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Radical cystectomy in women: Impact of the robot-assisted versus open approach on surgical outcomes

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Abstract

Objectives: To perform a comparison of complications following open versus robot-assisted radical cystectomy (RC) among women who undergo the procedure. Studies comparing robotic to open RC have been mixed without a clear delineation of which patients benefit the most from one modality vs. the other, leading to continued debate.

Patients and methods: This was a retrospective study of women who underwent either open or robotic RC at the MD Anderson Cancer Center from 1/2014 to 6/2018. Co-morbidities, pathologic data, and complications were assessed with descriptive statistics, along with uni- and multivariable logistic regression.

Results: 122 women underwent either open ($n = 76$) or robotic ($n = 46$) RC. Open RC was associated with greater intraoperative blood loss (median EBL 775 ml vs. 300 ml, $P < 0.001$). In both uni- and multivariable analyses, open RC was associated with a greater odds of intraoperative transfusion compared to robotic RC (odds ratio 6.49, 95% CI 2.85−14.78, $P < 0.001$). Women undergoing open RC were also at greater odds of receiving 4 or more units of packed red blood cells (odds ratio 5.46 (1.75−17.02), $P = 0.003$). Robotic RC conferred a higher median lymph node yield (27 vs. 20 nodes, P, <0.001) and operative times (median 513 min vs. 391.5 min, $P < 0.001$). There were no differences in margin positivity, length of stay, or readmission rates at 30 and 90 days.

Conclusions: Robotic RC was associated with a significantly lower risk of transfusion and EBL, and a higher median lymph node yield and operative time. Unique anatomic considerations may in part be responsible for these findings.

Keywords: Blood loss; Female; Radical cystectomy; Robot-assisted; Robotic cystectomy; Women

1. Introduction

Radical cystectomy (RC) with bilateral pelvic lymph node (LN) dissection remains the gold-standard for patients with muscle-invasive bladder cancer, as well as those with recurrent high-grade nonmuscle invasive disease.

Since its original description by Menon et al in 2003 [1], the robotic approach to RC has been increasingly utilized. Studies comparing robotic to open RC have found that the robotic approach confers noninferior oncologic outcomes while potentially decreasing morbidity [2−7], but with added costs and no clear delineation of which patient populations benefit the most from the robotic modality. Although a bladder cancer diagnosis is nearly 4 times more common in men

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[8], women are more likely to have locally advanced disease at the time of diagnosis and may have a greater risk of bladder cancer mortality, recurrence, and progression after treatment [9–13]. Women who undergo RC receive an operation that is technically different from the male cystectomy. In addition to removal of the bladder, the RC in females is classically described to include an anterior exenteration, requiring removal of the uterus, fallopian tubes, ovaries, and anterior vaginal wall. Laterally investing vascular pedicles are often encountered during dissection of the cardinal and uterosacral ligaments [14]. As such, women undergoing RC may be at a higher risk for urethral margin positivity, wound complications, and bleeding compared to males [14,15]. These anatomic challenges could potentially be ameliorated by advantages conferred by the robot-assisted approach.

To date there have been no comparisons of the RC approach performed exclusively in women. We sought to characterize the differences in postoperative complications in women undergoing open vs. robot-assisted RC.

2. Materials and methods

We reviewed the records of all female patients who underwent either open or robot-assisted RC with any urinary diversion at our institution between January 2014 and June 2018. We excluded patients who were undergoing RC concomitantly with another major abdominal procedure (i.e. ventral hernia repair), so as to avoid confounding. Patient characteristics, Charlson comorbidity index (CCI), American Society of Anesthesiologists score (ASA), operative time, estimated blood loss (EBL), transfusion requirements, length of hospitalization, clinical and final pathologic stage and outcomes, as well as 30- and 90-day complication rates were recorded. The study was approved by the MD Anderson Cancer Center Institutional Review Board.

Open RC was performed through a standard lower midline abdominal incision. The robot-assisted approach was performed using the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA), with 3 ports for the robotic arms (2 on the right, 1 on the left), a supraumbilical camera port, and most commonly 2 assistant ports (a 12 mm left upper quadrant assistant port, as well as a 15 mm left lower quadrant assistant port). Most of the open RC procedures were 2 team procedures in which one team performed the extirpative part and the other performed the reconstructive part. In the robot RC group, the entire procedure was performed by a single team. The decision to perform open or robot-assisted cystectomy was based on surgeon experience and patient preference. Some surgeons within the cohort performed only open radical cystectomy, while others performed both. All surgeons whose patients were included in the cohort are high-volume surgeons (>50 cystectomies per year) and were beyond their learning curve for the procedure being performed. As an experienced tertiary-care referral center, close coordination with our anesthesiology teams have allowed us to offer both surgical options to patients routinely even in the setting of morbid obesity and prior abdominal surgery, 2 factors that have historically been cited as requiring special considerations for the robotic approach in particular. There were no systematic criteria that were used to mandate that certain patients undergo one modality over the other.

