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Evaluation of brachytherapy and external beam radiation therapy for early stage, node-negative uterine carcinosarcoma

Nirav Patel[1], Sarah E. Hegarty[2], Leigh A. Cantrell[3], Mark V. Mishra[4], Timothy N. Showalter[1,*]

[1]*Department of Radiation Oncology, University of Virginia School of Medicine, Charlottesville, VA*

[2]*Division of Biostatistics, Department of Pharmacology & Experimental Therapeutics, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA*

[3]*Division of Gynecology Oncology, Department of Obstetrics & Gynecology, University of Virginia School of Medicine, Charlottesville, VA*

[4]*Department of Radiation Oncology, University of Maryland School of Medicine, Baltimore, MD*

ABSTRACT

PURPOSE: There is limited evidence to guide treatment decision making for patients with early stage uterine carcinosarcoma (UCS) regarding the use of pelvic external beam radiation therapy (RT) vs. vaginal brachytherapy (BT) after hysterectomy. We analyzed a population-based database to compare survival outcomes after adjuvant BT vs. pelvic external beam RT for patients with Stages I–II UCS.

METHODS AND MATERIALS: We searched the Surveillance, Epidemiology, and End Results registry to identify a cohort of patients with International Federation of Gynecology and Obstetrics I/II UCS diagnosed during 1998–2010, who received a total hysterectomy and for whom radiotherapy type was known. χ^2 tests were used to test associations between patient characteristics and radiotherapy type. Overall and cancer-specific survival, measured from date of diagnosis, were summarized within each covariate. Cox proportional hazards models were used to model the impact of RT type on survival while adjusting for other factors.

RESULTS: A total of 1581 subjects were identified, including 803 (50.8%) no radiotherapy; 636 (40.2%) external beam radiotherapy ± BT; and 142 (9.0%) BT alone. The use of BT alone increased from 4.5% in 1988–1999 to 12.5% in 2005–2010. Multivariate models of overall and cause-specific survival showed that radiotherapy type was not associated with survival after adjustment for other covariates.

CONCLUSIONS: For patients with Stages I–II UCS, adjuvant radiotherapy type did not influence survival after hysterectomy. This study addresses an existing evidence gap and identifies a trend toward increasing utilization of BT alone. Prospective trials are warranted to provide high-quality evidence to guide adjuvant therapy decisions for these patients. © 2015 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Brachytherapy; Radiation therapy; Uterine cancer; Carcinosarcoma

Introduction

Uterine carcinosarcoma (UCS), which was previously classified as malignant mixed mullerian tumor and malignant mixed mesodermal tumor, is a rare and aggressive malignancy that arises in the uterus. In the United States, the annual incidence is less than two per 100,000 women per year (1). Prognosis for UCS remains relatively poor; despite accounting for less than 5% of uterine malignancies, they are associated with greater than 15 percent of uterine cancer–related deaths (1, 2). Five-year survival rates remain less than 50%, and median survival is only 21 months (1, 3).

Standard staging and treatment for UCS includes total hysterectomy and bilateral salpingo-oophorectomy with pelvic and para-aortic lymph node dissection, cytology of peritoneal washings, omentectomy, and biopsies of peritoneal surfaces (4). After surgery, adjuvant therapy options for patients with no extrauterine spread include observation, chemotherapy, pelvic external beam radiation therapy

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* Corresponding author. Department of Radiation Oncology, University of Virginia School of Medicine, PO Box 800383, Charlottesville, VA 22908. Tel.: +1-434-982-6282; fax: +1-434-982-3262.

E-mail address: tns3b@virginia.edu (T.N. Showalter).

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(EBRT), and/or vaginal brachytherapy (BT) (4). Although multimodality therapy is recommended, the optimal adjuvant therapy approach has not been clearly established (2). Because UCS is a rare tumor, there are few prospective studies to guide clinical decisions for adjuvant therapy, and most of the existing evidence comes from small, retrospective studies (2). The role of adjuvant chemotherapy has increased in recent years, based on limited data that suggest a clinical benefit from adjuvant chemotherapy (2). Although radiation therapy (RT) has been shown to provide some benefit in local control within the pelvis (5, 6), it is not clear how RT should be combined with chemotherapy and which modality (BT or EBRT) should be delivered (2).

