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## Best Practices in Robot-assisted Radical Cystectomy and Urinary Reconstruction: Recommendations of the Pasadena Consensus Panel

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### Abstract

**Context:** Robot-assisted surgery is increasingly used for radical cystectomy (RC) and urinary reconstruction. Sufficient data have accumulated to allow evidence-based consensus on key issues such as perioperative management, comparative effectiveness on surgical complications, and oncologic short- to midterm outcomes.

**Objective:** A 2-d conference of experts on RC and urinary reconstruction was organized in Pasadena, California, and the City of Hope Cancer Center in Duarte, California, to systematically review existing peer-reviewed literature on robot-assisted RC (RARC), extended lymphadenectomy, and urinary reconstruction. No commercial support was obtained for the conference.

**Evidence acquisition:** A systematic review of the literature was performed in agreement with the PRISMA statement.

**Evidence synthesis:** Systematic literature reviews and individual presentations were discussed, and consensus on all key issues was obtained. Most operative, intermediate-term oncologic, functional, and complication outcomes are similar between open RC (ORC) and RARC. RARC consistently results in less blood loss and a reduced need for transfusion during surgery. RARC generally requires longer operative time than ORC, particularly with intracorporeal reconstruction. Robotic assistance provides ergonomic value for surgeons. Surgeon experience and institutional volume strongly predict favorable outcomes for either open or robotic techniques.

**Conclusions:** RARC appears to be similar to ORC in terms of operative, pathologic, intermediate-term oncologic, complication, and most functional outcomes. RARC consistently results in less blood loss and a reduced need for transfusion during surgery. RARC

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can be more expensive than ORC, although high procedural volume may attenuate this difference.

**Patient summary:** Robot-assisted radical cystectomy (RARC) is an alternative to open surgery for patients with bladder cancer who require removal of their bladder and reconstruction of their urinary tract. RARC appears to be similar to open surgery for most important outcomes such as the rate of complications and intermediate-term cancer-specific survival. Although RARC has some ergonomic advantages for surgeons and may result in less blood loss during surgery, it is more time consuming and may be more expensive than open surgery.

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## 1. Introduction

Bladder cancer is one of the most common [1] and expensive malignancies to manage [2]. Radical cystectomy (RC) with urinary reconstruction is a complex, time-consuming surgery associated with significant morbidity [3]. Approximately 7000 RCs were performed annually from 2001 to 2010 in the United States [4]. The number of these procedures performed with robotic assistance rose dramatically (0.6–12.8%) from 2004 to 2010 [5].

The expanding evidence base for robot-assisted RC (RARC) now allows preliminary conclusions to be drawn about the comparative effectiveness of RARC versus open RC (ORC). This consensus summarizes existing data using up-to-date systematic reviews of the literature (presented elsewhere in this issue of *European Urology* [6,7]) and best practices for cystectomy and urinary reconstruction as developed by an international panel of expert ORC and RARC surgeons who met in Pasadena, California, and at the City of Hope Cancer Center, Duarte, California, USA, in May 2014.

## 2. Evidence acquisition

A systematic review of published literature related to RARC was performed in September 2013 using Medline, Scopus, and Web of Science, with an update performed in April 2014. The keywords *robot-assisted radical cystectomy*, *da Vinci radical cystectomy*, and *robot\* radical cystectomy* were used across these search fields: *surgical series* (prospective and retrospective) and *comparative studies* (prospective and retrospective, randomized and nonrandomized) evaluating RARC. Partial cystectomy, prostate-sparing cystectomy, salvage surgery, urachal cancer, cystectomy for benign condition, concomitant/combined procedures, and single-case reports were excluded from our review. Intraoperative and perioperative outcomes (including complications) as well as pathologic, intermediate-term oncologic, and functional results were evaluated. The development of the systematic reviews followed the PRISMA guidelines [8].

The systematic review and the personal experiences of expert surgeons provided context for the development of individual presentations by attendees of the Pasadena meeting. Over the course of the 2-d conference, the Pasadena Consensus Panel (PCP) developed best practice recommendations that were incorporated into a draft manuscript reviewed by all panelists.

## 3. Evidence synthesis

### 3.1. Perioperative management

Perioperative management of patients undergoing RARC is identical to that for patients undergoing ORC. The PCP considered systematic review data, recent high-quality studies, and existing guidelines of the European Association of Urology (EAU) [9], the International Consultation on Urological Diseases [10], and the Enhanced Recovery After Surgery (ERAS) Society [11]. The evidence-based guidelines for pre- and postoperative care after RC developed by ERAS, in particular, were judged to provide an excellent framework for the specifics of care before, during, and after RARC [11,12]. The use of ERAS protocols has been shown to reduce both length of stay (LOS; <30%) and postoperative complications (<50%) in colorectal surgeries [13]. Only limited studies exist in cystectomy patients, but they suggest that these protocols can shorten LOS without increased morbidity [11].

#### 3.1.1. Patient selection

The indications for RARC are identical to ORC (Table 1). There are no absolute contraindications for RARC, although the PCP noted that certain cases should be performed only by experienced surgeons because of their complexity (Table 2). Although no accepted definition of *experienced surgeon* exists, the PCP noted that data on surgeon learning curves with RARC suggest that at least 20–30 procedures are needed to flatten the initial learning curve. Surgeons should strive to achieve the parameters established by existing surgical criteria, such as those in the 2014 EAU guidelines [9], before attempting higher risk cases.

RARC is feasible in patients who have had prior surgery or radiation, although the decision to proceed is determined primarily by surgeon experience. In cases of prior pelvic radiation, the posterior dissection can be very challenging, and care must be taken to avoid rectal injury. In patients with prior lower intra-abdominal surgery, extensive laparoscopic lysis of adhesions may be needed for port placement.

#### 3.1.2. Preoperative considerations

Before surgery, patients should be counseled extensively about the risks and benefits of RARC including the possibility of conversion to an open approach.

