

ONCOLOGY

Patterns of care for locally advanced vulvar cancer

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OBJECTIVE: Patients with locally advanced vulvar carcinoma can be treated with primary surgery or neoadjuvant chemoradiation. Neoadjuvant treatment appears to be associated with decreased morbidity and acceptable long-term outcomes. We examined the patterns of care for women with locally advanced vulvar cancer.

STUDY DESIGN: Data from the Surveillance, Epidemiology, and End Results (SEER) database was used to examine women with stage III-IVA vulvar cancer treated from 1988 to 2008. Primary therapy was classified as surgery or radiation. Multivariable logistic regression models were developed to examine the use of primary radiotherapy.

RESULTS: We identified a total of 2292 women including 1757 who underwent primary surgery (76.7%) and 535 treated with primary radiation (23.3%). The use of primary radiation increased with time

from 18.0% in 1988 to 30.1% in 2008. In a multivariable model, older women (odds ratio [OR], 1.33; 95% confidence interval [CI], 1.03–1.72), black women (OR, 1.59; 95% CI, 1.14–2.23), and patients with stage IVA tumors (OR, 2.23; 95% CI, 1.78–2.81) were more likely to receive primary radiation. Among women treated with primary radiotherapy, only 17.8% ultimately underwent surgical resection.

CONCLUSION: The use of primary radiation for locally advanced vulvar cancer is limited but has increased over time. Multiple patient and tumor factors influence use. The majority of patients with stage III-IVA vulvar cancer treated with primary radiation therapy did not undergo surgical resection.

Key words: advanced vulvar carcinoma, morbidity, neoadjuvant chemoradiation, surgery, vulvar cancer, vulvectomy

Cite this article as: Sharma C, Deutsch I, Herzog TJ, et al. Patterns of care for locally advanced vulvar cancer. *Am J Obstet Gynecol* 2013;209:60.e1-5.

Vulvar cancer is the fourth most common gynecological malignancy with an estimated 4340 new cases and 940 deaths projected in the United States in 2012.¹ The incidence of vulvar cancer is increasing, and the disease affects not

only postmenopausal women but also younger women.¹ For patients diagnosed with vulvar cancer, stage and the status of the inguinofemoral lymph nodes are the most important prognostic factors.² Although women with early-stage tumors have a high cure rate, those patients with metastatic spread to the groin lymph nodes are at substantial risk for recurrence and death.

Surgery remains the mainstay of treatment for the majority of women with vulvar cancer. Historically, en bloc radical vulvectomy with bilateral inguinofemoral lymphadenectomy was the treatment of choice.³⁻⁶ Although associated with a high-rate of local tumor control, the procedure is also accompanied by substantial morbidity including wound infections and long-term lymphedema.³⁻⁶ For women with smaller primary tumors, less aggressive local resections have emerged as a viable treatment.³⁻⁶ The morbidity of groin dissection has also decreased with the use of unilateral lymphadenectomy for small tumors away from the midline and the incorporation of sentinel lymph node biopsy into practice.^{3,6,7}

For women with large primary tumors or locally advanced disease, less radical

resection is often not a therapeutic option. When the urethra or anus is involved or when the primary tumor is large, primary surgical management often requires pelvic exenteration and may entail complex reconstructive surgery often with urinary or gastrointestinal diversion.^{8,9} To minimize morbidity and to maximize cosmesis, primary radiotherapy has been offered as an alternative to upfront surgery. Several observational studies as well as 2 phase II trials by the Gynecologic Oncology Group (GOG) have described the outcomes of primary chemoradiation followed by surgical resection.¹⁰⁻¹⁴ These studies have suggested that radiation decreases local tumor burden and often allows a less radical resection.¹⁰⁻¹⁴

Despite the promising data surrounding primary chemoradiation for women with vulvar cancer, little is known about the patterns of use in the United States. We performed a population-based analysis to determine the use of primary radiotherapy for women with stage III-IV vulvar cancer and examined the factors associated with treatment choice.

MATERIALS AND METHODS

The National Cancer Institute's Surveillance, Epidemiology, and End Results

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Received Dec. 28, 2012; revised March 9, 2013; accepted March 11, 2013.

The authors report no conflict of interest.

