Open versus robotic cystectomy: Comparison of outcomes

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Open radical cystectomy (ORC) is the current gold standard treatment for muscle invasive bladder cancer. As surgeons become more proficient in minimally invasive and robotic surgical techniques, the number of patients undergoing robotic-assisted radical cystectomy (RARC) is increasing. Although minimally invasive methods are on the rise, research that critically compares open surgery with robotic methods is limited. In this review, we surveyed and appraised the current literature comparing ORC and RARC with regards to perioperative, functional, and oncologic outcomes in order to distinguish the benefits and disadvantages of each method. Here we report that RARC is associated with several perioperative advantages over ORC such as lower estimated blood loss and transfusion rate, and possibly faster gastrointestinal recovery, lower narcotic requirement, and shorter length of stay. ORC is less costly and permits less time in the operating room. Recent data suggests that there is no difference between ORC and RARC when comparing urinary continence and postoperative quality of life. Moreover, ORC and RARC are both associated with similar rates of obtaining positive surgical margins, lymph node yield, and recurrence. However, RARC patients had an increased likelihood of having distant metastases to extrapelvic lymph nodes and the peritoneum. At this point, it is unclear if ORC or RARC has superior patient outcomes, and more research is needed to ascertain management-altering conclusions.

Keywords: Cystectomy; Outcome assessment; Robotic surgical procedures; Urinary bladder neoplasms; Urinary diversion

INTRODUCTION

Bladder cancer is the ninth most common type of cancer, with an estimated 430,000 new cases diagnosed each year [1]. For patients with muscle invasive or high-risk nonmuscle invasive bladder cancer, radical cystectomy (RC) is traditionally the hallmark of treatment [2,3]. Between 2003 and 2010, 49,540 patients underwent RC [4] with open radical cystectomy (ORC) currently regarded as the gold standard. However, as more surgeons become proficient in minimally invasive surgery (MIS) techniques, robotic-assisted radical cystectomy (RARC) is increasing in popularity. From 2004 to 2010, the number of RARCs increased from 0.6% to 12.8%, highlighting that trend [3,5].

Several reports have suggested numerous advantages of RARC over ORC, including lower estimated blood loss (EBL) and shorter length of hospital stay [6]. However, it remains unclear if there is a difference between ORC and RARC for perioperative factors, postoperative complications, total costs, morbidity and mortality, quality of life and oncologic
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As the number of urologists trained in robotic surgery increases, it is important to distinguish the advantages and disadvantages between ORC and RARC to improve patient-important outcomes and maximize patient satisfaction. In this nonsystematic review of the literature, we critically analyze and compare perioperative, functional, and oncologic outcomes between open and RARC.

METHODS

We identified articles for this nonsystematic review in PubMed, Google Scholar, and Embase during January 2016. All authors used the search terms “open versus robotic radical cystectomy” and “radical cystectomy.” We did not set a restricted range for publication date. Articles were excluded from our review if they were not published in English or if they were unavailable for viewing in PubMed, Google Scholar, or Embase. Together, the authors considered the most relevant articles for inclusion. We ultimately selected studies that focused on surgical, oncologic, and quality of life outcomes as well as total procedural costs. In this review, we summarize and evaluate these articles.

PERIOPERATIVE FACTORS

A minimally invasive surgical approach to several urologic organs has consistently demonstrated perioperative benefits over an open approach, including superior outcomes with respect to EBL, length of stay (LOS), narcotic requirements, and transfusion rates [7,8]. By extension, the chief purported benefits of RARC over ORC are also thought to involve the perioperative period.

The majority of the comparative literature of RARC versus ORC is based on retrospective, single-center series of consecutive cystectomy patients. A recent systematic review and meta-analysis was conducted by Novara et al. [9] and identified comparative studies of RARC versus ORC through the year 2014. Of note, there are four prospective, randomized trials (RCTs) in the literature comparing RARC to ORC, two of which were published after the meta-analysis by Novara et al. (Table 1) [6,10-12].