**3.1.2.1. Neoadjuvant chemotherapy.** Given the relatively high risk of disease recurrence following RC, attempts have been made to improve survival with neoadjuvant chemotherapy

**Table 1 – Indications for radical cystectomy\***

Indication
Patients with T1 tumors at high risk of progression (ie, high grade, multifocality, carcinoma in situ, and tumor size)
T1 patients failing intravesical therapy
Patients with muscle-invasive bladder cancer T2–T4a, N0–Nx, M0–I
Patients with high-risk and recurrent superficial tumors, BCG-resistant Tis, T1G3, as well as extensive papillary disease that cannot be controlled with TURB and intravesical therapy alone
Salvage cystectomy is indicated for nonresponders to conservative therapy, recurrence after bladder-sparing treatment, and nonurothelial carcinoma
As a purely palliative intervention, including in fistula formation, for pain, or recurrent visible hematuria
BCG = bacillus Calmette-Guérin; TURB = transurethral resection of the bladder.
* From the European Association of Urology guidelines, 2014 edition [9].

**Table 2 – Challenging cases recommended for experienced robot-assisted radical cystectomy surgeons only**

Types of challenging cases
Patient with high body mass index
Salvage cystectomy following chemotherapy and radiation treatment
Patient with clinical lymphadenopathy
Patient with clinically advanced disease (ie, T4)
Patient who has had previous prostatectomy, abdominoperineal resection surgery, or low anterior resection surgery
Patient with large bulky tumor
Patient with multiple prior lower abdominal surgeries
Patient with prior pelvic radiation for pelvic malignancy such as prostate or rectal cancer

(NAC). Level 1 evidence from randomized controlled trials (RCTs) has demonstrated that cisplatin-based NAC confers a benefit in overall survival for cT2–cT4 patients. A meta-analysis of 3005 patients comparing cisplatin combination therapy with controls found a 5% absolute improvement in survival and a 9% improvement in disease-free survival at 5 yr [14]. The PCP concurred with EAU and International Consultation on Urological Diseases recommendations to offer NAC to patients with cT2–cT4 disease who are cisplatin eligible [9,10]. Neoadjuvant regimens not containing cisplatin have not shown a benefit and therefore cannot be recommended [9]. Incorporating routine combined consultation with both urology and medical oncology has been shown to improve the adoption of NAC (11–55% in 1 yr) [15].

**3.1.2.2. Bowel preparation.** Formal bowel preparation may not be necessary for cystectomy with urinary reconstruction and is not considered mandatory according to the EAU guidelines [9]. A 2011 Cochrane review of 18 RCTs with >5800 patients showed no statistically significant benefit from mechanical bowel preparation or rectal enemas in colorectal surgery [16]. A randomized study of 86 patients undergoing ORC with ileal conduit compared a 3-d bowel preparation regimen with no bowel preparation and found no significant differences for a variety of outcomes including wound infections, ileus, sepsis, and median hospital stay [17]. In another study, bowel preparation was associated with *more* urinary tract infection or sepsis and *Clostridium difficile* infections [18].

After reviewing the level 1 evidence, the PCP suggested that bowel preparation can be safely omitted for cystectomy with urinary reconstruction using the ileum. Data regarding the need for bowel preparation when using the colon in the reconstruction are not available; therefore, a recommendation cannot be made in this situation.

**3.1.2.3. Preoperative fasting and carbohydrate loading.** US and European guidelines recommend no solid food 6 h before surgery but allow liquids up to 2 h prior to surgery including for patients classified American Society of Anesthesiologists class 3 and 4 and/or with diabetes mellitus. In addition, carbohydrate fluid intake 2 h before surgery may be beneficial [19]. A meta-analysis of 13 randomized studies of preoperative carbohydrate loading for various surgical procedures found benefits in terms of thirst and hunger, and it also showed less postoperative nausea and vomiting [20].

**3.1.2.4. Alvimopan.** Alvimopan (Entereg) is a  $\mu$ -opioid antagonist that can minimize undesirable side effects of opioid analgesics on bowel motility without affecting pain control or precipitating withdrawal. Alvimopan is approved by the US Food and Drug Administration for the treatment of postoperative ileus and accelerates gastrointestinal (GI) recovery [21]. Only one RCT has been conducted in cystectomy patients. It found that the alvimopan cohort experienced quicker GI recovery, shorter LOS, and significantly less ileus-related morbidity [22]. The PCP concluded that the perioperative use of alvimopan should be considered in patients undergoing RARC.

**3.1.2.5. Deep vein thrombosis prophylaxis.** The incidence of clinically significant deep vein thrombosis (DVT) after cystectomy is estimated at 5–8% [23–25], although the PCP noted that because DVTs can occur months after surgery, such estimates probably underestimate the true incidence. The PCP also noted wide international variations in DVT prophylaxis protocols that may be driven by differing reimbursement and insurance regulations. Nonetheless, the PCP noted that RCTs support prolonged thromboprophylaxis for up to 4 wk after oncologic pelvic surgery. These data have shown a significant decrease in the incidence of DVT compared with in-hospital prophylaxis, without increasing the risk of bleeding complications [26].

ERAS [11] and other guidelines (eg, National Institute for Health and Clinical Excellence [NICE] [27]) recommend thromboprophylaxis using low-molecular-weight or unfractionated heparin for all major pelvic surgery, with the addition of compression stockings and intermittent pneumatic compression devices that can further decrease risk.

**3.1.2.6. Antibiotics.** None of the studies reviewed by the PCP suggested any benefits from one antibiotic or skin preparation over another, although it was noted that antimicrobial agents in cystectomy patients should be effective against aerobes and anaerobes. The PCP consensus was that a single course of a second- or third-generation cephalosporin is recommended before skin incision and

<1 h before surgery, with treatment continued for 24 h after surgery for men and 48 h after surgery for women.