Patient characteristics were summarized using descriptive statistics. Univariable and multivariable logistic regression models were fitted to assess the association between patient characteristics (Table 1) and surgical outcomes. A backward stepwise model selection approach was applied using Akaike Information Criteria (AIC) [16] to build a multivariable model for each outcome, which starts with the largest model and eliminates the variables sequentially in a way to decrease the AIC maximally. This process continues until the AIC stops improving. A Kaplan-Meier analysis was performed to compare survival. Statistical analysis was performed by designated biostatisticians using R v.3.5.1 (R Core Team, www.r-project.org).

3. Results

A total of 122 women underwent either open ($n = 76$) or robot-assisted ($n = 46$) RC during the study period. The vast majority of urinary diversions in the robot-assisted cohort were performed intracorporeally (40 of 46 cases; 87%). Baseline characteristics are summarized in Table 1. There were no statistically significant differences between groups with respect to age, body mass index (BMI), smoking history, exposure to NAC, CCI, prior pelvic surgery, intraoperative vaginal sparing, or cTNM stages.

Overall 30- and 90-day readmission rates were 24% (29 patients) and 29.8% (36 patients), respectively, with no difference observed between the open or robotic groups ($P = 0.67$ and $P = 0.68$). Outcomes by procedure type are summarized in Table 2. The overall complication rate was 75.4%, with no difference in rates between groups (76.3% vs. 73.9%, respectively, $P = 0.83$). The majority of complications (87%) were grades 1 and 2 by Clavien-Dindo classification. There were no grade 5 complications in either group. The most common complication encountered among both cohorts was anemia requiring transfusion, which occurred in 21.2% of cases (41 patients), followed by urinary tract infection in 9.8% (19 patients), and ileus 9.8% (19 patients). Length of hospitalization and overall survival were not statistically different between the groups (Table 2; Supplemental Fig. 1). Operative time was longer for patients undergoing robotic RC compared with open RC [median 513 minutes (range 365–810) vs. 392 minutes (range 208–875), respectively, $P < 0.001$].

In both univariable and multivariable analyses (Table 3), women who underwent open RC were significantly more likely to require an intraoperative blood transfusion (Table 3). The odds ratio (OR) for requiring an intraoperative transfusion of at least 1 unit of packed red blood cells (pRBCs)

Table 1
Baseline characteristics

Variable	Open ($N = 76$)	Robotic ($N = 46$)	P value
Age, median (IQR)	68 (62, 77)	68.5 (58, 74)	0.16
Race, No. (%)			
White	64 (84.21%)	38 (82.61%)	0.81
Other	12 (15.79%)	8 (17.39%)	
BMI, median (IQR)	26.55 (23.2, 30.2)	27.14 (24.4, 32.6)	0.18
HX of smoking, No. (%)			
Never smoker	37 (48.68%)	23 (50%)	1
Smoker	39 (51.32%)	23 (50%)	
NAC, No. (%)			
No	33 (43.42%)	19 (42.22%)	1
Yes	43 (56.58%)	26 (57.78%)	
ASA, No. (%)			
< 3	6 (7.89%)	3 (6.52%)	1
≥3	70 (92.11%)	43 (93.48%)	
Charlson score, No. (%)			
1−2	2 (2.63%)	5 (10.87%)	0.18
3−4	20 (26.32%)	11 (23.91%)	
≥5	54 (71.05%)	30 (65.22%)	
Prior pelvic surgery, No. (%)	35 (46.1%)	13 (28.3%)	0.06
Clinical T Stage, No. (%)			
Ta or T1	19 (25%)	13 (28.89%)	0.99
T2: Invasive into muscularis propia	28 (36.84%)	16 (35.56%)	
T3: Invasive into perivesical fat	24 (31.58%)	13 (28.89%)	
T4: Invades into surrounding organs	4 (5.26%)	2 (4.44%)	
Tis: Carcinoma in situ	1 (1.32%)	1 (2.22%)	
Clinical N Stage, No. (%)			
N0: No regional lymph node spread.	66 (86.84%)	39 (86.67%)	0.71
N1: Cancer has spread to a single lymph node in true pelvis.	6 (7.89%)	2 (4.44%)	
N2: Cancer has spread to 2 or more lymph nodes in true pelvis.	1 (1.32%)	2 (4.44%)	
N3: Cancer has spread to lymph nodes along the common iliac artery.	3 (3.95%)	2 (4.44%)	
Clinical M Stage, No. (%)			
M0: (no metastasis)	76 (100%)	45 (100%)	