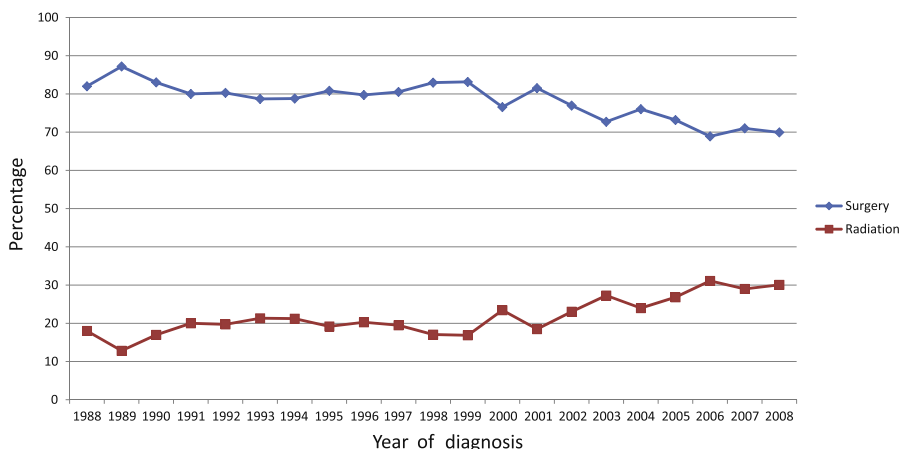
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0002-9378/\$36.00

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<http://dx.doi.org/10.1016/j.ajog.2013.03.013>

FIGURE
Patterns of radiation and surgery use



Patterns of radiation and surgery use for patients with locally advanced vulvar cancer stratified by year of diagnosis.

Sharma. Patterns of care for locally advanced vulvar cancer. *Am J Obstet Gynecol* 2013.

(SEER) database was utilized. SEER is a population-based tumor registry that includes approximately 26% of the US population. SEER is composed of several geographically distinct tumor registries. Data from SEER 17 registries were used.¹⁵ Data from all of the available SEER registries were included in the analysis.

Women with stage III-IVA squamous cell carcinomas of the vulva diagnosed from 1988 to 2008 were analyzed. Based on coding for primary treatment, women were stratified as having undergone either primary surgery or primary radiation. Patients who underwent only an incisional biopsy were excluded from analysis. We also examined surgery after radiation in the primary radiation group. Performance of any incisional or excisional procedure was considered surgical evaluation after radiation.

Clinical and pathological data including age at diagnosis (younger than 60, 60-75, and older than 75 years of age), race (white, black, other), and marital status (single, married, other) were collected. Year of diagnosis was classified as 1988-1994, 1995-2001, or 2002-2008. Subjects were categorized based on the geographic area of residence within the United States at the time

of diagnosis: central (Detroit, MI; Iowa; Kentucky; Louisiana; Utah), eastern (Connecticut, New Jersey, Atlanta, GA; rural Georgia), and western (Alaska; California; Hawaii; Los Angeles, CA; New Mexico; San Francisco, CA; San Jose, CA; Seattle, WA). Staging information was derived from the American Joint Cancer Committee staging information and recorded extent of disease codes. Tumor differentiation was grouped as well differentiated, moderately differentiated, and poorly differentiated.

Frequency distributions between categorical variables were compared using χ^2 tests. A logistic regression model was developed to examine predictors of primary radiation use, controlling for other clinical and demographic characteristics. The vital status of each patient was recorded. All hypothesis tests were 2 sided. All analyses were conducted using SAS version 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 2292 patients were identified. The cohort included 1757 patients who underwent primary surgery (76.7%) and who received primary radiotherapy 535 (23.3%). Use of primary radiation increased with time from 18.0% in 1988 to 30.1% in 2008 (Figure).

The clinical and demographic characteristics of the cohort are displayed in Table 1. Among women older than 75 years of age, 26.0% were treated with primary radiation compared with 23.2% of those whose age was younger than 60 years ($P = .04$). Primary radiation was administered to 22.9% of white patients compared with 32.0% of black women ($P = .005$). Similarly, use of primary radiation was more common in women with stage IV tumors; primary radiation was given to 20.0% of patients with stage III neoplasms compared with 36.5% of those with stage IV cancers ($P < .0001$). Among women who underwent primary radiation, 95 (17.8%) subsequently had a vulvar surgical procedure.

In a multivariable model of factors associated with the use of primary radiation, year of diagnosis and stage were the strongest predictors of use of radiation (Table 2). Compared with women treated from 1988 to 1994, those diagnosed from 2002 to 2008 were 64% more likely to receive primary radiation (odds ratio [OR], 1.64; 95% confidence interval [CI], 1.22–2.21). Likewise, the odds ratio for the use of radiation for stage IVA compared with stage III neoplasms was 2.23 (95% CI, 1.78–2.81). Older women were more likely to receive primary radiation (OR, 1.33; 95% CI, 1.03–1.72), and black women were 59% (OR, 1.59; 95% CI, 1.14–2.23) more likely to receive primary radiotherapy than their white counterparts.

COMMENT

These findings suggest that the use of primary radiation for women with locally advanced vulvar cancer is increasing. Over the last 2 decades, the use of primary radiotherapy for patients with stage III-IVA vulvar cancer increased from 18% in 1988 to 30% by 2008. Both patient and tumor characteristics appear to strongly influence treatment choice.

A growing body of literature supports the use of primary chemoradiation for locally advanced vulvar cancer. In addition to several single-institution observational studies, the GOG has undertaken 2 prospective trials of neoadjuvant chemoradiation.^{10-14,16-21} GOG protocol 101 examined radiation in combination

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