### 3.1.3. Postoperative considerations

Postoperative care of patients after RARC is identical to care given to ORC patients. Specifics of care regimens depend on the type of surgery and urinary reconstruction. The goals are to minimize complications and educate patients and families to set realistic expectations for recovery and improve communication between the patient and healthcare providers.

ERAS guidelines for postoperative care should be followed [11]. These procedures are particularly relevant to cystectomy patients:

- Routine postoperative intensive care unit (ICU) monitoring is not necessary. ICU placement may be appropriate for sicker patients, although such patients represent only approximately 6% of the cystectomy population [28]
- Monitoring and treatment of metabolic abnormalities (eg, hyperammonemia, hypokalemia, hypomagnesemia, hypocalcemia) [28]
- For patients with orthotopic neobladders, frequent irrigation of urinary catheters to clear the neobladder of mucus, beginning the evening of surgery (typically needed until the catheter is removed) [28]
- Placement of ureteral stents (at least 5 d) [29]
- Avoidance of routine or long-term use of nasogastric tubes (a Cochrane review showed no benefit in major abdominal surgery) [11,30]
- Avoidance of total parenteral nutrition (no benefit, more complications) [31]
- Early oral nutrition (eg, 4 h after surgery) [11]
- Gum chewing (two studies show shorter time to flatus and first bowel movement) [32,33]
- Early ambulation [11]
- Multimodal postoperative analgesia to minimize opioids (use of epidural catheters, local anesthesia, and patient-controlled analgesia [PCA] recommended) [11]
- Incentive spirometry, coughing, and deep-breathing exercises to help minimize postoperative respiratory complications [11].

### 3.1.4. Key consensus recommendations

The following recommendations are made regarding perioperative management:

- There are no absolute contraindications to RARC.
- Obesity, previous abdominal surgery, bulky bladder tumors, and previous radiation are not absolute contraindications for RARC, although such cases should be performed by experienced surgeons.
- There are no differences in patient evaluation between RARC and ORC.
- NAC should be offered to patients who are eligible.
- Bowel preparation is unnecessary unless there is need to involve the colon.
- A single course of a second- or third-generation cephalosporin is recommended before skin incision and <1 h before surgery.

- A total of 4 wk of DVT prophylaxis is recommended; national or institutional guidelines, such as the NICE guidelines, should be followed.
- Preoperative use of carbohydrate loading may decrease postoperative thirst and nausea.
- Perioperative use of alvimopan may decrease the risk of postoperative ileus and reduce hospital stay.

## 3.2. Surgical techniques

### 3.2.1. Technique overview

The surgical principles for cystectomy and urinary reconstruction are identical whether conducted with open, laparoscopic, or robot-assisted techniques. A detailed discussion and video demonstration of robot-assisted techniques has been prepared simultaneously with this report and can be viewed in the “Surgery in Motion” section of the *European Urology* Web site [34].

### 3.2.2. Surgical experience

RC with urinary reconstruction is associated with relatively high 90-d complication rates [35]. A clear learning curve exists in the acquisition of proficiency in RARC and extended lymphadenectomy. There is wide variation in how to define such proficiency. With robot-assisted radical prostatectomy (RARP), for example, the number of cases at which a surgeon is considered proficient varies in the literature from 20 to 250 cases [36–38].

In the RARC literature, three papers have explored the nature of the learning curve and its effects on outcomes. Hayn et al used defined cut-off points for operative time, lymph node yield (LNY), estimated blood loss (EBL), and positive surgical margins (PSMs) in a study of 496 patients who underwent RARC by 21 surgeons at 14 institutions [39]. Using statistical models, it was estimated that 21 patients were required for operative time to reach 6.5 h, and 8, 20, and 30 patients were required to reach an LNY of 12, 16, and 20, respectively. An estimated 30 patients were necessary to achieve PSM rates <5%. For patients with pathologic stage T2 or higher, PSM rates of <15% were achieved after 24 patients. The overall conclusion was that approximately 30 cases were required, on average, to achieve proficiency in RARC, although many variables exist, such as a surgeon’s previous experience with robot-assisted surgeries and the presence of an experienced mentor to train junior faculty.

Richards et al reviewed the first 60 cases at a single high-volume institution with experienced surgeons and analyzed key factors such as operating room time, EBL, LOS, and complications by tertiles [40]. The authors found a significant drop in total complications from 70% after the first tertile to 30% after both the second and third tertiles [40].

Collins et al looked prospectively at the learning curve effect in a series of 67 patients undergoing RARC with orthotopic intracorporeal neobladder performed by two primary surgeons [41]. This group found a significant drop in overall complications with time, although the rate of major complications was not significant. There were

nonsignificant differences across time in EBL, LOS, and LNY. Total operative times dropped significantly for one of the surgeons (from a median of 565 min to a median of 345 min) but were not significantly different for the second surgeon (413 min to 385 min), suggesting that the second surgeon learned from the first. The authors also noted that current assessments of learning curves for robotic urologic surgery are subjective and based on nonvalidated metrics [41].

### 3.2.3. Case-volume effects

Data from the ORC literature consistently show that larger volumes of cystectomy procedures are associated with better outcomes [42]. Leow et al found a clear inverse relationship between surgeon volume of RCs and the development of postoperative 90-d major complication rates as well as direct hospital costs [43]. As such, the Improving Outcome Guidance in the United Kingdom has mandated a minimum of five RCs per surgeon per year [27]. Some data specifically for RARC suggest that similar case-volume patterns apply to robotic surgery and are expected due to the complexity of the procedures, particularly with intracorporeal reconstructions [5]. Table 3 lists specific recommendations based on surgeon experience.

A study of lymph node dissection (LND) and RARC found that high-volume surgeons are more likely to perform extended LND (eLND), presumably reflecting their increased comfort with advanced vascular dissection [44].

