of life is also affected by the surgical treatment of vulvar cancer as women report worsening body image and psychosexual disturbances including a decrease in sexual frequency [25–26]. Among women with stage I and II disease in our study, we noted widespread use of radical local excision, which is less disfiguring than radical vulvectomy. Nonetheless, 47% of women with FIGO I/II disease underwent radical or total vulvectomy; while 45% of FIGO III and 54% of FIGO IV underwent a radical or total vulvectomy.

Sentinel lymph node assessment remains experimental among women with vulvar cancer. In our study, we observed that lymph node evaluation was almost always performed with inguinal lymphadenectomy. As data matures from the ongoing studies of sentinel node assessment in

vulvar cancer conducted by the Gynecologic Oncology Group and the European Organization for Research and Treatment of Cancer, it is possible that sentinel lymph node assessment may become more common.

We do not have data on the training or board certification of the physicians treating these patients, so we cannot determine how many of these women were treated by gynecologic oncologists. Nonetheless, our data suggest that the majority of patients with vulvar cancer, especially those with late stage disease, were treated at generally large, teaching hospitals with at least one approved residency training program.

Our analysis of mortality from cancer, although limited, mirrors that of previous studies that reported higher risks of death associated with older age and higher stage [19,27]. However, after adjusting for stage and age, race/ethnicity was not associated with cancer mortality.

This study has several limitations. We do not have data on whether the entire course of therapy was received, the side-effects of treatment, and quality of life measurements. In addition, we do not have data on the training or board certification of the treating physicians, which might influence treatment. However, the database does have major strengths. It is a population-based dataset that captures characteristics of treatment facilities, therapy provided in the community, patient comorbidity, and interventions confirmed by the treating physicians.

This “snapshot” of vulvar cancer in 1999 demonstrates that it is a disease most often diagnosed at early stages. Radical surgery was still commonly performed for all stages of invasive vulvar cancer, and the use of radiation was more common in women with FIGO III and IV. Although clinical trials data support the use of primary chemoradiation for patients with advanced disease, its use remained limited in the treatment of vulvar cancer among the general population in 1999. Vulvar cancer in most cases is local or loco-regional at the time of diagnosis. Definitive therapy is associated with high cure rates. We must make every effort, therefore, to ensure the treatment will produce the best possible chance at a cure as well as the least impact upon health related quality of life. Future research may collect similar data for 2007 diagnoses to assess more contemporary practice patterns in the United States.

We need to ensure that women with vulvar cancer are referred to specialists with appropriate training. Women must have access to a multidisciplinary treatment team encompassing expertise in gynecologic oncology, radiation oncology, oncology nursing, and psycho-social rehabilitation. In addition, we need to ensure that primary surgery is tailored to the size and location of the lesion, sparing the morbidity and disfigurement of the traditional radical vulvectomy. We need to encourage the use of primary chemoradiation for larger primary tumors, as this approach will permit more limited surgical resection and preservation of function.

The relative rarity of vulva cancer probably precludes phase III trials. We need to encourage participation in available national and international trials aimed at improving cure, local control, and health related quality of life.

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Table 1

Distribution of Demographic and Health Systems Characteristics for Women Diagnosed With Vulvar Cancer by FIGO Stage at Diagnosis, 1999

FIGO Stage	Stage 0	Stage I/II	Stage III	Stage IV	Unstaged	
Number of Cases	328	141	35	8	11	p value
Age	WT%	WT%	WT%	WT%	WT%	<0.001
20–24	3.1	0.0	0.0	0.0	0.0	
25–29	4.5	1.3	0.0	0.0	0.0	
30–34	5.8	1.4	0.0	0.0	0.0	
35–39	12.7	5.3	5.1	12.9	11.8	
40–44	17.5	6.2	8.1	0.0	11.8	
45–49	13.7	13.5	0.0	20.4	8.0	
50–54	9.7	6.7	13.2	0.0	0.0	
55–59	9.7	5.1	5.2	12.6	0.0	
60–64	5.0	3.4	2.5	0.0	9.3	
65–69	3.3	6.7	2.6	10.4	0.0	
70–74	5.9	8.7	8.9	20.8	8.0	
75–79	4.7	12.1	7.7	12.6	17.3	
80–84	2.0	14.7	16.7	0.0	17.3	
85+	2.5	15.1	29.9	10.4	16.4	
Race/ethnicity						<0.001
NHWhite	80.9	88.3	88.3	87.2	92.5	
NHBlack	10.6	6.3	2.4	0.0	0.0	
Hispanic	8.4	5.4	9.4	12.9	7.6	
Other/unk						
Insurance Type						<0.001
Private*	73.6	59.7	53.1	43.4	8.4	
Any Medicaid	6.9	7.4	20.4	12.6	29.1	
Medicare Only	5.1	20.5	20.6	31.2	17.3	
No Insurance	3.1	3.7	2.9	12.9	0.0	
Unknown	11.4	8.8	3.1	0.0	45.2	
Hosp Code-Hospital Classification						
Not for profit	69.7	66.2	62.4	56.4	47.3	
For-profit	19.0	9.3	8.9	30.8	33.4	
Non-Federal	10.6	19.3	28.7	12.9	7.6	
Unk/Not Given	0.8	5.3	0.0	0.0	11.8	
Hosp Code-Residency Training Approval						0.06
Yes	56.5	56.7	77.8	66.6	36.7	
No/Unk	43.5	43.4	22.2	33.4	63.3	
Hosp Code-Bed Size						<0.001
<200 beds	21.6	18.0	22.2	20.4	0.0	
200 – 299 beds	20.3	18.8	10.4	10.4	29.9	
300 – 399 beds	17.8	14.1	20.9	25.2	16.8	
400+ beds	24.7	41.3	46.5	33.6	8.0	
OPD	14.8	2.5	0.0	10.4	45.2	
Unk	0.8	5.3	0.0	0.0	0.0	

