European Association of Urology

Bladder Cancer

Long-term Oncologic Outcomes Following Robot-assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium

Syed Johar Raza [a], Timothy Wilson [b], James O. Peabody [c], Peter Wiklund [d], Douglas S. Scherr [e],
Ali Al-Daghmin [a], Shiva Dibaj [a], Muhammad Shamim Khan [f], Prokar Dasgupta [f],
Alex Mottrie [g], Mani Menon [c], Bertram Yuh [b], Lee Richstone [h], Matthias Saar [i], Michael Stoeckle [i],
Abolfazl Hosseini [d], Jihad Kaouk [j], James L. Mohler [a], Koon-Ho Rha [k], Gregory Wilding [a],
Khurshid A. Guru [a,*]

[a] Roswell Park Cancer Institute, Buffalo, NY, USA; [b] City of Hope and Beckman Research Institute, Duarte, CA, USA; [c] Henry Ford Health System, Detroit, MI,
USA; [d] Karolinska University Hospital, Stockholm, Sweden; [e] Weill Cornell Medical College, New York, NY, USA; [f] Guy's and St Thomas's Hospital, London, UK;
[g] Onze-Lieve-Vrouw Ziekenhuis, Aalst, Belgium; [h] Arthur Smith Institute for Urology, New Hyde Park, NY, USA; [i] University Clinics of Saarland, Homburg,
Germany; [j] Cleveland Clinic Foundation, Cleveland, OH, USA; [k] Yonsei University Health Systems Severance Hospital, Seoul, Korea

Article info

Abstract

Background: Long-term oncologic data on patients undergoing robot-assisted radical cystectomy (RARC) are limited and based largely on single-institution series.
Objective: Report survival outcomes of patients who underwent RARC $\geq$5 yr ago.
Design, setting, and participants: Retrospective review of the prospectively populated International Robotic Cystectomy Consortium multi-institutional database identified 743 patients with RARC performed $\geq$5 yr ago. Clinical, pathologic, and survival data at the latest follow-up were collected. Patients with palliative RARC were excluded. Final analysis was performed on 702 patients from 11 institutions in 6 countries.
Intervention: RARC.
Outcome measurements and statistical analysis: Outcomes of interest, recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS) were plotted using Kaplan-Meier survival curves. A Cox proportional hazards model was used to identify factors that predicted outcomes.
Results and limitations: Pathologic organ-confined (OC) disease was found in 62% of patients. Soft tissue surgical margins (SMs) were positive in 8%. Median lymph node (LN) yield was 16, and 21% of patients had positive LNs. Median follow-up was 67 mo (interquartile range: 18–84 mo). Five-year RFS, CSS, and OS were 67%, 75%, and 50%, respectively. Non-OC disease and SMs were associated with poorer RFS, CSS, and OS on multivariable analysis. Age predicted poorer CSS and OS. Adjuvant chemotherapy and positive SMs were predictors of RFS (hazard ratio: 3.20 and 2.16; $p < 0.001$ and $p < 0.005$, respectively). Stratified survival curves demonstrated poorer outcomes for positive SM, LN, and non-OC disease. Retrospective interrogation and lack of contemporaneous comparison groups that underwent open radical cystectomy were major limitations.
Conclusions: The largest multi-institutional series to date reported long-term survival outcomes after RARC.
Patient summary: Patients who underwent robot-assisted radical cystectomy for bladder cancer have acceptable long-term survival.

* Corresponding author. Department of Urology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. Tel. +1 716 845 3389; Fax: +1 716 845 3300.
E-mail address: khurshid.guru@roswellpark.org (K.A. Guru).

CrossMark

1. Introduction

Recent technological advancements in minimally invasive surgery have increased the diversity of options for surgical management of oncologic diseases. Robot-assisted radical cystectomy (RARC) has been compared with open radical cystectomy (ORC) in randomized and prospective studies and appears to reduce operative blood loss and complications while providing similar early oncologic outcomes [1–4]. However, ORC and pelvic lymph node dissection (PLND) remain the gold standard for muscle-invasive or recurrent noninvasive bladder cancer, since open operation provides >60% 10-yr recurrence-free survival (RFS) [5,6].

RARC has been criticized for limited reports of long-term oncologic outcomes [7]. Published series report outcomes from individual institutions with smaller numbers of patients, representative of selected patient cohorts [8–10]. The International Robotic Cystectomy Consortium (IRCC) has a prospectively populated quality-assurance database that contains >2000 RARC patients. The IRCC has reported on learning curve, margin status, lymph node (LN) yield, and complications [11–14]. The IRCC database was queried to report the long-term oncologic outcomes for a large series of patients who underwent RARC.