### 3.2.4. Previous history of surgery

After reviewing the literature, the PCP concluded that only experienced surgeons should perform RARC in patients with either previous pelvic surgery or radiation to the pelvic region. Studies find no association with such prior treatments and EBL, transfusion rates, operative time, lysis of adhesion time, reoperation, length of time in the ICU, or

overall LOS [45,46]. Data do show an association between previous surgery or radiation treatment and lower LNY and higher overall complication rates, which is why the PCP recommended that these cases be limited to experienced surgeons.

### 3.2.5. Soft tissue surgical margins

Positive soft tissue surgical margins may arise from locally advanced disease extending into surrounding structures, such as the pelvic side wall or the pubic bone, or from inadvertent cutting across tumor during cystectomy, and they are associated with a very poor prognosis. Soft tissue surgical margins are a measure of surgical experience and skill, but they are also related to the local extent of the primary tumor. The PCP recommended stage-specific soft tissue surgical margin goals for RARC that are similar to those obtained from experienced surgeons performing ORC. The proposed acceptable soft tissue surgical margins based on final pathologic T stage of the tumor are <3% for pT2, <10% for pT3, <25% for pT4, and <7% overall [47].

Case number and institutional volume are not generally associated with soft tissue surgical margins, whereas pathologic stage higher than pT2 is associated with a 5-times-higher chance of positive soft tissue surgical margins [48]. In large-volume tumors and/or cases of suspected extravesicle disease, wide dissection of the perivesicle tissue is mandatory to minimize positive soft tissue surgical margins.

### 3.2.6. Lymph node dissection

The PCP recommended that the template for lymphadenectomy be identical to that of open surgery. The data consistently show that an adequate lymphadenectomy can be routinely performed during RARC. Controversy exists as to the optimal proximal limit of the template, but the panel agreed that for RARC there should be no compromise in oncologic principles.

**Table 3 – Recommended goals for robot-assisted radical cystectomy surgeons**

Level of surgeon experience	Recommendations
Learning curve (first 20–30 cases)	<ul style="list-style-type: none"> <li>• Supervision by an experienced mentor</li> <li>• Operative times &lt;7 h</li> <li>• Blood loss &lt;400 ml</li> <li>• Complete lymphadenectomy</li> <li>• Overall margin status &lt;7%</li> <li>• Use caution when operating on bulky tumors; obese patients; or patients with previous radiotherapy, surgery, or adhesions</li> <li>• Perform ileal conduit reconstructions only</li> </ul>
Experienced (30–100 cases)	<ul style="list-style-type: none"> <li>• Operative times with ileal conduit ≤5 h, or with neobladder, ≤6 h</li> <li>• Blood loss ≤300 ml</li> <li>• Complete lymphadenectomy</li> <li>• Build ICUD experience</li> </ul>
Very experienced (>100 cases)	<ul style="list-style-type: none"> <li>• Few contraindications</li> <li>• Operative times with ileal conduit ≤4 h, or with neobladder, ≤5 h</li> <li>• Blood loss ≤300 ml</li> <li>• Complete lymphadenectomy</li> <li>• Use neobladder or continent reconstruction in 25–50% of cases, as the case mix allows</li> <li>• Aim for Clavien-Dindo grades 3–5 complication rates of &lt;30% of patients</li> <li>• Aim for length of stay of 5–10 d</li> </ul>

ICUD = intracorporeal urinary diversion.

No recommendation was made on a minimum number of lymph nodes (LNs) to remove because node yield may be influenced by factors unrelated to the extent of the surgery. However, the panel agreed that an extended node dissection should include nodes up to the common iliac vessels and lateral to the genital femoral nerve. Within the pelvis, the nodes are removed from the bladder wall laterally to the pelvic sidewall and distally to the femoral canal. All nodes above and below the obturator nerve are removed. The proximal extent should include all nodes up to the proximal common iliac vessels. No consensus was reached about whether or not the lymphadenectomy should extend above the aortic bifurcation or include the presacral area. A thorough LND should include removal of all fatty soft tissue surrounding the vessels and over to the pelvic sidewall within the template. High-volume institutions (>100 procedures per year) are 3.5 times more likely to perform an extended pelvic LND (ePLND) [44].

### 3.2.7. Nerve-sparing procedures

Standards for deciding on nerve-sparing procedures are similar for ORC and RARC. Nerve sparing appears to be safe in the absence of bulky tumor around the bladder neck and prostate, and it may allow preservation of erectile function in potent men. There is also a suggestion that it may improve continence in patients undergoing neobladder reconstruction [49].

### 3.2.8. Key consensus recommendations

The following recommendations are made regarding surgical techniques:

- Goals for PSMs: <3% for pT2, <10% for pT3, <25% for pT4, and <7% overall.
- In appropriate patients, ePLND should be performed according to oncologic principles.
- All surgeons, but particularly those in the early phase of the learning curve, should be open to conversion from RARC to ORC as needed, guided by what is in the patient's best interest.
- Standards for deciding on nerve-sparing procedures are similar for ORC and RARC, with nerve sparing generally preferred except in cases of a bulky tumor.

## 3.3. Urinary reconstruction

Three options for urinary reconstruction are mainly used after cystectomy: (1) incontinent cutaneous diversion, (2) continent orthotopic diversion, and (3) continent cutaneous diversion.

A large majority of patients undergoing ORC and RARC in the United States have received an ileal conduit diversion. Rates of neobladder vary in open series from 10% to >70% depending on the institution [50].

### 3.3.1. Intracorporeal versus extracorporeal reconstruction

To date, most surgeons have used extracorporeal urinary diversion (ECUD) for the urinary reconstruction following

RARC because it is simpler and faster to perform than an intracorporeal urinary diversion (ICUD) [4]. ICUD is becoming more common as surgical experience increases and the potential benefits from a totally intracorporeal approach become apparent. However, ICUD use in the United States remains low, accounting for roughly 3% of RARCs [51]. ICUD appears to be more common in Europe and at a few high-volume centers [9].