* Includes HMO, Tricare, Military, VA

Table 2

Distribution of Clinical Characteristics for Women Diagnosed With Vulvar Cancer by FIGO Stage at Diagnosis, 1999

FIGO Stage	Stage 0	Stage I/II	Stage III	Stage IV	Unstaged
Number of Cases	328	141	35	8	11
	WT%	WT%	WT%	WT%	WT%
Charlson Score					
0	87.3	70.5	51.9	87.4	90.7
1	10.5	23.2	29.4	0.0	0.0
2+	2.2	6.4	18.7	12.6	9.3
Size of primary tumor					
Microscopic	2.3	11.6	0.0	0.0	0.0
< 2 cm	17.9	25.4	11.1	0.0	11.8
2 – <4 cm	8.7	22.6	17.6	0.0	8.0
4+ cm	3.2	14.4	59.7	68.8	9.3
Not stated	68.0	26.1	11.6	31.2	70.9
Depth of invasion					
Micro/No depth	6.6	3.3	0.0	0.0	0.0
<2 cm	1.7	54.8	31.4	33.6	8.0
2 – <4 cm	0.0	3.4	0.0	0.0	0.0
4+ cm	0.0	3.6	8.3	0.0	0.0
Not stated	91.8	34.9	60.3	66.4	92.0
Evaluation of lymph nodes by laterality					
No LND done	99.7	46.6	49.2	33.4	424.0
Unilateral lymph node evaluation	0.3	20.4	9.4	43.7	0.0
Bilateral lymph node evaluation	0.0	29.9	41.4	23.0	0.0
Not stated	0.0	3.1	0.0	0.0	0.0
Sentinel Lymph Nodes Biopsy	0.0	3.5	0.0	0.0	0.0
Number of lymph nodes examined					
Zero	98.6	44.3	46.7	33.4	100.0
1–2	0.3	5.3	5.7	12.9	0.0
3–9	0.0	10.5	9.3	20.4	0.0
10+	0.0	34.2	33.3	23.0	0.0
Aspiration	0.0	0.0	2.5	0.0	0.0
Number Unknown	0.0	2.0	2.5	10.4	0.0
1+, exact number unknown	1.1	3.8	0.0	0.0	0.0
Number of positive lymph nodes					
None	1.4	33.3	19.5	0.0	0.0
1–2	0.0	14.3	12.1	43.7	0.0
3–4	0.0	3.8	11.0	12.6	0.0
5–9	0.0	2.8	8.2	0.0	0.0
At least 1	0.0	0.0	2.5	10.4	0.0
None exam	98.6	44.3	46.7	33.4	100.0
Unk	0.0	1.5	0.0	0.0	0.0
Lymph Node Involvement					
Unknown	0.3	17.1	19.2	20.8	78.9
No Lymph Node Involvement	99.8	62.0	35.7	0.0	21.1
Unilateral	0.0	12.8	22.7	45.9	0.0
Bilateral/Contralateral Regional	0.0	5.4	19.9	10.4	0.0
Distant	0.0	2.8	2.6	23.0	0.0
Grade					
Well	1.4	27.4	31.0	20.4	17.3
Moderately	0.8	38.2	45.2	33.6	35.8
Poorly/Undifferentiated	4.0	12.0	11.4	25.2	0.0
Unknown	93.8	22.4	12.4	20.8	46.9
POC Hist					
Epithelial	0.3	0.0	0.0	0.0	0.0
Verrucuous, NOS	0.0	0.0	8.7	0.0	0.0