2. Patients and methods

The study is a retrospective review of the prospectively populated and maintained, institutional review board–approved (I97906) database. The IRCC database comprises 2187 patients from 37 institutions in 17 countries who were treated with RARC for clinically localized bladder cancer from 2003 to date. Overall, 743 patients underwent RARC ≥5 yr earlier. Patients with missing pathologic information or palliative RARC were excluded at the time of analysis.

Primary outcome measures included RFS, cancer-specific survival (CSS), and overall survival (OS). OS was defined as time from date of cystectomy to death due to any cause. CSS was defined as the time to death due to bladder cancer, whereas RFS was defined as time from date of cystectomy to local and or metastatic recurrence, based on histologic or radiologic evidence. Patients who were still alive without experiencing the event of interest at their last follow-up date were considered censored in analyses. Univariable and multivariable analyses were performed to determine the influence of perioperative factors on the primary outcome. Considered predictors included age, gender, pathologic tumor stage, pelvic LN (PLN) status, soft tissue surgical margins (SMs), adjuvant chemotherapy, and histology. Tumor grade and pathologic stage were determined using, respectively, the 2002 American Joint Committee on Cancer TNM staging system and the 2004 World Health Organization/International Society of Urologic Pathologists classification of papillary urothelial neoplasms [15]. Positive SM (PSM) included radial bladder soft tissue margins. Pathologic specimens were not reviewed at a central pathology facility.

Patients were followed using clinical, radiologic, and pathologic evaluation, at the treating physician's discretion. Follow-up data were entered prospectively in the centralized database, using preset parameters. Any missing information from any institution was acquired to generate the most recent and thorough data set possible for this analysis.

Descriptive analyses consisted of frequencies and relative frequencies for all categorical variables. Numeric variables were summarized using median and interquartile range (IQR). The estimated distributions of RSF, CSS, and OS were obtained using the product limit–based Kaplan-Meier method. The comparison of time-to-event distributions for groups defined by categorical predictors was done using the log-rank test. The univariable statistical assessment of numeric predictors was done using the Cox proportional hazards model. Furthermore, the Cox proportional hazards model was used in examining the multivariable associations among RFS, CSS, and OS and considered predictors. Because the predictive nature of each variable in the presence of the other considered predictors was of interest, all variables were included in the multivariable model regardless of univariable results. A nominal significance level of 0.05 was used throughout, and all analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA).

3. Results

Overall, 702 patients were included in the analysis. The median age was 69 yr (IQR: 61–76 yr), and 569 patients (82%) were male. Median operative time was 438 min (IQR: 360–515 min). Most of the patients (62%) had pathologic organ-confined (OC) disease. SMs were positive in 8%. Median PLN yield was 16 (IQR: 10–24 nodes), and 21% of PLNs were positive (Table 1).

Table 1 – Patient characteristics and operative and pathologic findings

Characteristic	Result
Patient characteristics	
Age, yr, median (IQR)	69 (61–76)
Gender, male, n (%)	569 (82)
BMI, median (IQR)	26.6 (24–30)
ASA score >2, n (%)	273 (47)
Neoadjuvant chemotherapy, yes, n (%)	94 (15)
Operative data	
Overall operative time, median (IQR)	438 (360–515)
Estimated blood loss, median (IQR)	400 (250–600)
Pathologic data	
Positive soft tissue margins, yes, n (%)	55 (8)
LN yield, median (IQR)	16 (10–24)
Positive LNs, yes, n (%)	137 (21)
pT stage, n (%)*	
pT0	116 (17)
pIS	78 (11)
pT1	80 (12)
pT2	148 (22)
pT3	197 (29)
pT4	60 (9)
pN stage, n (%)	
N0	484 (75)
N1	54 (8)
N2–3	83 (13)
Nx	27 (4)
Adjuvant chemotherapy, yes, n (%)	134 (24)
Histology, n (%)	
Transitional cell	349 (68)
Squamous cell	133 (26)
Adenocarcinoma	21 (4)
Small cell	7 (1)
Sarcomatoid	4 (1)
Extent of LN dissection, n (%)	
Standard	30 (4)
Extended	507 (72)
Unknown	138 (20)
None	27 (4)

ASA = American Society of Anesthesiology; BMI = body mass index; IQR = interquartile range; LN = lymph node.
* Percentages may not add up to a total of 100, due to rounding off or due to missing values.