When performed by an experienced surgeon, ICUD may offer decreased fluid loss from evaporation, reduced body cooling, reduced EBL, lower pain, a smaller incision in women (ie, better cosmesis), and quicker return to bowel function [41]. Potential disadvantages include the technical challenge, longer learning curve, and longer operative times. At present, a limited number of studies have evaluated the benefits of ICUD compared with ECUD. These suggest a small benefit of ICUD over ECUD in terms of fewer complications, although the extent of this benefit is not clear and the evidence quality is low [6].

### 3.3.2. Patient selection

The eligibility criteria and contraindications for robot-assisted continent or noncontinent urinary reconstruction are the same as for ORC. A full discussion of the pros and cons of each type of diversion is beyond the scope of this paper. The extent of tumor, patient comorbidities such as impaired cardiac, pulmonary, and renal function; preexisting bowel disease; and cognitive function are all important factors that should be considered in a decision about what reconstruction is appropriate, along with patient preference [9]. The options for urinary diversion should not be limited by the surgical approach.

### 3.3.3. Choice of reconstruction and quality-of-life issues

The decision-making process regarding reconstruction choice should not differ between RARC and ORC. Few data report the relationship between surgical technique, choice of urinary reconstruction, and patient health-related quality of life (HRQoL) [9]. Important covariables such as a patient's age, mental status, coping ability, and sex have rarely been considered in studies of postoperative HRQoL [52,53]. Finally, individual differences in symptom tolerance and the fact that people adapt relatively quickly to whichever kind of reconstruction they have reduce the ability to detect differences in HRQoL over longer time periods. Evidence is mixed with regard to whether reconstruction type is associated with differences in HRQoL [53,54]. When asked, however, most patients state a preference for orthotopic reconstruction rather than an ileal conduit [55].

Some studies, perhaps reflecting improvements in surgical techniques for creating orthotopic bladders, have shown statistically significant differences in HRQoL in favor of neobladders [56,57]. Patients in these studies who had an orthotopic bladder had significantly better physical function and a more active lifestyle compared with patients with an ileal conduit, although these attributes may have been present preoperatively.

### 3.3.4. Key consensus recommendations

The following recommendations are made with regard to urinary reconstruction:

- The principles of reconstruction are similar for RARC and ORC, and decisions about which approach to use should not be influenced by surgical approach.
- ICUD may offer some advantages over ECUD when surgical experience and patient selection allow this route, although existing data are weak.
- Particularly early in the learning curve of either individual surgeons or entire surgical centers, a team approach to cystectomy with urinary reconstruction, whereby one surgeon performs the extirpative phase and another performs the reconstruction phase, may be effective.

## 3.4. Outcomes

### 3.4.1. Complication rates

RC is a morbid procedure. Historically, reports of complications following ORC have used inconsistent definitions [58]. Standardized reporting using objective criteria, such as the Martin criteria [59] or EAU recommendations [60], is now strongly recommended. Using this approach, complication rates for RARC vary between 34% and 80% [61–64]. For example, a multi-institutional database of 939 patients reported a total complication rate of 41% at 30 d and 48% at 90 d [58]. Overall, 52% of patients did not have a complication (Clavien grade 0); 29% of complications were grades 1–2; and 19% were grades 3–5 [58]. Most types of complications were GI (27%), infectious (23%), and genitourinary (17%) [58]. The PCP systematic review of reports comparing major complications for RARC with ORC found significantly lower rates for RARC at both 30 d (40 total events for RARC across 6 studies vs 80 events for ORC; odds ratio [OR]: 0.64) and at 90 d (55 total events across 4 studies for RARC vs 93 events for ORC; OR: 0.54) [6]. Other series of experienced surgeons found rates of high-grade complications with RARC equal to or higher than those reported from ORC series [25]. All of these retrospective series may be affected by selection bias.

Most recently, Bochner et al conducted a prospective RCT comparing ORC with RARC, both with reconstruction performed extracorporeally [65]. The authors powered this study assuming RARC would lower grade 2–5 perioperative complications by  $\geq 20\%$  and shorter LOS. The trial was closed before full recruitment when a planned interim analysis found no difference in 90-d grade 2–5 complications. In the 118 randomized patients, 90-d complications were similar (ORC = 66% vs RARC = 62%; 95% confidence interval [CI], –21 to 13;  $p = 0.7$ ) according to intention to treat [65]. The authors concluded that although EBL was decreased, operative time was longer and LOS was unchanged. RARC provided similar pathologic outcomes compared with ORC, and HRQoL measures at 3 and 6 mo postoperatively failed to demonstrate a benefit of RARC over conventional open surgery [65].

**3.4.1.1. Blood loss and transfusion rates.** The PCP systematic review found that mean EBL during surgery was lower for

RARC than for ORC (weighted mean difference [WMD]: 568 ml; 95% CI, 405–730 ml;  $p < 0.00001$ ).

Comparative transfusion rates have been reported for RARC and ORC in only one RCT. This study found nonsignificantly lower transfusion rates for RARC (8 transfusion events of 20 cases for RARC vs 10 of 20 for ORC) [66]. The PCP systematic review of 14 nonrandomized studies, however, found a highly significant difference in transfusion events favoring RARC: 126 events among 654 cases for RARC versus 428 events among 775 cases for ORC [6].

**3.4.1.2. Intraoperative complications.** The PCP systematic review found no statistically significant differences in the rates of intraoperative complications for RARC compared with ORC across four comparative studies (total complications: 6 events of 235 cases for RARC vs 2 events of 116 cases for ORC;  $p = 0.65$ ) [6].

### 3.4.2. Operative time

The PCP systematic review of 20 studies found that mean operative times were longer for RARC than for ORC (WMD: 78.3 min; 95% CI, 48.7–107.9 min;  $p < 0.00001$ ) [6]. As with open surgery, the PCP agreed that operative times with RARC are surgeon and experience driven.