1. Blood loss and LOS

With respect to blood loss, Novara et al. [9] determined that the weighted mean difference in EBL was 521 mL less for RARC compared to ORC (95% confidence interval [CI], −644 to −399; p<0.00001), while the odds ratio for transfusion requirements was 0.16, indicating that RARC patients are less likely to receive a transfusion (95% CI, 0.1 to 0.27; p<0.00001). Similarly, three of four RCTs found that EBL was significantly less in the RARC arm [6,10,12]. These findings can be attributed to the hemostatic effects of pneumoperitoneum in RARC and the absence of a large abdominal incision. Moreover, these benefits may have, in part, translated into a reduction in the mean LOS, as RARC patients stayed in the hospital 1.26 days less than their ORC counterparts (95% CI, −2.08 to −0.43; p=0.003) in a cumulative analysis by Novara et al. [9]. This finding, however, may reflect a selection bias in the various retrospective series included in the meta-analysis, as all four RCTs found no difference in LOS between groups. Parekh et al. [6], however, in their RCT of 40 consecutive patients did report a nonsignificant trend (p=0.11) towards decreased length of extended stay (>5 days) in the RARC group.

Table 1. Perioperative and intraoperative parameters among RCTs comparing RARC vs. ORC

| Source                  | No. of patients | Mean/median operative time (min) | EBL (mL) | Transfusion rate (%) | Intraoperative complications (%) |
|-------------------------|----------------|---------------------------------|----------|----------------------|---------------------------------|
| Nix et al. [10], 2010   | 21 RARC        | 252                             | 258      | -                    | -                               |
|                         | 20 ORC         | 211*                            | 575*     | -                    | -                               |
| Bochner et al. [12], 2015 | 60 RARC       | 456                             | 516      | -                    | 5.0                             |
|                         | 58 ORC         | 329*                            | 676*     | -                    | 5.2                             |
| Parekh et al. [6], 2013 | 20 RARC        | 300                             | 400      | 40                   | -                               |
|                         | 19 ORC         | 285.5                           | 800*     | 50                   | -                               |
| Khan et al. [11], 2016  | 20 RARC        | 389                             | 585      | -                    | -                               |
|                         | 20 ORC         | 293*                            | 808      | -                    | -                               |

Comparison between four randomized control trials (RCTs) between perioperative and intraoperative factors during open radical cystectomy (ORC) or robotic-assisted radical cystectomy (RARC). Patients were analyzed for the mean operative time, estimated blood loss, transfusion rate as well as intraoperative complications.

EBL, estimated blood loss.

*Statistically significant, p<0.05.
2. Narcotic requirements and bowel function

Gastrointestinal and pain outcomes are described by only a few level I evidence studies. Nix et al. [10] conducted a prospective, RCT of 41 patients undergoing cystectomy (21 RARC, 20 ORC). They found that the RARC cohort had a shorter time to both flatus (p=0.001) and bowel movement (p=0.001) and used less morphine equivalents (89 mg) compared to the ORC group (147 mg, p=0.019). Conversely, Parekh et al. [6] found no difference in median days to diet between RARC (4 days) and ORC (5.5 days, p=0.5). Khan et al. [11], meanwhile, found that the time to solids was faster in their RCT of RARC versus ORC (4.0 days vs. 7.5 days, p=0.049), but that time to flatus was not statistically different (36 days vs. 37 days, p=0.3). Knox et al. [13] in a retrospective analysis of 142 cystectomy patients reported a shorter mean time to flatus (4.3 days vs. 5.9 days, p=0.028) and regular diet (5.4 days vs. 8.1 days, p=0.009) in their RARC cohort. The current literature consensus is that RARC may afford some improvement in gastrointestinal recovery, though additional studies are needed for more definitive conclusions.

3. Operative time

Although RARC has certain advantages compared to ORC, including those outlined above, there are several perioperative drawbacks to this approach. One of the chief disadvantages to RARC is the increased operative time compared to ORC. Novara et al. [9] reported a weighted mean difference of 836 minutes (95% CI, 570.6–1101.4; p<0.00001) for operative time, favoring ORC as a faster operation. Moreover, three of the four RCTs also support this finding [10–12]. These results are somewhat expected, as a robotic approach requires docking, more complex patient positioning, and is associated with certain surgical factors such as laparoscopic suturing that are inherently slower. While ORC is a faster operation, intraoperative complications differed between RARC and ORC in neither the meta-analysis nor in the RCTs with data available on intraoperative complications [11].

