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Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial

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Abstract

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Background—Open radical cystectomy (ORC) and urinary diversion in patients with bladder cancer (BCa) are associated with significant perioperative complication risk.

Objective—To compare perioperative complications between robot-assisted radical cystectomy (RARC) and ORC techniques.

Design, setting, and participants—A prospective randomized controlled trial was conducted during 2010 and 2013 in BCa patients scheduled for definitive treatment by radical cystectomy (RC), pelvic lymph node dissection (PLND), and urinary diversion. Patients were randomized to ORC/PLND or RARC/PLND, both with open urinary diversion. Patients were followed for 90 d postoperatively.

Intervention—Standard ORC or RARC with PLND; all urinary diversions were performed via an open approach.

Outcome measurements and statistical analysis—Primary outcomes were overall 90-d grade 2–5 complications defined by a modified Clavien system. Secondary outcomes included comparison of high-grade complications, estimated blood loss, operative time, pathologic outcomes, 3- and 6-mo patient-reported quality-of-life (QOL) outcomes, and total operative room and inpatient costs. Differences in binary outcomes were assessed with the chi-square test, with differences in continuous outcomes assessed by analysis of covariance with randomization group as covariate and, for QOL end points, baseline score.

Results and limitations—The trial enrolled 124 patients, of whom 118 were randomized and underwent RC/PLND. Sixty were randomized to RARC and 58 to ORC. At 90 d, grade 2–5 complications were observed in 62% and 66% of RARC and ORC patients, respectively (95% confidence interval for difference, −21% to −13%; $p = 0.7$). The similar rates of grade 2–5 complications at our mandated interim analysis met futility criteria; thus, early closure of the trial occurred. The RARC group had lower mean intraoperative blood loss ($p = 0.027$) but significantly longer operative time than the ORC group ($p < 0.001$). Pathologic variables including positive surgical margins and lymph node yields were similar. Mean hospital stay was 8 d in both arms (standard deviation, 3 and 5 d, respectively; $p = 0.5$). Three- and 6-mo QOL outcomes were similar between arms. Cost analysis demonstrated an advantage to ORC compared with RARC. A limitation is the setting at a single high-volume, referral center; our findings may not be generalizable to all settings.

Conclusions—This trial failed to identify a large advantage for robot-assisted techniques over standard open surgery for patients undergoing RC/PLND and urinary diversion. Similar 90-d complication rates, hospital stay, pathologic outcomes, and 3- and 6-mo QOL outcomes were observed regardless of surgical technique.

Patient summary—Of 118 patients with bladder cancer who underwent radical cystectomy, pelvic lymph node dissection, and urinary diversion, half were randomized to open surgery and half to robot-assisted laparoscopic surgery. We compared the rate of complications within 90 d after surgery for the open group versus the robotic group and found no significant difference between the two groups.

Keywords

Bladder cancer; Complications; Cystectomy; Lymph node dissection; Quality of life; Randomized controlled trial; Robot assisted; Robotic; Urinary diversion

1. Introduction

Primary bladder cancer (BCa) is a serious worldwide health risk [1], commonly affecting the elderly and smokers [2]. Radical cystectomy (RC) is the standard management of nonmetastatic, invasive BCa and is curative in the majority of patients with localized disease. Since smoking is common among patients with BCa [3,4], many present with significant cardiovascular, pulmonary, and renal disease. The combination of an extensive extirpative procedure with urinary tract reconstruction in this elderly, comorbid population leads to a significant perioperative morbidity and recovery time following standard open surgery.

Minimally invasive surgical (MIS) techniques have been rapidly adopted for the treatment of benign and malignant diseases, with the promise of improving perioperative morbidity and ease of recovery. Technical advances and the ability to use smaller incisions may ease recovery, limit complications, and decrease in-hospital recovery time. A more limited in-hospital length of stay (LOS) potentially may offset the additional equipment-related costs. Most reported robotassisted laparoscopic RCs (RARCs) consist of a combined approach in which the cystectomy and pelvic lymph node dissection (PLND) are performed using the MIS approach, and the urinary diversion is then created through an open laparotomy incision [5]; however, a total incorporeal technique has gained interest [6]. Nonrandomized RARC series have reported lower rates of complications, improved recovery, and equivalent oncologic outcomes compared with open RC (ORC) outcomes [7–12]. The majority of RARC reports are retrospective series from single- or combined multi-institutional data sets. The absence of properly powered randomized studies, lack of standardized reporting methods, and short duration of follow-up have limited the level of evidence supporting whether a benefit exists for RARC versus ORC.

We have previously reported the outcomes for overall complications and LOS in this study [13]. In this paper, we present the detailed results of our randomized controlled surgical trial that assessed the perioperative 90-d complication rates, surgical and pathologic performance, patient-reported quality of life (QOL), and costs associated with RARC versus ORC, both with extracorporeal urinary diversion. We hypothesized that the minimally invasive approach of RARC could provide a reduction in complications, improved patient recovery, improved patient-reported QOL outcomes, reduced or comparable costs, and decreased LOS.

