

Oncologic Outcomes after Anterior Exenteration for Muscle Invasive Bladder Cancer in Women



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Abbreviations and Acronyms

BCa = bladder cancer
GU = genitourinary
NB = neobladder
RC = radical cystectomy

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See Editorial on page 979.

For another article on a related topic see page 1270.

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Purpose: We investigated oncologic and urinary outcomes after anterior exenteration for urothelial cell carcinoma in females, identifying tumor characteristics associated with female pelvic organ involvement. We hypothesized that a lack of trigonal or bladder floor tumor, intraoperative palpable posterior mass and clinical lymphadenopathy is associated with a lack of female pelvic organ involvement.

Materials and Methods: We retrospectively reviewed the charts of female patients who underwent radical cystectomy at our institution from 1999 to 2014. Patient and operative characteristics were extracted from the electronic medical record, and performance of hysterectomy was tested for association with disease recurrence. Categorical and continuous variables were analyzed with the chi-square and Student t-test, and Kaplan-Meier analysis was performed to determine recurrence-free survival according to hysterectomy performance. Women who had neobladder creation were additionally evaluated for an association between hysterectomy status, and nighttime wetting and catheter use.

Results: Of 322 eligible patients 160 with urothelial cancer did not have a hysterectomy before cystectomy. Mean followup was 2.2 years (SD 2.8). There were 22 patients (13.8%) who had recurrence during followup. No patient or surgical factor other than use of adjuvant chemotherapy or radiation ($p < 0.01$) was associated with recurrence. Of 139 women 32 (23.0%) who underwent exenteration had female pelvic organ involvement. At least 1 of the 3 characteristics of interest were present in 28 of 99 (28.3%) women with any genitourinary organ involvement compared to only 4 of 40 (10.0%) of those who did not ($p = 0.01$). Nighttime continence ranged between 21.9% and 48% but there was no significant association with continence and hysterectomy status.

Conclusions: Lack of trigonal/bladder floor tumor, palpable posterior mass and clinical lymphadenopathy is associated with the absence of pelvic organ involvement. Individualized risk assessment using these factors along with patient preferences should be used to guide surgical planning.

Key Words: urinary bladder neoplasms, cystectomy, hysterectomy, female

THERE will be an estimated 76,960 new cases of bladder cancer in the U.S. in 2016, of which more than 18,000 will be in women.¹ While

women represent approximately 25% of BCa cases, there is a well established disparity in screening and survival outcomes. Several studies

have demonstrated lower cancer specific and overall survival, although there is some controversy as to whether this is a stage driven phenomenon or a reflection of hormonal influence on bladder malignancy.²⁻⁷

Approximately a third of new BCa cases present with muscle invasive disease, with the standard treatment being radical cystectomy, extended pelvic lymphadenectomy and urinary diversion.⁸⁻¹¹ In women concurrent total hysterectomy, bilateral salpingo-oophorectomy and anterior vaginectomy are performed to provide optimal cancer control and reduce the risk of pelvic recurrence.¹² The reported rate of gynecologic organ involvement varies from 2.5% to 7.5% in the existing literature, with the anterior vagina being the most commonly involved organ.¹³⁻¹⁶

Previous reports have suggested that female pelvic organ sparing can be performed safely with satisfactory oncologic outcomes but few have defined the parameters that would guide surgical planning for organ preservation.^{13,17,18} One group determined that palpable mass, hydronephrosis and pathological lymph node status were associated with involvement.¹⁴ With the aim of determining the clinical factors associated with involvement, we hypothesized that preoperative palpable mass on pelvic examination, tumor located at the trigone and/or bladder floor and clinical lymphadenopathy would be associated with gynecologic organ involvement at RC. To examine this hypothesis we retrospectively queried our prospective cystectomy database. In addition, we examined the functional urinary outcomes among women who had pelvic organ sparing surgery.

METHODS

We identified 322 consecutive women who underwent RC for urothelial carcinoma at Vanderbilt University Medical Center from January 1999 through December 2014. RC was performed and postoperative care administered as previously described by Lowrance et al.¹⁹ Institutional review board approval was obtained for the creation of a prospective database and completion of this study. Clinical, pathological and outcome data were collected prospectively, and were supplemented by review of the medical records. Performance of pelvic gynecologic organ sparing was determined entirely at the discretion of the operating surgeon.

Covariates including age, race, smoking status, American Society of Anesthesiologists® classification, receipt of neoadjuvant chemotherapy, urinary diversion type, pathological TNM classification according to the American Joint Commission on Cancer, 7th edition and lymph node status were obtained through patient charts. Vital status was ascertained through patient charts. Patients were censored at the date of last followup or date of death up to June 2015.

All covariates as well as the preoperative variables of interest (clinical lymphadenopathy greater than 1 cm on imaging, bladder floor or trigone tumor involvement on transurethral resection of bladder tumor and intraoperative palpable posterior mass) were evaluated for association with disease recurrence using the chi-square test for categorical variables and Student's t-test for continuous variables in the cohort of women who did not previously undergo hysterectomy. We estimated disease recurrence according to performance of anterior exenteration using Kaplan-Meier analysis. A Cox proportional hazards model was used to evaluate time to recurrence, and included presence of hysterectomy, patient age and pathological tumor stage.

The primary objective was to determine the association of a lack of clinical lymphadenopathy, bladder floor/trigonal tumor and posterior palpable mass with female pelvic organ involvement. Therefore, these covariates were evaluated for this association in women who underwent intraoperative anterior exenteration.

The secondary objective was to investigate urinary function in women who received orthotopic NB urinary diversion. We hypothesized that female pelvic organ sparing would result in decreased rates of NB catheterization and nighttime leakage. Clinical notes of all female patients who underwent NB diversion were reviewed to extract these data, and the presence of preoperative or intraoperative hysterectomy and other clinical characteristics were evaluated for association with urinary outcomes at the second and third postoperative visits using chi-square analysis. All tests of significance were 2-tailed and $p < 0.05$ was considered significant. Statistical analyses were performed using Stata® 10.0 software.

RESULTS

Of 322 women who underwent radical cystectomy 164 had not previously undergone radical hysterectomy. Among these women 160 (49.7%) had pure or mixed urothelial cell carcinoma on final pathology and were included in the final analysis. Mean followup for the cohort was 2.2 years (SD 2.8). Patient and operative characteristics and pathological characteristics are summarized in table 1. Mean patient age was 67.7 ± 11.2 years and 138 patients (86.2%) were Caucasian.

We analyzed the proportion of patients with presence or absence of the preoperative characteristics of interest (clinical lymphadenopathy, palpable mass, trigonal/posterior bladder mass) with pathological female pelvic organ involvement (table 2). Of 139 women 32 (23.0%) who underwent exenteration had female pelvic organ involvement. Preoperative clinical lymphadenopathy, trigonal or bladder floor tumor and/or intraoperative palpable posterior mass were not associated with uterine ($p=0.14$), fallopian/ovarian ($p=0.97$) or vaginal ($p=0.19$) involvement, individually. However, at least 1 of these 3 characteristics was present in 28 of

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