### 3.4.3. Bowel function

An analysis of six series reports of RARC found mean times to flatus ranging from 1.9 to 3.4 d, with a mean of 2.5 d [6]. Three comparative studies of mean time to flatus found shorter times for RARC compared with ORC (2.1 d vs 2.9 d [67]; 2.3 d vs 3.2 d [68]; and 4.3 d vs 5.9 d [69]).

An analysis of six series reports of RARC found mean times to first bowel movement ranging from 2.6 d to 4 d, with a mean of 3.1 d [6]. Three comparative studies of mean time to bowel movement found shorter, or equal, rates for RARC compared with ORC (2.8 d vs 3.8 d [67]; 3.2 d vs 4.3 d [68]; and 2.3 d for both RARC and ORC [70]). Similar figures have been reported in ORC series adopting enhanced recovery protocols [71].

### 3.4.4. Length of hospital stay

Data on LOS following RC can be difficult to interpret because LOS is often driven more by institutional, insurance, or government policies than by actual patient morbidity. The PCP systematic review found wide variations in mean LOS, with average hospital stay duration slightly shorter following RARC (WMD: 1.2 d; CI, –0.43 to –2.08;  $p = 0.03$ ) [6]. Bochner et al, however, found no difference in LOS between RARC and ORC patients (8 d for each) [65].

### 3.4.5. Mortality

The PCP systematic review found similar mortality rates for RARC compared with ORC at both 30 d (two deaths across six comparative studies in 248 RARC patients vs nine deaths in 313 ORC patients;  $p = 0.18$ ) and at 90 d (two deaths across three comparative studies in 218 RARC patients vs nine deaths in 308 ORC patients;  $p = 0.23$ ) [6].

**Table 4 – Recurrence-free specific survival: robot-assisted radical cystectomy series**

Reference	Cases, no.	Study design	Follow-up, mo	Neoadjuvant chemotherapy, %	Adjuvant therapy, %	RFS estimates, %		
						1 yr	3 yr	5 yr
Murphy et al, 2008 [75]	23	Retrospective	17	29	NA	91 <sup>*</sup>	–	–
Josephson et al, 2010 [76]	58	Retrospective	12	22	NA	–	76 <sup>**</sup>	–
Kang et al, 2010 [77]	104	Retrospective	12	NA	NA	96	–	–
Kauffman et al, 2010 [62]	85	Retrospective	18	20	12	79	73 <sup>**</sup>	–
Martin et al, 2010 [78]	59	Retrospective	21	17	NA	82	71	–
Canda et al, 2012 [79]	27	Not reported	6	NA	4	85 <sup>***</sup>	–	–
Mmeje et al, 2013 [80]	50	Multi-institutional	41.5	12	46	–	43	39
Tyritzis et al, 2013 [82]	70	Prospective	30.3	24	NA	–	81 <sup>**</sup>	–
Xylinas et al, 2013 [81]	175	Retrospective	37	NA	19	–	67	63
Raza et al, 2014 [72]	99	Retrospective	30.9	6	29	74	55	52
Yuh et al, 2014 [73]	162	Retrospective	52	23	9	–	76	74

NA = not available; RFS = recurrence-free survival.

<sup>\*</sup> 17 mo.

<sup>\*\*</sup> 24 mo.

<sup>\*\*\*</sup> 6 mo.

### 3.4.6. Oncologic outcomes

Limited evidence from a few RARC surgical series from high-volume centers reporting data at follow-up duration of about 5 yr suggests that RARC and ORC are similar in terms of early to intermediate-range safety and oncologic outcomes [72–74]. RARC recurrence-free survival rates (which are more specific and relevant than overall survival rates) across studies range from 74% to 96% at 1 yr to 39–74% at 5 yr that compare favorably with similar rates for ORC (Table 4). No evidence exists for any significant risk of port-site metastases.

### 3.4.7. Lymph node dissection and yields

The PCP systematic review found that LNY was similar in RARC and ORC (WMD: 2.94 nodes; 95% CI, –0.28 to 6.1;  $p = 0.80$ ) [7]. The eLND was shown to be feasible with robotic assistance, although operative times were significantly longer compared with standard LND, for example, mean operative times of 44 min for standard LND [83] compared with a mean of 107 min for eLND in a study by Lavery et al [84] and a mean of 117 min in a study by Davis et al [85].

### 3.4.8. Positive surgical margins

PSM rates in ORC are 6.3% overall but vary significantly with stage (see sect. 3.2.5) [47]. In comparative studies, overall PSM rates following RARC were 4.8% compared with 6.7% in ORC (OR: 0.71; 95% CI, 0.46–1.08;  $p = 0.11$ ), indicating a similarity between RARC and ORC [86]. Looking at RARC series, as far as it can be assessed from the limited available evidence, PSM in pT2 (about 2%) and pT3 cancers (about 8%) seem similar to those reported in ORC series [87]. Conversely, the PSM rate in pT4 cancers among RARC patients (18 of 46 patients included in the analysis) was 39%, which is significantly higher than the 24% reported in similar multicenter ORC series [46,47].

### 3.4.9. Functional outcomes

Data on functional outcomes (eg, continence and sexual function) associated with RARC are limited to a few surgical series, suggesting results at least comparable with ORC,

although case numbers tend to be small, studies are retrospective, and definitions of key terms such as *potency* are often variable or are not provided. Hence these conclusions must be considered tentative [82].