2. Patients and methods

2.1. Patients

BCa patients scheduled for definitive treatment by RC plus PLND and urinary diversion were recruited from the urology clinics at Memorial Sloan Kettering Cancer Center

(MSKCC) between March 2010 and March 2013. Approximately 25% of eligible patients agreed to enrollment and randomization. The protocol had been approved by the MSKCC institutional review board. All patients provided written consent prior to enrollment and surgery. All patients were followed ≥6 mo to provide 90-d complications and QOL data.

Eligible patients were medically cleared for RC plus PLND, aged ≥18 yr, and had BCa clinical stage Ta–T3/N0–3/M0. Exclusion criteria included previous pelvic radiation, clinical stage T4 or M1, any contraindication for Trendelenberg position, or extensive prior abdominal surgery. Postoperatively, all patients were placed on the identical treatment pathway, which is designed for a 4- to 5-d LOS.

2.2. Study design and objectives

Based on historical data [14], we expected the rate of grade 2–5 complications occurring within 90 d after surgery to be 50% among patients undergoing ORC. For the primary objective, we hypothesized that the rate of grade 2–5 complications would be 20% lower in absolute terms for RARC compared with ORC; that is, we expected grade 2–5 complications to be 30% in the RARC group. A trial with an α of 5% and 80% power required 93 patients per arm. However, due to a mandated interim analysis to occur halfway through enrollment, we intended to accrue 105 patients per arm to maintain 80% power. For the interim analysis, we would calculate the upper bound of a one-sided 95% confidence interval (CI) for the difference in rate of grade 2–5 complications between surgery groups. If the upper bound was ≤20%, we would require stopping the trial for futility. All complications were graded on the MSKCC modified Clavien grading scale [14]; complications data were collected prospectively by unblinded MSKCC research study staff at the initial postoperative, 3-mo, and 6-mo follow-up visits using the institution's standard reporting method for postoperative complications. All pathologic specimens were reviewed blinded to surgical technique.

Secondary end points included number of grade 2–5 complications, rate and number of grade 3–5 complications, surgical time, intraoperative blood loss, PLND nodal yield, rates of positive surgical margins (PSM), LOS, 3- and 6-mo patient-reported QOL outcomes, and total surgical and admission costs by surgery type. As a further unplanned sensitivity analysis, we used an analysis of covariance (ANCOVA) model to compare nodal yield between RARC and ORC adjusted for the extent of dissection the patient received. Differences in binary outcomes were assessed with the chi-square test, with differences in continuous outcomes assessed by ANCOVA with randomization group as the covariate and, for QOL end points, baseline score.

2.3. Surgical interventions

The trial was designed as an expertise-based study in which all patients randomized to open surgery were treated by one of four surgeons extensively experienced in ORC and urinary diversion. Similarly, all RARC procedures were performed by one of three surgeons with extensive robotic pelvic surgery experience. All urinary diversions were performed as open surgeries; therefore, one of the surgeons experienced in open procedures completed them

regardless of randomization arm. All surgeons were urologic oncology fellowship-trained and had a minimum of 10 yr operative experience in practice after fellowship.

Men underwent removal of the prostate if present and women underwent hysterectomy and bilateral salpingo-oophorectomy if those organs were present. The extent of the PLND was left to the discretion of the surgeon based on clinician preference and judgment (extent of disease, vascular disease) and determined prior to randomization. The extent of PLND was alterable intraoperatively based on clinical findings (vascular disease, fibrosis, adenopathy). Once the RC plus PLND was completed, the open urinary diversion was performed based on preoperative and intraoperative assessments and previous patient discussion. Bowel mobilization was performed robotically for all RARC patients. Incision site for diversion depended on type of reconstruction (periumbilical for conduit and lower midline for neobladder).

2.4. Randomization and treatment evaluation

Consenting patients were stratified by age (≤64 vs ≥65 yr) and American Society of Anesthesiologists score (1–2 vs 3–4), then randomly assigned 1:1 to undergo RARC or ORC using randomly permuted blocks of random length. Randomization was conducted by an independent office, where allocation concealment was ensured by a password-protected database, such that the randomization group could not be predicted prior to receiving group assignment and group could not be changed after randomization. The primary analysis was conducted according to intention-to-treat (ITT). Analyses of the main and secondary end points were also repeated according to actual treatment received.

2.5. Quality-of-life assessment

To assess patient-reported outcomes (PROs) of QOL, patients completed the validated European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) survey [15]. EORTC scores for each of the six functional domains and items are scaled from 0 to 100 using linear transformation. PROs were assessed at baseline (within 4 wk prior to cystectomy and after neoadjuvant chemotherapy when applicable) and at 3 and 6 mo postoperatively. Differences in QOL measures were assessed at 3 and 6 mo after cystectomy using ANCOVA, with randomization group and baseline score as the covariates. PROs are reported according to standards recommended by the 2010 Consolidated Standards of Reporting Trials (CONSORT) PRO extension [16].