ASA = American Society of Anesthesiologists scor; BMI = body mass index; NAC = neoadjuvant chemotherapy.

when undergoing an open RC was 6.49 (95% CI 2.85−14.78, $P < 0.001$) on univariable logistic regression and 16.86 (95% CI 4.69−59.98, $P < 0.001$) on multivariable logistic regression. These findings were driven by the fact that nearly 68% (51 of 76) of women who underwent open RC received an intraoperative blood transfusion, compared with only 24% (11 of 46) of those who were managed robotically. EBL was also significantly greater in the open group, with a median EBL of 762 ml (IQR 600) compared to a median EBL of 275 ml (IQR 350 ml) among women undergoing robot-assisted radical cystectomy ($P < 0.01$) (Fig. 1). Exposure to NAC was associated with receiving an intraoperative pRBC transfusion (OR 5.16, 95% CI 1.28−20.73, $P = 0.02$) on multivariable regression, but not on univariable analysis. The same was true for patients who had no prior history of smoking (OR 3.49, 95% CI 1.26−9.67, $P = 0.02$) and for those who did not undergo vaginal sparing (OR 0.25, 95% CI 0.08−0.78, $P = 0.02$). Postoperative blood transfusions were not different between the 2 groups (36% open vs. 26% robotic, $P = 0.32$; Table 4). When considering intraoperative and postoperative transfusions together, women undergoing open RC were significantly more likely to have undergone transfusions of 4 or more units of pRBCs compared to those undergoing robotic RC, with odds of 5.46 (univariable, 95% CI 1.75−17.02, $P = 0.003$) and 24.11 (multivariable, 95% CI 7.0−82.67, $P < 0.001$) (Table 5).

The positive margin rate was low overall (4.9%, 6 of 122 patients), with no statistically significant difference between the 2 techniques (4 cases for open RC and 2 for robot RC). Approximately 27% of patients were pT0 at the time of cystectomy, which comprised of 17 patients (22.4%) in the open cohort and 16 patients (35.6%) of the robot-assisted cohort ($P = 0.72$). LN yield was higher for women undergoing robot-assisted RC compared with the open approach, with a median of 27 nodes (range 7−57) removed robotically compared with a median of 20.5 nodes (range 0−57) removed during open pelvic LN dissection ($P < 0.001$). The overall rate of LN positive disease was low between both groups, with 86.8% (106 of 122 patients) found to be N0 at the time of cystectomy.

Table 2
Outcomes by procedure type in women

Variable	Open $N = 76$	Robotic $N = 46$	P value
Length of stay, days, median (IQR)	6 (5, 8)	5 (4, 7)	0.13
Operative time, minutes, median (IQR)	391.5 (327, 488)	513 (465, 587)	**<0.001**
Total nodes removed, median (IQR)	20.5 (13, 28)	27 (19, 41)	**<0.001**
Pathologic T Stage, No. (%)			
T0: No residual tumor	17 (22.37%)	16 (35.56%)	0.72
Ta or T1	13 (17.11%)	7 (15.56%)	
T2: Invasive into muscularis propia	11 (14.47%)	4 (8.89%)	
T3: Invasive into perivesical fat	19 (25%)	11 (24.44%)	
T4: Invades into surrounding organs	6 (7.89%)	2 (4.44%)	
Tis: Carcinoma in situ	10 (13.16%)	5 (11.11%)	
Pathologic N Stage, No. (%)			
N0: No regional lymph node spread.	65 (86.67%)	41 (91.11%)	0.89
N1: Cancer has spread to a single lymph node in true pelvis.	2 (2.67%)	1 (2.22%)	
N2: Cancer has spread to 2 or more lymph nodes in true pelvis.	6 (8%)	3 (6.67%)	
N3: Cancer has spread to lymph nodes along the common iliac artery.	2 (2.67%)	0 (0%)	
Pathologic M Stage, No. (%)			
M1: Distant metastasis	1 (1.32%)	0 (0%)	1
M0 or Mx:	75 (98.68%)	46 (100%)	
Lymphovascular invasion, No. (%)	16 (21.05%)	7 (13.04%)	0.65
Margin Status, No. (%)			
Negative	72 (94.74%)	43 (95.56%)	1
Positive	4 (5.26%)	2 (4.44%)	
Intraoperative pRBC, No. Transfused (%)			
≥1	51 (67%)	11 (23.91%)	**<0.001**
0	25 (33%)	35 (76.09%)	
Post-operative pRBC, No. Transfused (%)			
≥1	27 (36%)	12 (26%)	0.32
0	49 (64%)	34 (74%)	
Overall transfusion, No. Transfused (%)			
≥ 4	26 (34%)	4 (8.7%)	**0.002**
< 4	50 (66%)	42 (91.3%)	
EBL (ml)			
Median (min, 25th, 75th, max)	762 (100, 500, 1,100, 7,000)	275 (150, 150, 500, 800)	**<0.01**
Overall complications (%)	58 (76.32%)	34 (73.91%)	0.83
Wound complications, No. (%)	14 (18.42%)	3 (6.52%)	0.1
Anemia with transfusion, No. (%)	27 (35.53%)	14 (30.43%)	0.69
GI complications, No. (%)	24 (31.58%)	14 (30.43%)	1
UTI, No. (%)	12 (15.79%)	4 (8.7%)	0.41
Other complications, No. (%)	15 (19.74%)	13 (28.26%)	0.37
30-day Readmission Rate (%)	17 (22.67%)	12 (26.09%)	0.67
90-day Readmission Rate (%)	21 (28%)	15 (32.61%)	0.68
Surgical complications within 90 days by Clavien-Dindo grade			
I	34 (29.5%)	20 (32.3%)	
II	69 (60%)	31 (50%)	
III	10 (8.7%)	8 (12.9%)	
IV	2 (1.7%)	3 (4.8%)	
V	0 (0%)	0 (0%)	

