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Platinum Priority – Bladder Cancer

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Recurrence Patterns After Open and Robot-assisted Radical Cystectomy for Bladder Cancer

Daniel P. Nguyen [a,b,*], *Bashir Al Hussein Al Awamlh* [a], *Xian Wu* [c], *Padraic O'Malley* [a], *Igor M. Inoyatov* [a], *Abimbola Ayangbesan* [a], *Bishoy M. Faltas* [d], *Paul J. Christos* [c], *Douglas S. Scherr* [a]

[a] *Department of Urology, Weill Cornell Medical College-New York Presbyterian Hospital, New York, NY, USA;* [b] *Department of Urology, Bern University Hospital, Bern, Switzerland;* [c] *Department of Healthcare Policy and Research, Division of Biostatistics and Epidemiology, Weill Cornell Medical College, New York, NY, USA;* [d] *Department of Medicine, Division of Hematology/Medical Oncology, Weill Cornell Medical College-New York Presbyterian Hospital, New York, NY, USA*

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Abstract

Background: Concerns remain whether robot-assisted radical cystectomy (RARC) compromises survival because of inadequate oncologic resection or alteration of recurrence patterns.
Objective: To describe recurrence patterns following open radical cystectomy (ORC) and RARC.
Design, setting, and participants: Retrospective review of 383 consecutive patients who underwent ORC ($n = 120$) or RARC ($n = 263$) at an academic institution from July 2001 to February 2014.
Intervention: ORC and RARC.
Outcome measurements and statistical analysis: Recurrence-free survival estimates were illustrated using the Kaplan-Meier method. Recurrence patterns (local vs distant and anatomic locations) within 2 yr of surgery were tabulated. Cox regression models were built to evaluate the effect of surgical technique on the risk of recurrence.
Results and limitations: The median follow-up time for patients without recurrence was 30 mo (interquartile range [IQR] 5–72) for ORC and 23 mo (IQR 9–48) for RARC ($p = 0.6$). Within 2 yr of surgery, there was no large difference in the number of local recurrences between ORC and RARC patients (15/65 [23%] vs 24/136 [18%]), and the distribution of local recurrences was similar between the two groups. Similarly, the number of distant recurrences did not differ between the groups (26/73 [36%] vs 43/147 [29%]). However, there were distinct patterns of distant recurrence. Extrapelvic lymph node locations were more frequent for RARC than ORC (10/43 [23%] vs 4/26 [15%]). Furthermore, peritoneal carcinomatosis was found in 9/43 (21%) RARC patients compared to 2/26 (8%) ORC patients. In multivariable analyses, RARC was not a predictor of recurrence. Limitations of the study include selection bias and a limited sample size.
Conclusions: Within limitations, we found that RARC is not an independent predictor of recurrence after surgery. Interestingly, extrapelvic lymph node locations and peritoneal carcinomatosis were more frequent in RARC than in ORC patients. Further validation is warranted to better understand the oncologic implications of RARC.
Patient summary: In this study, the locations of bladder cancer recurrences following conventional and robotic techniques for removal of the bladder are described. Although the numbers are small, the results show that the distribution of distant recurrences differs between the two techniques.

* Corresponding author. Department of Urology, Weill Cornell Medical College, 525 E 68th St, New York, NY 10021, USA. Tel. +1 646 6331322; Fax: +1 212 7468941.
E-mail address: danielphatnguyen@hotmail.com (D.P. Nguyen).

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1. Introduction

Open radical cystectomy (ORC) is the mainstay of therapy for patients with muscle-invasive and high-risk non–muscle-invasive bladder cancer (BCa) [1]. Following successful adoption of minimally invasive techniques in kidney and prostate surgery, the last few years have seen growing interest in robot-assisted radical cystectomy (RARC). In retrospective studies [2,3] and in the Memorial Sloan Kettering Cancer Center randomized trial [4], large differences in complication rates between RARC and ORC have not been observed.

However, the introduction of RARC into surgical practice has been accompanied by legitimate concerns regarding its oncologic efficacy [5]. To date, favorable outcomes in terms of positive surgical margin (PSM) rates and lymph node yield have been published [2,3,6]. Early oncologic outcomes appear to be acceptable [7–9]. Nevertheless, the use of RARC remains controversial and restricted to specialized centers [3,6,7,9]. Furthermore, there is anecdotal evidence of peritoneal seeding during minimally invasive surgery [10], and pneumoperitoneum may impact BCa cell seeding [11].

In light of the possibility of unusual recurrence locations after RARC, limited information is available for the robotic approach with regard to patterns of disease recurrence. In the present study we describe recurrence patterns in patients who underwent ORC and RARC.