2.6. Cost analysis

Cost data were determined using activity-based costing. Resources consumed were assigned to groups of charges by category and treatment location from the general ledger, payroll, and purchasing and were aggregated at the patient level. Total patient costs include both direct costs (ie, a particular charge or service) and indirect costs (ie, an overhead cost not attributable to a specific charge or service).

Average total costs for the RARC and ORC arms were compared separately by urinary diversion type. These prices were normalized to the average Medicare reimbursement, using a ratio of the accounting-based prices compared with the Medicare reimbursement for that

service in a theoretical *generic* hospital. Medicare reimbursement was calculated at the diagnosis-related group (DRG) level according to a method developed by the Centers for Medicare and Medicaid Services [17]. A weighted average of DRG-level, normalized Medicare reimbursements was used to calculate separate multipliers for the RC with ileal conduit and RC with neobladder groups. The differences can thus be interpreted as the amount that would be reimbursed to an average hospital by Medicare if it paid differentially for the open or robotic-based procedures. Cost differences between open and robotic procedures were calculated as the difference between the average total cost for an ORC procedure and the average total cost for an RARC procedure. Statistical significance was assessed using two-sided *t* tests and an α of 5%. Prior to performing *t* tests, costs were logged to account for positive skew in the cost distribution and normalized as described.

3. Results

3.1. Patient disposition

Study participant flow and reasons for exclusion are shown in Figure 1. Overall, 124 patients were accrued, 4 did not receive surgery due to progression of disease, and 2 were deemed ineligible after registration due to prior pelvic radiation. Of the 60 patients assigned to RARC, 4 refused to proceed with RARC and underwent ORC. No patient assigned to RARC required conversion to open surgery. All 58 patients assigned to ORC underwent ORC. The planned interim analysis was performed after 100 accrued patients (49 RARC, 51 ORC) had 90-d postsurgical follow-up. The interim analysis demonstrated that the upper bound of the CI for the difference in rate of grade 2–5 complications (primary end point) between surgery groups at 3 mo was 18.6%. The trial was therefore stopped for futility based on the predefined criterion that the upper bound was <20%. Accrual continued until the interim analysis was completed, such that the final cohort for the trial included 118 patients: 60 randomized to receive RARC and 58 to ORC.

3.2. Baseline characteristics and complications outcomes

Baseline and intraoperative characteristics of the two groups were similar (Table 1). In the ITT analysis, the rates of grade 2–5 perioperative complications were 62% and 66% of RARC and ORC patients, respectively (difference: −4%; 95% CI, −21 to 13%; $p = 0.7$) (Table 2). Overall, 21% of patients (25 of 118) experienced high-grade complications (grade 3–5), with no differences observed between treatment groups (difference: 1.0%; 95% CI, −14 to 16%; $p = 0.9$). There were no deaths in the RARC group and a single death at 90 d in the ORC group (1 of 58, 1.7%). Intraoperative complications were experienced by 5% of patients regardless of surgical technique ($p > 0.9$). When patients were analyzed based on actual surgical procedure received rather than ITT, nearly identical results were observed (Table 2). The types of complications observed were similar in each arm, with infectious complications the most commonly identified (Table 3). The only statistically significant difference identified was related to wound complications, more commonly observed in ORC.

Based on the ITT analysis, intraoperative estimated blood loss favored the RARC group by a mean of 159 ml ($p = 0.027$) (Table 2). Operative time, however, favored the ORC group by

a mean time of 127 min (95% CI, 98–156; $p < 0.001$). Mean LOS was 8 d in both arms (standard deviation [SD], 3 and 5 d in RARC and ORC, respectively; $p = 0.5$). These findings were similar for both the ITT and actual-procedure-received analyses.

3.3. Pathologic outcomes

Pathologic outcomes are shown in Tables 1 and 2. Residual disease lower than pT2 was present on final pathologic review in 35 of 60 patients (58%) and 32 of 58 patients (55%) in the RARC and ORC groups, respectively; while 17 of 60 patients (28%) and 19 of 58 patients (33%) had pT3 or higher disease (Table 1). All patients received the extent of PLND that had been determined preoperatively. Lymph node yield adjusted for the extent of the dissection demonstrated no significant differences based on technique (adjusted difference of 1.5; 95% CI, −2.9 to 5.9; $p = 0.5$). PSM rates were similar between arms (Table 2).

3.4. Patient-reported quality-of-life data

PRO outcomes are summarized in Table 4. Fifty-eight patients returned evaluable baseline surveys and 53 returned follow-up surveys at 3 and 6 mo. At baseline, measures of functioning were similar between arms. There were no clinical or statistical differences between the two arms in QOL change from baseline to 3 mo or from 3 to 6 mo in any of the evaluated domains (Table 4).