Bold values signify statistical significance $p<0.05$.
EBL = estimated blood loss; GI = gastrointestinal; pRBC = packed red blood cell unit; UTI = urinary tract infection.

4. Discussion

4.1. Principal findings

Women who undergo robot-assisted RC have lower blood loss and are significantly less likely to require an intraoperative blood transfusion compared with those undergoing open RC, despite no significant differences between the 2 groups with respect to patient characteristics or disease pathology. Further, when considering both intraoperative and postoperative blood transfusion rates, more female patients undergoing open RC required transfusions of 4 or more pRBC units compared with those undergoing RC. Higher volumes of transfusion have been associated with worse outcomes in multiple studies [17]. There were no differences in overall complication rates or margin positivity. Women undergoing robotic RC were also found to have a higher LN yield compared to their open RC counterparts, although this may be explained by a difference in practice patterns with

Table 3
Logistic regression: need for intraoperative transfusion in women undergoing open versus robot-assisted radical cystectomy

Variable	Univariable OR (95% CI)	*P* value	Multivariable OR (95% CI)	*P* value
Race (non-white vs. white)	2.01 (0.74–5.46)	0.17	2.98 (0.77–11.5)	0.11
History of smoking (never smoker vs. smoker)	1.81 (0.88–3.75)	0.10	2.57 (1.01–6.62)	**0.05**
Neoadjuvant chemotherapy (yes vs. no)	1.88 (0.91–3.88)	0.09	3.76 (1.01–13.92)	**0.05**
ASA (≥3 vs. <3)	0.81 (0.21–3.21)	0.77	0.7 (0.11–4.36)	0.70
Prior pelvic surgery (yes vs. no)	0.83 (0.4–1.71)	0.61	0.84 (0.31–2.29)	0.74
Open vs. robot-assisted approach for cystectomy	6.49 (2.85–14.78)	**<0.001**	9.97 (3.39–29.31)	**<0.001**

ASA = American Society of Anesthesiologists score; CI = Confidence interval; OR = Odds ratio.

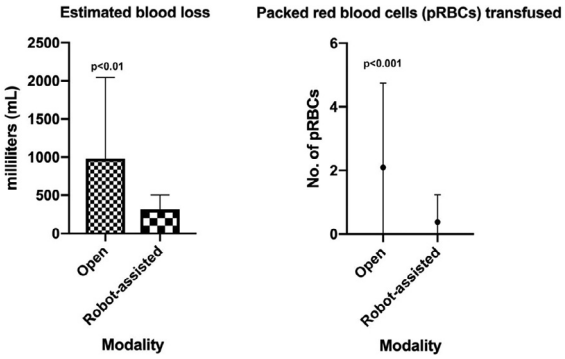

Fig. 1. Comparison of mean blood loss and transfusion requirements by surgical modality among female patients.

the open surgeons generally sending the LNs in fewer packets, a practice that has been shown to affect node counts [18].