2. Patients and methods

2.1. Patient population

Institutional review board approval was obtained to use data prospectively maintained in our BCa registry. A total of 411 RCs (136 ORC, 275 RARC) were performed at Weill Cornell Medical College by one surgeon from July 2001 to February 2014. Patients with non-bladder primary tumors ($n = 24$; 14 ORC, 10 RARC) and for whom RC had only palliative indication ($n = 4$; 2 ORC, 2 RARC) were excluded. A total of 383 patients (120 ORC, 263 RARC) remained for final analysis. Clinical stage was assigned based on a combination of specimen pathology at transurethral resection of the bladder tumor, evaluation during examination under anesthesia, and imaging studies. By definition, preoperative chemotherapy was administered to patients with clinically metastatic disease in lymph nodes and/or unresectable disease. In the case of a clinical response, surgical consolidation with RC and pelvic lymph node dissection (PLND) was offered. Neoadjuvant chemotherapy was proposed to patients with clinically nonmetastatic disease [12], and its use steadily increased during the study period. For instance, for patients with clinical T2–T4 disease, the rate of neoadjuvant therapy increased from 27% in 2001–2009 to 47% in 2010–2014. Adjuvant chemotherapy was proposed within 3 mo of surgery according to pathologic stage (T3–4, positive nodes) [12]. Institution of any chemotherapy was also discussed according to the patient's performance status, and the decision was ultimately made at the discretion of the patient and the genitourinary medical oncologist. To reduce the effect of variable use of chemotherapy on outcome, all three chemotherapy regimens were grouped into a single variable, perioperative chemotherapy, in the analyses.

2.2. Surgical techniques

The standard techniques for ORC and RARC have been described previously [13,14]. In both techniques, the limits of the PLND were the upper border of the common iliac artery superiorly, Cooper's ligament (including the node of Cloquet) inferiorly, the genitofemoral nerve laterally, and the bladder and sacral promontory medially. Although we attempt PLND in every RC candidate, this was not surgically feasible in eight patients because of prior pelvic irradiation, in two patients because PLND had been performed previously (in the context of nephroureterectomy in one case and an aborted RC attempt elsewhere in the other), and in five patients for other reasons (elderly morbid patients in three cases, one case of marked retroperitoneal desmoplastic reaction in the context of acute myelogenous leukemia and status after chemotherapy, and one case in which the tumor was unexpectedly found to be infiltrating adjacent structures in the pelvis).

2.3. Outcomes measures

2.3.1. Pathologic data

Bladder specimens were evaluated according to a standard pathology protocol. Pathologic data included histologic type, tumor grade according to the World Health Organization/International Society of Urological Pathology consensus classification [15], tumor and nodal stage according to the 2002 TNM classification [16], the presence of lymphovascular invasion, and surgical margin status. A soft-tissue PSM was defined as the presence of tumor at the bladder and urethral and/or ureteral margin.

2.3.2. Oncologic outcomes

During the entire study period, the follow-up protocol comprised history, physical examination, urine cytology, and laboratory measurements every 3–4 mo in the first year, semi-annually in the second year, and annually thereafter. Diagnostic imaging was performed at least annually or when clinically indicated. Documentation of events was based on clinical and radiologic findings, and categorized as the first evidence of local recurrence, distant recurrence, or secondary urothelial carcinoma. Local recurrences, by definition, occurred within the soft-tissue field of exenteration (cystectomy bed and PLND template). Distant recurrences were defined as those that occurred at any other site. Peritoneal carcinomatosis was diagnosed either by imaging (nodular or solid peritoneal masses, focal or nodular peritoneal thickening in abdominopelvic computed tomography [CT]) [17] or intraoperatively during surgery for abdominal symptoms. Histologic confirmation was obtained whenever possible.

2.3.3. Statistical analysis

The χ^2 test (or Fisher's exact test) and Mann-Whitney U test were used to compare baseline variables between the two groups. Kaplan-Meier curves were used to illustrate the probability of recurrence-free survival (RFS) for the entire cohort. Because our cohort was not balanced in terms of stage (Table 1), Kaplan-Meier curves for patients with pathologic stage T0/Ta/Tis/T1 ($n = 181$), T2–T4 ($n = 202$), N0/Nx ($n = 301$), and N1–N3 ($n = 82$) were generated to reduce the effect of selection bias. Recurrence patterns within 2 yr of surgery were also described. Each patient was followed to recurrence or 2 yr of follow-up, whichever came first. For descriptive purposes, percentages were calculated as: number of patients with event within 2 yr/(number of patients with event within 2 yr + number of patients without event and follow-up $\geq$2 yr). Finally, a multivariable Cox regression model including all patients of the cohort tested for the effect of surgical technique on the risk of recurrence, adjusting for patient age (continuous), female gender (yes/no), clinical stage (T0/Ta/Tis, T1, T2, T3, T4), perioperative (i.e. preoperative, neoadjuvant, or adjuvant) chemotherapy (yes/no), pathologic stage (T0/Ta/Tis, T1, T2, T3, T4), nodal stage (N0/Nx, N1-3), lymphovascular invasion (yes/no), and PSM (yes/no). Collinearity between predictors was evaluated before formulating the final multivariable model. Competing-risks survival regression was also performed to correct the univariate and multivariable hazard ratios for the competing event of