3.5. Cost analysis

The average normalized total operating room and inpatient costs for RARC and ORC were compared based on type of urinary diversion (Table 5). For RC with neobladder, RARC generated an average additional cost of $3920 compared with ORC ($p < 0.0001$). For RC with ileal conduit, RARC generated an average additional cost of $1740 compared with ORC ($p < 0.05$). Additional costs due to RARC were primarily related to operating room costs (robot, supplies, and facilities) and physician costs. For RC with ileal conduit, the operating room and physician costs together accounted for 98% of the additional costs due to RARC. For RC with neobladder, the operating room and physician costs together accounted for 69% of the additional costs due to RARC.

4. Discussion

The primary goal of this study was to determine whether robotic surgical techniques could substantially decrease the morbidity associated with RC, PLND, and urinary diversion in a BCa population. BCa is a smoking-related tumor [3,4], and many patients manifest cardiac, pulmonary, and renal dysfunction, complicating recovery after major surgery. Our hypothesis was that RARC would lower grade 2–5 perioperative complications by ≥20%, shorten hospital LOS, and improve patients' QOL. The results of our randomized trial showed complication rates out to 90 d after surgery of 62% and 66% in the RARC and ORC arms, respectively, using an ITT analysis. At the mandated interim analysis of this protocol, the similarity in complication rates met the trial's predetermined futility criteria and led to the early closure of the trial. The validity of the results of this trial is partly dependent on whether the outcomes of our primary end point (90-d complications) were comparable to

those reported in large, expert ORC and RARC series. Comparative evaluation of complications between surgical series poses many challenges related to variations in the method, consistency, and documentation of data reporting. Documented variations in the quality of surgical complications reporting are found across surgical disciplines [18]. Our trial design collected data prospectively, using a defined, previously published complications grading system [14]; several ORC and RARC series have used a similar grading system for complications reporting [8,12,14]. In a group of 1142 consecutive BCa patients managed by standard ORC and urinary diversion, the perioperative 90-d complication rate was 64% [14], nearly identical to that observed in our randomized ORC arm. Most common complications were infectious (25%), gastrointestinal (29%), and wound related (15%) [14].

Rates of complications after RARC have varied greatly in published series and likely reflect variations in reporting methods and patient selection [7–9,12,19]. The observed 62% complication rate in our RARC arm was similar to that reported in one of the largest single-institution series of RARC, in which the overall 90-d complication rate was 80% [12]. The majority of complications identified after ORC or RARC are low grade. We observed a 21% overall high-grade complication rate in the current trial, including 21% and 22% for RARC and ORC, respectively. Reported high-grade complication rates in RARC-treated patients have ranged from 19% in a 939-patient, RARC, multi-institutional series to 35% in the largest single-center report [8,12]. We have previously reported a 2.7% 90-d mortality rate in 1142 consecutive ORC patients [14]. The current trial observed no deaths in the RARC group and a single mortality at 90 d in the ORC group (1 of 58, 1.7%). The International Robotic Cystectomy Consortium (IRCC) reported a 4.2% 90-d mortality in 939 patients [8].

Hospital LOS following RC and urinary diversion is associated with the extent and severity of complications encountered [20]. Several RARC reports have suggested a benefit in LOS compared with ORC [10,21], whereas others have not [22,23]. The IRCC data set of 939 RARC patients demonstrated a median LOS of 8 d [8]. Our randomized trial displayed a similar median LOS of 8 d for both RARC and ORC, and thus showed no advantage for the robotic technique. LOS after RC is a function of recovery from both the extirpative and reconstructive parts of the operation. Despite a uniform postoperative pathway that allowed for early feeding, mobilization, and discharge by day 4 or 5 regardless of diversion type, no benefit in LOS was observed in the RARC group; however, we did not directly quantify differences in intermediate measures of recovery, such as time to return of bowel function or postoperative pain.

Measures of surgical quality for RC include PSM rates and lymph node yields, both of which have implications for oncologic outcomes. A PSM affects local recurrence, doubles the metastatic progression risk, and adversely affects cancer-specific survival [24,25]. In two large ORC series comprising 3180 patients, PSM were identified in 0% of organ-confined tumors (pT2N0 or lower) and 3–9% of patients with extravesical disease [25,26]. In contrast, the 939-patient international RARC study reported an overall PSM rate of 6.8% in 513 patients, 1.5% for organ-confined tumors, and 17% for extravesical tumors, including 8.3% for pT3 and 39% for pT4 tumors [8]. In general, higher lymph node yield is associated with improved disease-specific survival and overall survival [27–29]. Several reports have

demonstrated that extended PLND is feasible using robotic techniques and that with increasing experience, similar lymph node yields may be obtained [12,22,30]. We confirm the previously noted observations [30–32] that RARC plus extended PLND is feasible in most patients and has similar lymph node yields as the open procedure, but requires substantial time to complete. Others have demonstrated that increased volume and greater experience of RARC in the surgeon is positively associated with the completion of a PLND and with increased lymph node yield [33].