4.2. Meaning of the study: Possible explanations and implications for clinicians

To date, most studies that have compared robotic versus open RC have considered whether the robotic approach confers appropriate perioperative morbidity and oncologic equivalency [2–4,6,7,19,20]. Soria and colleagues performed a retrospective cohort study of 1,887 patients comparing the modalities and found that although RC was associated with lower blood loss and length of stay, the operations were longer and associated with more readmissions [21]. Given the importance of providing value-driven and high-quality care, these findings and others like it underscore the need to identify which subpopulations of patients requiring RC, if any, may derive the most benefit from the robotic approach. Women who undergo RC receive an operation that is technically different from the male cystectomy and which may confer unique risks in this patient population. For example, the anterior vagina can be either resected with the bladder or preserved depending on oncologic factors; however, dissection along the anterior and posterior vaginal walls can be a source of bleeding not encountered in males [14,22]. Additionally, the infundibulopelvic ligaments encountered during the ureteral dissection may also lead to bleeding [22]. The pneumoperitoneum offered by laparoscopic approaches in general also limits blood loss. The hypothesis that these anatomic challenges could potentially be ameliorated by advantages conferred by the robot-assisted approach is supported by our finding that women undergoing robotic cystectomy were significantly less likely to lose blood intraoperatively, and more vitally, require a blood transfusion compared to those undergoing open RC.

Linder et al evaluated a cohort of 2,060 patients treated with radical cystectomy over a 25-year period at the Mayo Clinic, among which 62% of patients received a perioperative blood transfusion [23]. At a median follow-up period of 10.9 years, patients who received a perioperative blood transfusion were found to have significantly worse 5-year recurrence-free survival (58% vs. 64%, $P = 0.01$), cancer-specific survival (59% cs 72%, $P < 0.001$), and overall survival (45% vs. 63%, $P < 0.001$). Among the hypotheses posited to explain these findings is the potential immunosuppressive effect of red blood cell transfusions, perhaps secondary to transfusion-related immunological anergy caused by the large volume of antigens present in transfused blood products [24]. Data also suggest that transfusions

Table 4
Logistic regression: need for postoperative transfusion in women undergoing open versus robot-assisted radical cystectomy

Variable	Univariable OR (95% CI)	*P* value	Multivariable OR (95% CI)	*P* value
Race (non-white vs. white)	0.9 (0.32–2.53)	0.84	0.85 (0.24–2.99)	0.80
History of smoking (never smoker vs. smoker)	0.84 (0.39–1.8)	0.65	0.71 (0.3–1.69)	0.44
Neoadjuvant chemotherapy (yes vs. no)	1.81 (0.81–4.05)	0.14	1.66 (0.55–4.94)	0.37
ASA (≥3 vs. <3)	0.34 (0.09–1.36)	0.13	0.29 (0.06–1.35)	0.11
Prior pelvic surgery (yes vs. no)	0.69 (0.31–1.53)	0.35	0.72 (0.29–1.82)	0.49
Open vs. robot-assisted approach for cystectomy	1.56 (0.7–3.49)	0.28	1.81 (0.72–4.53)	0.21

ASA = American Society of Anesthesiologists score; CI = Confidence interval; OR = Odds ratio.

Table 5
Logistic regression: need for overall transfusion ≥4 units in women undergoing open versus robot-assisted radical cystectomy

Variable	Univariable OR (95% CI)	*P* value	Multivariable OR (95% CI)	*P* value
Race (non-white vs. white)	3.16 (1.16–8.58)	**0.02**	1.26 (0.33–4.87)	0.74
History of smoking (never smoker vs. smoker)	1.49 (0.65–3.39)	0.35	2.05 (0.79–5.37)	0.15
Neoadjuvant chemotherapy (yes vs. no)	1.71 (0.72–4.06)	0.22	0.88 (0.27–2.9)	0.83
ASA (≥3 vs. <3)	0.63 (0.15–2.68)	0.53	0.41 (0.04–3.72)	0.42
Prior pelvic surgery (yes vs. no)	1.25 (0.54–2.89)	0.61	0.75 (0.27–2.09)	0.58
Open vs. robot-assisted approach for cystectomy	5.46 (1.75–17.02)	**0.003**	21.06 (6.51–68.44)	**<0.001**

Bold values signify statistical significance $p<0.05$.
ASA = American Society of Anesthesiologists score; CI = Confidence interval; OR = Odds ratio.

may confer higher costs and prolong time to convalescence after surgery [23]. Kukreja et al used a decision analytic model to demonstrate that robotic RC was more cost-effective compared to open surgery when complications and blood transfusions are reduced [25]. Limiting blood loss and more crucially, blood transfusions, may therefore confer clinically significant advantages to patients undergoing radical cystectomy.