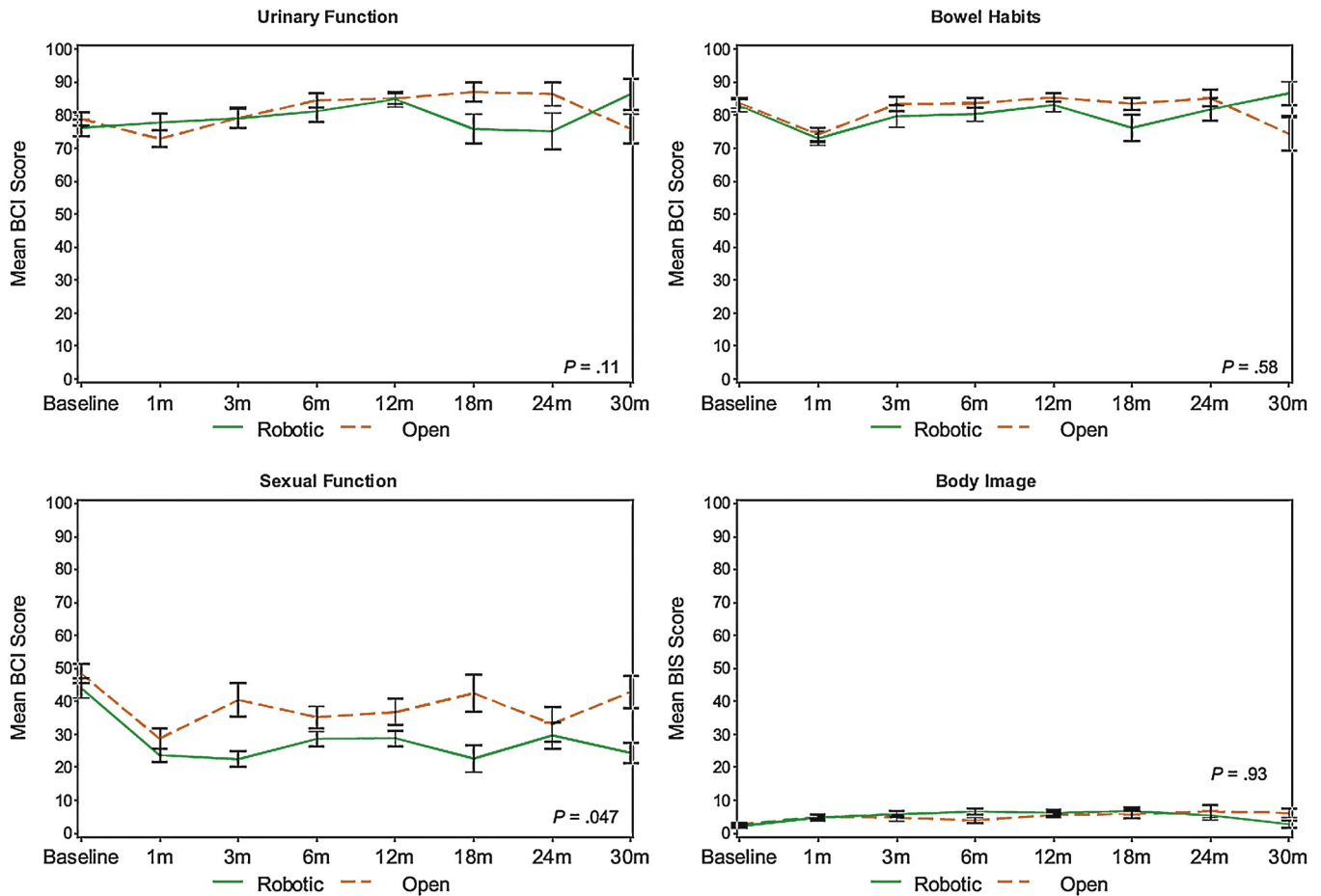
Aboumohamed et al found no significant differences in urinary function, sexual function, body image, and bowel habits between RARC and ORC procedures (Fig. 1) [87]. This retrospective study evaluated HRQoL using the validated bladder-specific Bladder Cancer Index and European Organization for Research and Treatment of Cancer Body Image scale in 82 patients who underwent RARC and 100 patients who underwent ORC. All patients underwent ileal conduit diversion. The two surgical approaches were performed at two separate institutions. Baseline urinary, bowel, sexual function, and body image measures were not different between the two groups [87]. Significantly, comparisons regarding reconstruction techniques showed similar findings at baseline and postoperatively on HRQoL data, with no significant differences in the HRQoL and body image domains but significantly better sexual function in the ORC group [87].

Some series have suggested an advantage of nerve-sparing procedures for open and robotic cystoprostatectomy with neobladder. Daytime continence was 83% in patients without nerve sparing versus 94% in patients with nerve sparing, and nighttime continence was 59% in patients without nerve sparing versus 75% in patients with nerve sparing ( $p < 0.002$  for both comparisons) [49]. Data for sexual function show similar advantages for nerve-sparing procedures. A study comparing 41 men with nerve-sparing RARC and 21 men with non-nerve-sparing RARC found significant benefits for the nerve-sparing procedure, although overall levels of sexual functioning were relatively low [82]. Both of these series were nonrandomized and likely affected by selection bias.

### 3.4.10. Complications of intracorporeal versus extracorporeal urinary reconstruction

Ahmed et al analyzed complications arising from intracorporeal and extracorporeal reconstructions and found more





**Fig. 1** – Comparison of robot-assisted radical cystectomy (RARC) and open radical cystectomy (ORC) quality-of-life data using the Bladder Cancer Index (BCI) questionnaire. Retrospective series of male patients undergoing cystectomy and ileal conduit from two separate institutions (82 patients RARC; 100 patients ORC). Reprinted from *Urology*, vol. 83, Aboumohamed AA, Raza SJ, Al-Daghmin A, et al, Health-related quality of life outcomes after robot-assisted and open radical cystectomy using a validated bladder-specific Instrument: a multi-institutional study, 1300–8 (2014), with permission from Elsevier [87]. BCI = Bladder Cancer Index; ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy.

GI and infectious complications with ECUD and a 32% lower risk of complications with ICUD (OR: 0.68; 95% CI, 0.50–0.94;  $p = 0.02$ ) [88]. Note, however, that only 167 patients in this series of 935 patients underwent ICUD, and the vast majority of these had ileal conduit diversion. Furthermore, this complicated surgical procedure involves a significant learning curve.