The only randomized control trial of adjuvant RT for UCS evaluated pelvic EBRT vs. observation (7). However, recent trends toward increasing role of lymphadenectomy for staging and the use of vaginal BT in node-negative patients with endometrioid adenocarcinoma, as well as trends toward increased use of chemotherapy for UCS, combine to encourage potential interest in BT for UCS. Studies comparing BT to pelvic radiation as adjuvant therapy after surgery in endometrial adenocarcinoma have shown that BT has similar rates of recurrence, metastases, and disease-free and overall survival (OS) (8–11). Although vaginal BT is a potential therapeutic option, there are limited data available regarding the potential benefit of BT added to chemotherapy for UCS (12, 13).

To provide evidence to inform treatment decisions regarding vaginal BT vs. pelvic EBRT for patients with early stage UCS, we used an existing large, population-based database to evaluate outcomes after pelvic EBRT and BT. We hypothesize that for patients with pathologically determined negative lymph nodes, disease-specific outcomes after BT will be similar to those observed after pelvic EBRT.

Methods and materials

Data source

The Surveillance, Epidemiology, and End Results (SEER) Program of the U.S. National Cancer Institute was used to identify a cohort of female patients who were diagnosed with UCS between 1988 and 2010 (14). The SEER database routinely collects and provides comprehensive cancer case data from various population-based registries located around the United States. The program provides data on patient demographics, tumor anatomical location, tumor morphology, disease stage, treatments, and survival (15). This retrospective analysis used the November 2012 SEER 18-Registries 1973–2010 data set, which represents 27.8% of the total US population. The study population is comparable to the general US population with respect to education level and poverty, although the patients recorded in the SEER database are more likely to be foreign-born and more often live in urban areas (15). This study was considered exempt from Institutional Review Board approval because the data provided by the SEER database is absent of any personal identifiers.

Patient cohort

SEER*Stat was queried for primary diagnosis of UCS (8950/3 mullerian mixed tumor, 8951/3 mesodermal mixed tumor, 8980/3 carcinosarcoma, not otherwise specified). This initial query yielded 1731 cases. Women were then excluded if they had International Federation of Gynecology and Obstetrics (FIGO) stage other than I or II and if they did not have a total hysterectomy (53 excluded). SEER tumor extent data were mapped to current FIGO staging for consistency across versions of SEER tumor extent coding. Women with unknown RT use or missing demographic information were also excluded (97 excluded) leaving 1581 subjects for analysis. The cohort selection strategy is summarized in Fig. 1.

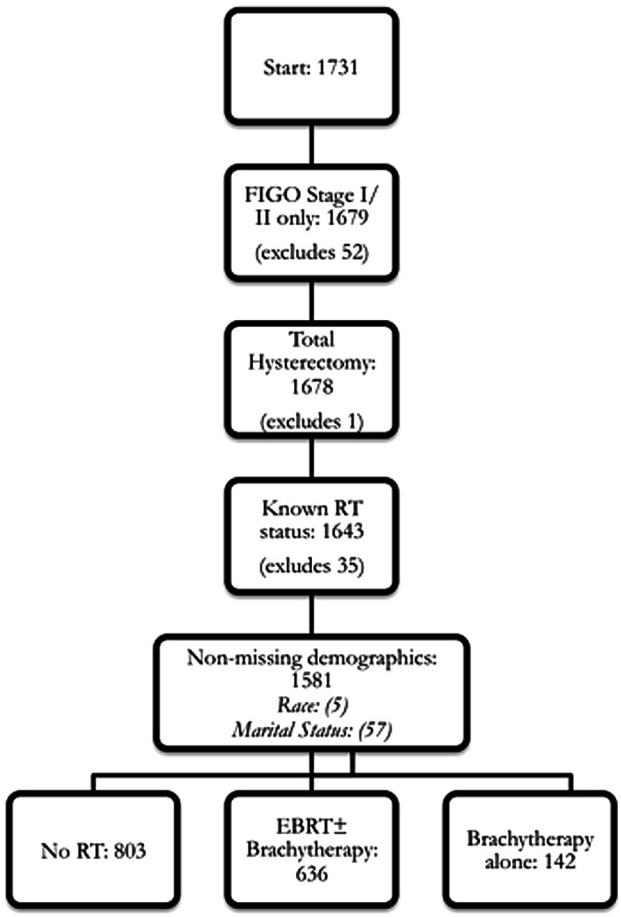

Fig. 1. Cohort selection strategy to identify patients in the SEER database who received hysterectomy for Stages I–II uterine carcinosarcoma. The EBRT ± brachytherapy cohort includes 176 patients who received both EBRT and brachytherapy and 460 patients treated with EBRT alone. SEER Surveillance, Epidemiology, and End Results; EBRT, external beam radiation therapy; RT, radiation therapy.

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