To our knowledge, this study is unique in comparing surgical outcomes of an exclusively female cohort undergoing either open or robot-assisted RC. Existing observational and randomized trial data are comprised of patient cohorts that are overwhelmingly male. Among randomized controlled trial (RCT) data comparing robot-assisted to open RC, women comprise a minority of the patients studied with the percent of enrollees ranging from only 15 to 24.4% of the overall cohort [26]. For example, in the trial by Bochner and colleagues in which no differences in oncologic outcomes were identified at a median of 5 years of follow-up, only 9 female patients were randomized to the robotic arm and 16 female patients were in the open arm, out of 118 patients [5]. The largest RCT published to date is the RAZOR trial, in which 350 participants were randomized to either open- or robot-assisted cystectomy. Women comprised of only 16% of the overall cohort [7]. Among the findings included lower EBL in the robotic arm (300 ml vs. 700 ml, $P < 0.001$) as well as lower rates of perioperative (24% vs. 45%, $P = 0.0002$) and postoperative (25% vs. 40%, $P = 0.0089$) blood transfusion [7]. Nevertheless, while these and other studies have provided sufficient data to date to confirm the oncologic acceptability of the robotic cystectomy [2–7,27,28], the optimal patient for whom a robotic cystectomy should be performed remains an ongoing topic of investigation.

This study did not compare outcomes between men and women, as our primary objective was to characterize an all-female patient cohort undergoing RC while comparing surgical modalities. Nevertheless, comparisons can be extrapolated from the existing literature. Sung and colleagues compared early complications between open versus robot-assisted RC and found that female gender was associated with an OR of 4.06 (1.13–14.11) in predicting a grade 2 or higher complications [29]. This finding is not reported uniformly among published series, however. For instance, Kang and colleagues noted that among 22 women who underwent robot-assisted RC (out of a series of 109 patients), there were no gender-based differences in oncologic outcomes, complication rates, or blood loss [30]. Smith and colleagues reported data from a multi-institutional analysis of 227 patients; in this cohort, 49 patients (22%) were women, and sex was not found to be a predictor of higher complications by Clavien grade [31]. Johar and colleagues, reporting for the International Robotic Cystectomy Consortium, found similarly in an analysis of 939 patients (of whom 20% were women) that gender was not associated with the occurrence of grade 3 complications or higher [19].

Our analysis also found that LN yield was higher among women undergoing the robotic approach by a median of 6.5 nodes. Existing literature suggests that LN yield is similar to that of the open surgery, and our findings could also be artefactual secondary to differences in pathologic examination techniques. At our institution, LN packets during open surgery are sent separately by side are but not further artificially stratified. In robotic cases, more nodal packets are sent, a practice that has been reported to be associated with increasing the "yield" of LNs removed [18]. Both open and robot-assisted procedures were performed with either a standard or extended pelvic LN template. The standard template included removal of nodal tissue from the genitofemoral nerve laterally, the internal iliac artery medially, Cooper's ligament inferiorly, and superiorly up to the approximate level at which the ureter crosses the common iliac artery. Patients with advanced disease (clinical T2 or greater) underwent an extended template dissection which included the entire common iliac LN basin and the presacral LNs. Care is routinely taken in both the open and robot-assisted approaches to remain meticulous during the lymphadenectomy, in part by following natural surgical planes and minimizing unnecessary division of individual LNs.

4.3. Strengths and weaknesses of the study

This is a single-institution cohort study with limitations inherent to the retrospective nature of the analysis, including selection bias. Additionally, the study was not large enough to adequately assess whether differences between the surgical modalities impacted rarer complications, such as wound complications (i.e. dehiscence). The overall rate of complications was observed to be higher in our study

(75.4%) than the roughly 40 to 60% complication rate frequently seen reported, although most were grades 1 to 2. The fact that our study was conducted at a tertiary care, high volume center may limit its generalizability to other institutions. Nevertheless, our study is unique in its focused comparison of an all-female cohort and was undertaken to identify specific subpopulations who may benefit the most from the robotic modality. The fact that women undergoing open cystectomy more frequently required a transfusion of 4 or more units of pRBCs compared to their robotic RC counterparts is an important finding that has implications for patient counseling, and in the selection of an appropriate surgical treatment modality for individuals who may have lower physiologic reserve.

Reduced transfusions have been a consistent benefit observed in other studies that have compared the modalities in both genders, but the magnitude of the benefit is a unique finding to this study [26]. We did not observe any difference in length of stay between the 2 groups, and although other studies have found benefit in this regard with the robotic approach, the differences reported may be clinically insignificant. Finally, the vast majority of our robotic cohort underwent an intracorporeal diversion, which is unique from much of the existing literature, including all of the RCT data to date in which urinary diversions were completed open.