FIGO Stage	Stage 0	Stage I/II	Stage III	Stage IV	Unstaged
Squamous cell, NOS	31.6	64.5	72.3	64.2	72.1
Squamous cell, keratinizing	0.3	22.9	19.1	23.0	16.1
Squamous cell, large cell	0.0	3.2	0.0	12.9	0.0
Squamous cell, microinvasive	0.0	9.4	0.0	0.0	0.0
Squamous Intraepithelial	59.5	0.0	0.0	0.0	0.0
Bowen's disease	8.4	0.0	0.0	0.0	11.8
Vital Status					
Deceased as of 12/31/2004	0.4	8.5	11.9	41.2	33.3

Table 3

Distribution of Diagnosis and Therapy for Women Diagnosed With Vulvar Cancer by FIGO Stage at Diagnosis, 1999

FIGO Stage	Stage 0	Stage I/II	Stage III	Stage IV	Unstaged
Number of Cases	328	141	35	8	11
CT/MRI	WT%	WT%	WT%	WT%	WT%
No CT or MRI	84.6	77.0	42.4	33.0	61.6
CT only	0.0	12.3	48.8	67.0	17.3
Unknown	15.4	10.8	8.8	0.0	21.1
Surgery Detail					
No surgery/biopsy of primary site	1.6	0.6	5.0	20.8	32.1
Incisional biopsy	4.3	3.1	27.2	25.4	56.1
Excisional biopsy	46.4	13.3	8.2	0.0	0.0
Wide local excision/radical local excision/partial vulvectomy	42.7	35.1	14.6	0.0	11.8
Radical or total vulvectomy	1.8	47.0	45.1	53.8	0.0
Surgery type unknown	3.2	0.9	0.0	0.0	0.0
Radiation					
None	99.5	81.9	46.7	41.2	65.8
External Beam	0.0	12.9	47.0	46.0	16.8
External Beam plus implants	0.0	0.0	6.3	0.0	0.0
Radiation, NOS	0.0	0.6	0.0	0.0	0.0
Refused	0.3	3.1	0.0	0.0	8.0
Recommended, unk	0.0	1.5	0.0	12.9	0.0
Unknown	0.3	0.0	0.0	0.0	9.3
Radiation Sequence with Surgery					
No/unknown radiation and/or cancer-directed surgery	100.0	86.5	72.7	66.6	100.0
Radiation before surgery	0.0	0.0	2.6	0.0	0.0
Radiation after surgery	0.0	13.6	24.8	33.4	0.0
Radiation Sequence with Chemotherapy					
No/unknown radiation and/or no/unknown chemotherapy	100.0	97.5	74.9	77.0	90.7
Radiation before chemotherapy	0.0	1.9	8.0	10.4	0.0
Radiation both before & after chemo	0.0	0.0	3.7	0.0	0.0
Concurrent radiation and chemo	0.0	0.6	8.3	0.0	9.3
Concurrent rad/chemo + other rad	0.0	0.0	2.5	0.0	0.0
Concurrent rad/chemo+ other chemo	0.0	0.0	2.6	12.6	0.0
Chemotherapy Given					
No	98.7	94.0	62.1	64.2	73.4
Yes	0.7	5.4	35.0	23.0	9.3
Ref	0.3	0.6	2.9	0.0	8.0
Rec, Unk	0.0	0.0	0.0	12.9	0.0
Unk	0.3	0.0	0.0	0.0	9.3
Chemotherapy agents given					
Carboplatinum	0.0	0.6	6.3	10.4	0.0
Cisplatin	0.0	1.5	21.8	12.6	0.0
5-Fluorouracil	0.0	2.4	28.7	23.0	9.3
Other	0.7	2.5	2.7	0.0	0.0
Taxanes	0.0	0.6	2.6	10.4	0.0

Table 4

Cancer Mortality Hazard Ratios at Last Known Follow-Up (December 31, 2004)

Effects	Hazard Ratio	95% Confidence Interval
Age		
20–49	1.00	Ref
50–74	6.83	0.85–54.92
75+	13.80	1.84–103.43
Presence of Residency Program		
Yes	1.00	Ref
No/Unknown	0.82	0.35–1.91
Charlson Comorbidity Score		
0 (none)	1.00	Ref
1	2.00	0.89–4.48
2+	1.27	0.47–3.41
Race		
Non-Hispanic White	1.00	Ref
Black/Hispanic	1.00	0.41–2.44
FIGO Stage		
Stage 0 (*in situ*)	1.00	Ref
Stage I/II	34.54	4.43–269.26
Stage III	64.17	7.09–580.41
Stage IV	186.06	15.26–2268.54
Unstaged	94.89	9.27–971.67