RC and urinary diversion can significantly alter QOL due to the required surgical recovery related to the associated complications and catabolic state induced by the trauma of treatment. A major purported benefit of MIS techniques is to ease the process of recovery, leading to improved QOL. Analysis of PRO in this study showed similar findings between ORC versus RARC at 3 or 6 mo after surgery. Our results are similar to those reported from a large, multicenter, randomized study of minimally invasive versus open colectomy for colorectal cancer, which showed no difference in QOL at 2 mo [34]. Unlike the latter study that showed a small difference in global rating scale favoring laparoscopic surgery at 2 wk, we did not evaluate PRO before 3 mo, which limits our ability to detect differences in very short-term QOL. Cost analyses have previously suggested a benefit in favor of RARC over ORC [35], whereas others have not [36]. Our study demonstrated increased total costs (operating room and inpatient) for RARC procedures whether the diversion was a conduit or neobladder, although the extent of the differences appeared lower for neobladder patients. The lack of difference in hospital LOS, the added equipment costs, and longer operating room times contributed to the greater costs associated with robotic procedures.

Limitations of this study include that it was completed at a single high-volume referral center, and the surgeons in this trial were highly experienced in performing ORC and RARC, respectively; thus these results may not be completely generalizable to surgeons less experienced in the RC/PLND procedure. As with most centers worldwide, our experience with ORC is significantly greater than with RARC. Although the surgeons using robotic techniques in this trial have performed thousands of robotic pelvic procedures, our results with RARC may improve as greater experience accumulates; however, the reported outcomes for our RARC arm compare favorably with the largest, multiyear RARC series reported to date [12]. Since our study was designed to detect a 20% difference in grade 2–5 complications, our negative results do not exclude the possibility that robotic techniques may reduce complication rates by 10–15%, which would not be clinically insignificant; however, we found no evidence of such a difference. Additionally, a lower rate of positive lymph nodes in our study population suggests that the distribution of patients enrolled had a more favorable oncologic outcome compared with previous reported ORC series.

5. Conclusions

This prospective, randomized trial observed 62% and 66% 90-d perioperative rates of grade 2–5 complications in RARC- and ORC-treated patients, respectively, thus excluding a large benefit in perioperative morbidity for RARC over ORC. While some surgical parameters were improved using RARC, others were not favorably enhanced and use of RARC did not result in a shorter LOS. Although RARC did provide similar pathologic outcomes compared

with ORC, costs and QOL measures at 3 and 6 mo postoperatively failed to demonstrate a benefit of RARC over conventional open surgery. While robotic technology holds promise in improving patient outcomes, this randomized study failed to confirm previously reported patient benefits.

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Take-home message

This randomized controlled trial demonstrated no advantage for robot-assisted radical cystectomy (RARC) with pelvic lymph node dissection (PLND) over standard open radical cystectomy with PLND (both with open diversion) with respect to 90-d complications, length of stay, 3- and 6-mo quality of life, or costs. While some surgical parameters were more favorable for RARC, others were not.