3.4.11. Surgeon ergonomic outcomes

Surgery, particularly standard laparoscopy procedures, can be physically demanding on surgeons, who frequently describe neck, back, and shoulder fatigue as well as various types of chronic pain [89]. Robot-assisted surgeries, in contrast, are associated with a significant reduction in neuromuscular pain in the shoulders and back and reduced overall physical demands [90]. Current robot models used in RARC allow a seated position for the surgeon, with adjustable supports for forehead, arms, and feet. These ergonomic supports effectively relieve the back and shoulders while maintaining sufficient mobility of the forearms and wrists to manipulate the master controls with minimal strain. It has been suggested that the rapidly

increasing use of robot-assisted laparoscopic surgery can be attributed in part to the benefits these devices confer to the surgeons who perform these complicated surgeries [90].

3.4.12. Economic considerations

Ongoing pressures to contain costs at all levels of health care systems globally, combined with the fact that bladder cancer incurs the highest treatment costs per patient of all cancers [91], mean that examining the cost effectiveness of technologies such as RARC is critical. Unfortunately, calculating cost effectiveness is complex because it must take into account highly variable costs related to physician salaries, hospital costs, laboratory testing, medications, loss of productivity, and rehospitalization costs. Also complicating an accurate assessment are cost variations related to the type of urinary reconstruction performed. For example, a 2011 study by Lee et al found that RARC was more cost efficient when performed with ileal conduits but that the cost benefit diminished when continent cutaneous reconstruction was performed and that RARC became less cost effective when orthotopic neobladders were used [92].

The largest study to date evaluating cost data is by Leow et al, who conducted a retrospective cohort study comparing 34 672 ORC patients with 2010 RARC patients [5]. This study found that RARC was \$4326 more expensive per procedure than ORC, even without accounting for the costs associated with purchase, installation, training, and setup of the robotic system itself [5]. Supplies specific to robotic surgery appeared to be the major contributor to the high cost for RARC. Costs in this study varied across institutions, with the disparities between RARC and ORC less pronounced in high-volume centers.

The authors speculate that the relative parity in costs among the highest volume providers may reflect the fact that surgeons in such centers are further along their learning curves or that these centers use streamlined postoperative care pathways that both improve outcomes and lower costs [5]. Significantly, the authors found that the slightly lower LOS for RARC patients did not translate into cost savings because costs tend to be front-loaded and follow a nonlinear pattern [5]. The cost figures in Leow et al, however, do not take into account potential differences in convalescence length or oncologic outcomes between RARC and ORC, which may affect overall cost differences [5].

#### 3.4.13. Key consensus recommendations

The following recommendations are made with regard to outcomes related to RARC outcomes:

- The key variable driving surgical and postsurgical outcomes is the skill and experience of the surgeon or surgical team, regardless of whether or not robot assistance is used.
- Reports of complications following RC and urinary reconstruction should use standardized criteria and be assessed from the intraoperative period until at least 3 mo postoperatively. Follow-up should be meticulous and include complications occurring outside of the home institution.
- RARC and ORC are comparable in terms of overall complication rates, rates of PSMs, LNYs, and intermediate-term oncologic outcomes. The lack of longer term studies limit the ability to assess the cancer-specific outcomes following RARC at 10-yr follow-up.
- Rates of EBL during surgery and need for transfusions are lower with RARC than with ORC. Other complications and LOS may not be decreased.
- Extended and highly extended robotic LNDs are feasible and should be performed, even though they add to overall operative time.
- Nerve-sparing procedures (whether RARC or ORC) may result in more favorable functional outcomes and should be pursued in appropriate patients.
- Hospital costs of RARC appear to be significantly higher than for ORC, although a complete accounting of costs associated with these surgeries has not been completed.
- Well-controlled cost-effectiveness studies are urgently needed, with the preferred method of cost analysis being quality-adjusted life expectancy in relation to total costs

of treatment, and using an incremental cost-effectiveness ratio as the key outcome measure.

#### 3.5. Research needs and priorities

As a surgical discipline, RARC is less mature than some other areas, such as RARP, hence there is a need for more high-quality research on the following topics:

- Routine and regular use of validated questionnaires for RC-specific HRQoL with particular emphasis on stoma complications such as leakage, skin problems, and stoma bandaging, and continence issues such as nighttime leakage and need for intermittent catheterization in patients with orthotopic neobladder
- Studies comparing HRQoL outcomes in RARC and ORC that capture early and long-term changes in QoL
- Postoperative pain levels in patients undergoing RARC compared with ORC and whether pain management protocols (eg, use of epidurals or PCA) differ with surgical techniques used
- Comparative outcome studies of ECUD versus ICUD
- Functional outcomes (eg, continence, erectile and sexual function) between RARC and ORC and between the different types and techniques of urinary reconstruction
- Longer term research on recurrence-free survival and cancer-specific survival in RARC compared with ORC
- Longer term and more thorough cost-effectiveness studies comparing RARC and ORC
- Prospective studies assessing the value of strict application of ERAS principles in the RARC setting.

#### 4. Conclusions

Robot-assisted techniques are increasingly used for RC and urinary reconstruction. This paper summarized existing data using a current set of systematic literature reviews and presented recommendations from an international panel of leading surgeons. RARC appears to be broadly equivalent to ORC in terms of morbidity and mortality, oncologic outcomes, and complication rates. RARC appears to result in less EBL and a reduced need for transfusion during surgery, and it provides ergonomic value for surgeons, but operative times tend to be longer for RARC than ORC (particularly early in the learning curve or with intracorporeal reconstruction), and, overall, RARC appears to be significantly more expensive than ORC, particularly in low-volume centers. Nonetheless, RARC is a viable alternative to ORC if performed by experienced surgeons in high-volume centers. Further research is needed on a range of issues that may help guide future clinical and policy decisions about this increasingly used surgical modality.

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