4.4. Unanswered questions and future research

Despite the oncologic safety of the robotic cystectomy, the optimal patient in whom this surgery offers the most benefit has yet to be ascertained. Robotic surgery is known to be more expensive, although these costs are mitigated if the procedure results in lower rates of complications and fewer blood transfusions [25]. Additional efforts to better identify these ideal treatment populations is essential.

5. Conclusion

In this cohort of women undergoing RC, the robotic approach was associated with a significantly lower risk of intraoperative transfusion and EBL, along with a higher median LN yield and operative time. Unique anatomic considerations in female patients may in part be responsible for these findings, particularly with respect to blood loss.

Conflicts of interest

The authors have no conflicts of interest relevant to the contents of this manuscript to report.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2019.12.005.

References

[1] Menon M, Hemal AK, Tewari A, Shrivastava A, Shoma AM, El-Tabey NA, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion. BJU Int 2003;92(Aug (3)):232–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12887473.

[2] Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. Eur Urol 2010;57(Feb (2)):196–201. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19853987.

[3] Parekh DJ, Messer J, Fitzgerald J, Ercole B, Svatek R. Perioperative outcomes and oncologic efficacy from a pilot prospective randomized clinical trial of open versus robotic assisted radical cystectomy. J Urol 2013;189(Feb (2)):474–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23017529.

[4] Bochner BH, Dalbagni G, Sjoberg DD, Silberstein J, Keren Paz GE, Donat SM, et al. Comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: a randomized clinical trial. Eur Urol 2015;67(Jun (6)):1042–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25496767.

[5] Bochner BH, Dalbagni G, Marzouk KH, Sjoberg DD, Lee J, Donat SM, et al. Randomized trial comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: oncologic outcomes. Eur Urol 2018;74(Oct (4)):465–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29784190.

[6] Khan MS, Gan C, Ahmed K, Ismail AF, Watkins J, Summers JA, et al. A Single-centre early phase randomised controlled three-arm trial of open, robotic, and laparoscopic radical cystectomy (CORAL). Eur Urol 2016;69(Apr (4)):613–21:Available from: http://www.ncbi.nlm.nih.gov/pubmed/26272237.

[7] Parekh DJ, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS, et al. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. Lancet 2018;391(Jun (10139)):2525–36. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673618309966.

[8] Fajkovic H, Halpern JA, Cha EK, Bahadori A, Chromecki TF, Karakiewicz PI, et al. Impact of gender on bladder cancer incidence, staging, and prognosis. World J Urol 2011;29(Aug (4)):457–63. Available from: http://link.springer.com/10.1007/s00345-011-0709-9.

[9] Dobruch J, Daneshmand S, Fisch M, Lotan Y, Noon AP, Resnick MJ, et al. Gender and bladder cancer: a collaborative review of etiology, biology, and outcomes. Eur Urol 2016;69(Feb (2)):300–10. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0302283815007824.

[10] Kluth LA, Rieken M, Xylinas E, Kent M, Rink M, Rouprêt M, et al. Gender-specific differences in clinicopathologic outcomes following radical cystectomy: an international multi-institutional study of more than 8000 patients. Eur Urol 2014;66(Nov (5)):913–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S030228381301302X.

[11] Palou J, Sylvester RJ, Faba OR, Parada R, Peña JA, Algaba F, et al. Female gender and carcinoma in situ in the prostatic urethra are prognostic factors for recurrence, progression, and disease-specific mortality in T1G3 bladder cancer patients treated with bacillus calmette-guérin. Eur Urol 2012;62(Jul (1)):118–25. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0302283811011353.

[12] Soave A, Dahlem R, Hansen J, Weisbach L, Minner S, Engel O, et al. Gender-specific outcomes of bladder cancer patients: a stage-specific analysis in a contemporary, homogenous radical cystectomy cohort. Eur J Surg Oncol 2015;41(Mar (3)):368–77. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0748798314003485.

[13] Mitra AP, Skinner EC, Schuckman AK, Quinn DI, Dorff TB, Daneshmand S. Effect of gender on outcomes following radical cystectomy for urothelial carcinoma of the bladder: a critical analysis of 1,994 patients. Urol Oncol Semin Orig Investig 2014;32(Jan (1)):52.

e1–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1078143913003177.

[14] Lee KL, Freiha F, Presti JC, Gill HS. Gender differences in radical cystectomy: complications and blood loss. Urology 2004;63(Jun (6)):1095–9. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0090429504001323.

[15] Chen ME, Pisters LL, Malpica A, Pettaway CA, Dinney CP. Risk of urethral, vaginal and cervical involvement in patients undergoing radical cystectomy for bladder cancer: results of a contemporary cystectomy series from M. D. Anderson Cancer Center. J Urol 1997;157 (Jun (6)):2120–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9146596.