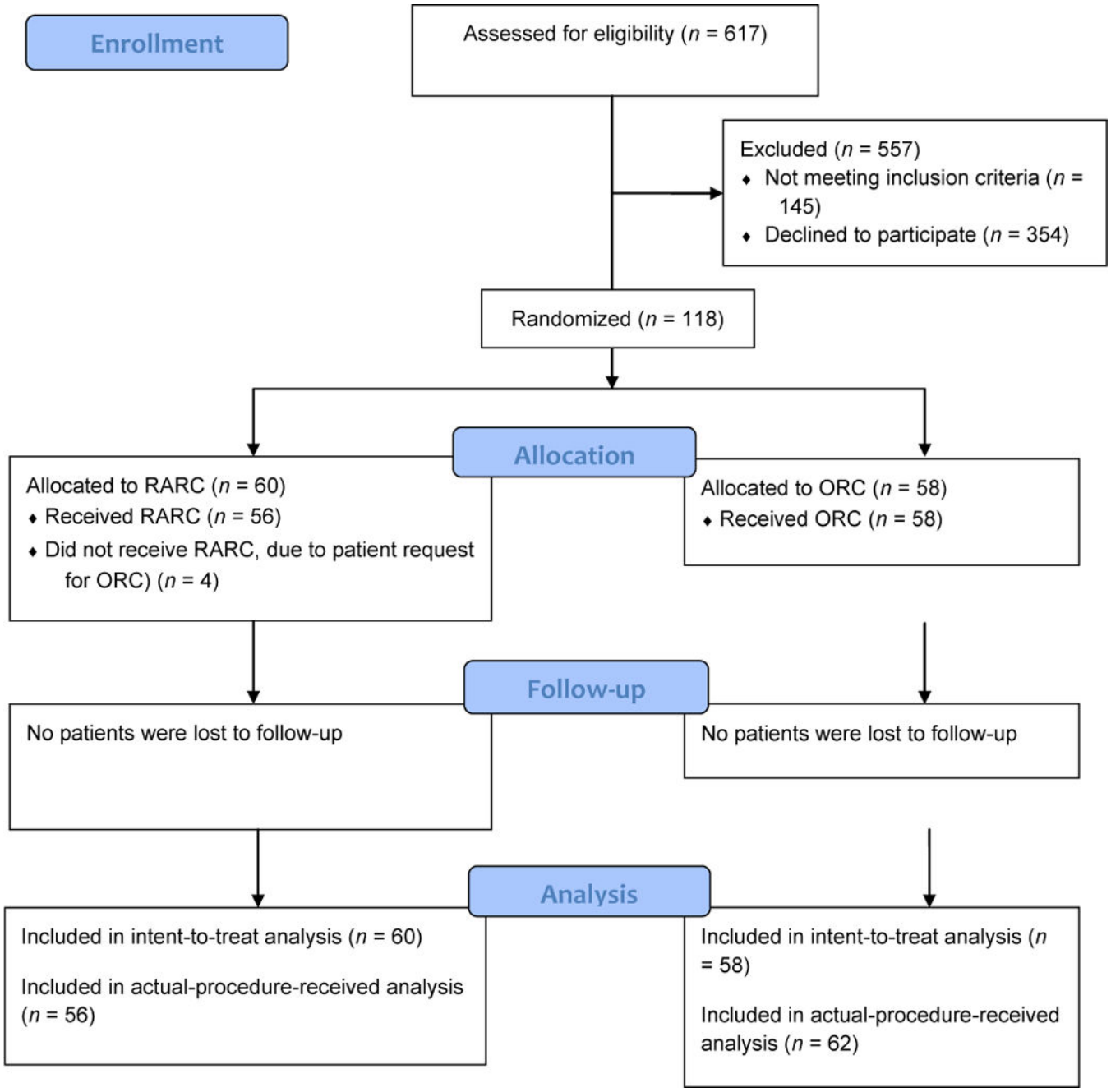

Fig. 1. Randomization and follow-up of study patients

ORC = open radical cystectomy; RARC = robot-assisted laparoscopic radical cystectomy.

Table 1

Participant characteristics

	Robotic (*n* = 60)	**Open (*n* = 58)**
Baseline		
Age, yr, median (IQR)	66 (60–71)	65 (58–69)
Male sex, *n* (%)	51 (85)	42 (72)
Body mass index, kg/m^2, median (IQR)	27.9 (24.7–31.0)	29.0 (26.3–33.7)
ASA score, *n* (%)		
2	17 (28)	12 (21)
3	42 (70)	43 (74)
4	1 (1.7)	3 (5.2)
Prior bacillus Calmette-Guérin therapy, *n* (%)	30 (50)	18 (31)
Clinical stage, *n* (%) *		
Tis	8 (14)	2 (3.5)
Ta	1 (1.7)	3 (5.3)
T1	21 (36)	19 (33)
T2	24 (41)	28 (49)
T3	4 (6.8)	5 (8.8)
T4	1 (1.7)	0 (0)
Neoadjuvant chemotherapy, *n* (%)	19 (32)	26 (45)
Intraoperative		
Urinary diversion type, *n* (%)		
Ileal conduit	27 (45)	23 (40)
Neobladder	33 (55)	32 (55)
Continent cutaneous	0 (0)	3 (5.2)
Level of lymph node dissection, *n* (%)		
External iliac	0 (0)	4 (6.9)
Common iliac	13 (22)	26 (45)
Aortic bifurcation	33 (55)	20 (34)
Inferior mesenteric artery	14 (23)	8 (14)
Received assigned surgery	56 (93.3)	58 (100)
Pathology from final cystectomy specimen		
Histology, *n* (%)		
Adenocarcinoma	0 (0)	1 (1.7)
Squamous cell carcinoma	1 (1.7)	1 (1.7)
Small cell carcinoma	1 (1.7)	1 (1.7)
Small cell plus transitional cell carcinoma	1 (1.7)	0 (0)
Transitional cell carcinoma	57 (95)	55 (95)
Pathologic stage, *n* (%)		

	Robotic (*n* = 60)	**Open (*n* = 58)**
T0	13 (22)	7 (12)
Tis	14 (23)	11 (19)
Ta	1 (1.7)	3 (5.2)
T1	7 (12)	11 (19)
T2	8 (13)	7 (12)
T3	12 (20)	15 (26)
T4	5 (8.3)	4 (6.9)

ASA = American Society of Anesthesiologists; IQR = interquartile range. Adapted from Bochner et al [13].

* Missing data for one participant in each of the two arms.

Table 2

Outcomes after radical cystectomy

	Robotic	Open	Difference, %	95% CI for difference, %	*p* value
By randomization arm/intention-to-treat	*n* = 60	*n* = 58			
Grade 2–5 complication, *n* (%)	37 (62)	38 (66)	−3.9	−21 to 13	0.7
Grade 3–5 complication, *n* (%)	13 (22)	12 (21)	1.0	−14 to 16	0.9
Total number of grade 2–5 complications, mean (SD)	1.4 (1.80)	1.5 (1.66)	−0.2	−0.8 to 0.5	0.6
Total number of grade 3–5 complications, mean (SD)	0.3 (0.58)	0.3 (0.76)	0.0	−0.3 to 0.2	0.7
Any intraoperative complications, *n* (%)	3 (5.0)	3 (5.2)	−0.2	−8 to 8	>0.9
Operative room time, min, mean (SD)	456 (82)	329 (77)	127	98 to 156	<0.001
Estimated blood loss, ml, mean (SD)	516 (427)	676 (338)	−159	−300 to −19	0.027
Hospital length of stay, d, mean (SD)	8 (3)	8 (5)	0	−2 to 1	0.5
Positive surgical margin, *n* (%)	2 (3.3)	3 (5.2)	−1.8	−9 to 5	0.6
Subgroup of patients ≥T3, *n/n* (%)	2/17 (12)	3/19 (16)	−4.0	−26 to 18	0.7
Lymph node–positive patients, *n* (%)	10 (17)	9 (16)	1.1	−12 to 14	0.9
By type of surgery received	*n* = 56	*n* = 62			
Grade 2–5 complication, *n* (%)	35 (63)	40 (65)	−2.0	−19 to 15	0.8
Grade 3–5 complication, *n* (%)	12 (21)	13 (21)	0.5	−14 to 15	>0.9
Total number of grade 2–5 complications, mean (SD)	1.4 (1.85)	1.5 (1.63)	−0.1	−0.7 to 0.6	0.9
Total number of grade 3–5 complications, mean (SD)	0.3 (0.59)	0.3 (0.74)	0.0	−0.3 to 0.2	0.8
Any intraoperative complications, *n* (%)	3 (5.4)	3 (4.8)	0.5	−7 to 8	0.9
Operating room time, min, mean (SD)	464 (79)	330 (75)	134	106 to 162	<0.001
Estimated blood loss, ml, mean (SD)	500 (437)	681 (328)	−181	−321 to −41	0.012
Hospital length of stay, d, mean (SD)	8 (4)	8 (5)	0	−2 to 1	0.9
Positive surgical margin, *n* (%)	2 (3.6)	3 (4.8)	−1.3	−8 to 6	0.7
Subgroup of patients ≥T3, *n/n* (%)	2/16 (13)	3/20 (15)	−2.5	−25 to 20	0.8
Lymph node yield, mean (SD)					
Extended dissection	31.9 (12)	30.0 (12)	2.0	−3.8 to 7.8	0.5
Standard dissection	19.5 (10)	18.9 (10)	0.6	−6.2 to 7.5	0.5
Lymph node-positive patients, *n* (%)	10 (18)	9 (15)	3.3	−10 to 17	0.6

CI = confidence interval; SD = standard deviation.

Adapted from Bochner et al [13].

Table 3

Complication types observed by randomization arm

	Robotic (*n* = 60), *n* (%)	Open (*n* = 58), *n* (%)	Difference, %	95% CI for difference, %	*p* value
Bleeding	3 (5.0)	3 (5.2)	−0.2	−8 to 8	>0.9
Cardiac	9 (15)	8 (14)	1.2	−11 to 14	0.9
Gastrointestinal	14 (23)	17 (29)	−6	−22 to 10	0.5
Genitourinary	3 (5.0)	8 (14)	−9	−19 to 1.7	0.10
Infectious	23 (38)	17 (29)	9	−8 to 26	0.3
Miscellaneous	2 (3.3)	3 (5.2)	−1.8	−9 to 5	0.6
Neurologic	5 (8.3)	2 (3.4)	4.9	−3.5 to 13	0.3
Pulmonary	1 (1.7)	3 (5.2)	−3.5	−10 to 3.1	0.3
Surgical	0 (0.0)	1 (1.7)	−1.7	−5 to 1.6	0.3
Thromboembolic	5 (8.3)	5 (8.6)	−0.3	−10 to 10	>0.9
Wounds	2 (3.3)	8 (14)	−10	−20 to −0.5	0.041

CI = confidence interval.