[16] Venables WN, Ripley BD. Exploratory multivariate analysis. In: Modern applied statistics with S. 2002.

[17] Shander A, Javidroozi M, Ozawa S, Hare GMT. What is really dangerous: anaemia or transfusion? Br J Anaesth 2011;107(Dec): i41–59. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0007091217325540.

[18] Bochner BH, Herr HW, Reuter VE. Impact of separate versus en bloc pelvic lymph node dissection on the number of lymph nodes retrieved in cystectomy specimens. J Urol 2001;166(Dec (6)):2295–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11696756.

[19] Johar RS, Hayn MH, Stegemann AP, Ahmed K, Agarwal P, Balbay MD, et al. Complications after robot-assisted radical cystectomy: results from the international robotic cystectomy consortium. Eur Urol 2013;64(Jul (1)):52–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0302283813000134.

[20] Raza SJ, Wilson T, Peabody JO, Wiklund P, Scherr DS, Al-Daghmin A, et al. Long-term oncologic outcomes following robot-assisted radical cystectomy: results from the international robotic cystectomy consortium. Eur Urol 2015;68(Oct (4)):721–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0302283815003231.

[21] Soria F, Moschini M, D'andrea D, Abufaraj M, Foerster B, Mathiéu R, et al. Comparative effectiveness in perioperative outcomes of robotic versus open radical cystectomy: results from a multicenter contemporary retrospective cohort study. Eur Urol Focus 2018 Nov; Available from: https://linkinghub.elsevier.com/retrieve/pii/S2405456918303341.

[22] Kurpad R, Woods M. Robot-assisted radical cystectomy. J Surg Oncol 2015;112(Dec (7)):728–35. Available from: http://doi.wiley.com/10.1002/jso.24009.

[23] Linder BJ, Frank I, Cheville JC, Tollefson MK, Thompson RH, Tarrell RF, et al. The impact of perioperative blood transfusion on cancer recurrence and survival following radical cystectomy. Eur Urol 2013;63(May (5)):839–45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23332883.

[24] Morgan TM, Barocas DA, Chang SS, Phillips SE, Salem S, Clark PE, et al. The relationship between perioperative blood transfusion and overall mortality in patients undergoing radical cystectomy for bladder cancer. Urol Oncol Semin Orig Investig 2013;31(Aug (6)):871–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1078143911002328.

[25] Kukreja JB, Metcalfe MJ, Qiao W, Kamat AM, Dinney CPN, Navai N. Cost-effectiveness of robot-assisted radical cystectomy using a propensity-matched cohort. Eur Urol Focus 2018 Jul; Available from: http://www.ncbi.nlm.nih.gov/pubmed/30033071.

[26] Sathianathen NJ, Kalapara A, Frydenberg M, Lawrentschuk N, Weight CJ, Parekh D, et al. Robotic-assisted radical cystectomy vs open radical cystectomy: systematic review and meta-analysis. J Urol 2018 Oct; Available from: http://www.ncbi.nlm.nih.gov/pubmed/30321551.

[27] Snow-Lisy DC, Campbell SC, Gill IS, Hernandez AV, Fergany A, Kaouk J, et al. Robotic and laparoscopic radical cystectomy for bladder cancer: long-term oncologic outcomes. Eur Urol 2014;65 (Jan (1)):193–200. Available from: https://linkinghub.elsevier.com/retrieve/pii/S030228381300849X.

[28] Khan MS, Elhage O, Challacombe B, Murphy D, Coker B, Rimington P, et al. Long-term outcomes of robot-assisted radical cystectomy for bladder cancer. Eur Urol 2013;64(Aug (2)):219–24. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0302283813000092.

[29] Sung HH, Ahn J-S, Seo S Il, Jeon SS, Choi HY, Lee HM, et al. A comparison of early complications between open and robot-assisted radical cystectomy. J Endourol 2012;26(Jun (6)):670–5. Available from: http://www.liebertpub.com/doi/10.1089/end.2011.0372.

[30] Kang SG, Kang SH, Lee YG, Rha KH, Jeong BC, Ko YH, et al. Robot-assisted radical cystectomy and pelvic lymph node dissection: a multi-institutional study from Korea. J Endourol 2010;24 (Sep (9)):1435–40. Available from: http://www.liebertpub.com/doi/10.1089/end.2009.0638.

[31] Smith AB, Raynor M, Amling CL, Busby JE, Castle E, Davis R, et al. Multi-institutional analysis of robotic radical cystectomy for bladder cancer: perioperative outcomes and complications in 227 patients. J Laparoendosc Adv Surg Tech 2012;22(Jan (1)):17–21. Available from: http://www.liebertpub.com/doi/10.1089/lap.2011.0326.