Table 4

Patient-reported quality-of-life outcomes by randomization group: measurements at baseline, at 3 mo after surgery, and at 6 mo after surgery*

	Patients with available data, *n*	Robotic, mean (SD)	Open, mean (SD)	Adjusted difference	95% CI for difference	*p* value
Baseline	–	***n* = 23**	***n* = 34**	–	–	–
Global health status/QoL	57	78 (20)	75 (19)	–	–	–
Cognitive function	58	90 (13)	87 (16)	–	–	–
Emotional function	58	73 (23)	75 (23)	–	–	–
Physical function	53	96 (8)	95 (7)	–	–	–
Role function	58	96 (14)	91 (17)	–	–	–
Social function	58	79 (21)	77 (23)	–	–	–
Appetite loss	53	7 (20)	8 (14)	–	–	–
Constipation	58	11 (19)	18 (24)	–	–	–
Diarrhea	58	1 (7)	6 (13)	–	–	–
Dyspnea	58	0 (0)	8 (17)	–	–	–
Fatigue	58	14 (17)	17 (17)	–	–	–
Financial problems	56	8 (14)	13 (18)	–	–	–
Insomnia	58	25 (30)	28 (30)	–	–	–
Nausea/vomiting	58	5 (9)	3 (8)	–	–	–
Pain	58	8 (16)	10 (20)	–	–	–
3 mo after radical cystectomy	–	***n* = 22**	***n* = 30**	–	–	–
Global health status/QoL	52	77 (12)	72 (21)	4	−5 to 14	0.4
Cognitive function	53	93 (12)	89 (14)	2	−5 to 9	0.5
Emotional function	53	81 (15)	82 (23)	1	−10 to 12	0.8
Physical function	53	91 (11)	87 (14)	4	−3 to 10	0.3
Role function	53	81 (22)	76 (25)	3	−10 to 16	0.6
Social function	53	80 (19)	76 (25)	4	−9 to 17	0.6
Appetite loss	53	12 (19)	17 (29)	−5	−19 to 9	0.5
Constipation	53	28 (30)	23 (25)	5	−10 to 21	0.5
Diarrhea	53	17 (28)	14 (21)	3	−11 to 17	0.6

	Patients with available data, *n*	Robotic, mean (SD)	Open, mean (SD)	Adjusted difference	95% CI for difference	*p* value
Dyspnea	53	7 (14)	12 (24)	0	−12 to 11	0.9
Fatigue	53	21 (20)	29 (20)	−5	−15 to 6	0.4
Financial problems	51	16 (25)	17 (24)	4	−7 to 15	0.5
Insomnia	53	22 (22)	27 (31)	−5	−20 to 9	0.5
Nausea/vomiting	53	4 (10)	5 (15)	−2	−8 to 4	0.5
Pain	53	13 (15)	17 (23)	−3	−14 to 8	0.6
6 mo after radical cystectomy	–	***n* = 23**	***n* = 30**	–	–	–
Global health status/QoL	53	76 (11)	78 (23)	−3	−12 to 7	0.5
Cognitive function	53	91 (10)	92 (13)	−1	−7 to 5	0.8
Emotional function	53	83 (13)	83 (20)	1	−8 to 10	0.9
Physical function	53	93 (8)	92 (10)	1	−4 to 6	0.7
Role function	53	91 (12)	89 (24)	0	−11 to 11	>0.9
Social function	53	84 (20)	85 (19)	−1	−12 to 9	0.8
Appetite loss	53	6 (13)	4 (12)	1	−5 to 8	0.7
Constipation	52	23 (24)	18 (24)	8	−6 to 21	0.3
Diarrhea	53	17 (26)	11 (20)	9	−4 to 22	0.2
Dyspnea	53	9 (15)	4 (12)	6	−1 to 14	0.09
Fatigue	53	18 (13)	21 (20)	−2	−12 to 7	0.6
Financial problems	51	11 (19)	13 (24)	2	−9 to 13	0.7
Insomnia	53	19 (22)	23 (25)	−4	−17 to 10	0.6
Nausea/vomiting	53	1 (3)	1 (3)	0	−2 to 1	0.9
Pain	53	8 (12)	9 (15)	−1	−8 to 7	0.8

CI = confidence interval; QoL = quality of life; SD = standard deviation.

*Adjusted differences, CIs, and *p* values are from an analysis of covariance model adjusted for baseline score. All scores are on a 0–100 scale. For function domains, higher scores represent better functioning. For symptom domains, higher scores represent worse symptoms.

Table 5

Cost comparison analysis of total adjusted operating room and inpatient-related costs by procedure received and type of urinary diversion*

Type of urinary diversion † and treatment arm	Patients, *n*	Average total cost		95% CI (Log $)	*p* value (difference >0)
		$	Log $		
Neobladder, robotic arm	30	19 231.26	9.84	9.77–9.92	–
Neobladder, open arm	35	15 311.00	9.61	9.54–9.69	
Difference	–	3920.26	0.23	0.13–0.33	$p < 0.0001$
Ileal conduit, robotic arm	26	18 388.19	9.80	9.72–9.87	–
Ileal conduit, open arm	24	16 648.58	9.64	9.50–9.79	
Difference	–	1739.61	0.16	0.001–0.317	$p < 0.05$

CI = confidence interval.

*Analysis includes actual procedure received by patients, not by intention to treat. We did not analyze the three patients who received continent cutaneous urinary diversion, as they were all in the open radical cystectomy arm.

†All urinary diversions were performed via an open surgical approach.