4. Postoperative complications

Postoperative complications after RARC and ORC are well documented; all four RCTs report postoperative complications. Nix et al. [10] found no significant difference in the rate of overall complications or the median Clavien-Dindo grade of complications between their two cohorts in the perioperative period. Khan et al. [11] performed a RCT with 20, 19, and 15 patients in the ORC, RARC, and laparoscopic cystectomy arms, respectively, and found no significant difference between groups with respect to both 30- and 90-day overall and major (Clavien-Dindo grade≥III) complications. Similarly, Bochner et al. [12] randomized 118 patients to RARC (60 patients) or ORC (58 patients) and failed to find a difference between groups in overall 90-day Clavien-Dindo grade II–V complications (62% vs. 66%, respectively; p=0.7) and in major complications (13% vs. 12%, respectively; p=0.9). Finally, Parekh et al. [6] found no difference in Clavien-Dindo grade II–V complications, as 25% of patients in both groups experienced a complication in the perioperative period (p=0.5) (Table 2). Of note, while all the RCTs found no differences in postoperative complications, Novara et al. [9] did report that RARC had a lower 90-day complication rate of any-grade and 90-day grade III complication rate (p<0.04). These findings may reflect the fact that several RCTs did not report Clavien-Dindo grade I complications, as their clinical significance is minor. Moreover, Novara et al. [9] also found that high-grade 90-day complication (p=0.06) and mortality (p=0.23) rates were not significantly different, suggesting that the complications with greatest clinical impact are not different based on the approach. Similar to postoperative complication rates, multiple studies demonstrated that readmission is common (e.g., Styn et al.: 28% [RARC] vs. 20% [ORC] readmission rates, p=0.25) but found no difference in the readmission rates between RARC and ORC cohorts [14,15]. A final point worth mentioning is that the majority of comparative series in the literature included an extracorporeal approach to urinary diversion. Small initial series show no significant difference in outcomes between the two diversion techniques, but until more robust data is published it has yet to be determined how this will affect the complication rates [16]. Overall, there is no significant advantage to either approach with respect to improvements in postoperative complications or readmission rates.

5. Cost

Cost of a surgery is an important metric to both hospitals and patients alike. Leow et al. [4] in a propensity-matched comparison of 34,672 ORC and 2,101 RARC patients showed that RARC was $4,326 costlier with respect to adjusted 90-day direct costs (p=0.004), which was mostly attributed to a higher supply cost ($6,041 vs. $3,638; p<0.0001). Similarly, an analysis of the US Nationwide Inpatient Sample showed that RARC was $3,797 more expensive than ORC (p=0.023) [17]. At an institution level, Smith et al. [18] demonstrated that RARC costs on average $1,640 more than ORC based on a financial analysis of 20 cases.

In short, the current literature supports the notion that
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RARC affords superior perioperative outcomes in terms of blood loss and transfusion rate. Some evidence also suggests a benefit with respect to gastrointestinal recovery, narcotic requirements and LOS, though additional study is needed for more definitive conclusions. These benefits come at the expense of increased operative times and cost. Equivalence is noted between the two approaches with respect to intraoperative complications, which are rare, and postoperative complications and readmissions, which are common.

FUNCTIONAL OUTCOMES

1. Urinary continence

Urinary continence after RC plays a direct role in patient satisfaction. Unfortunately, there are limited studies directly comparing urinary continence rates directly between patients who have undergone ORC versus RARC. There are, however, several retrospective studies evaluating continence rates postoperatively for each ORC and RARC, but varying definitions of continence and variable degrees of follow-up make direct comparisons difficult.

In a retrospective, nonsystematic review by Steers [19], 2,238 patients were evaluated for urinary continence after ORC with orthotopic neobladder for an average follow-up of 26±18 months. They found daytime incontinence rates of 13.3%±13.6% and nighttime incontinence rates of 28% (range, 0%–67%). They suggest that incontinence is largely related to the initial lack of neobladder functional capacity and, over time, as the neobladder functional capacity improves, the continence rates gradually improve. In a retrospective study by Steven and Poulsen [20], 166 patients who underwent ORC with an orthotopic neobladder at a single institution were evaluated for continence over a 5-year period. Daytime continence was assessed objectively by weight of pads while nighttime continence was objectively assessed as dryness without the need for protection. The daytime continence rates ranged from 87% to 100% while nighttime continence rates ranged from 70% to 95%. The study also established that continence rates improve with time, as the daytime continence rate improved from 74% at 6 months to 81.1% and 97.4% at 1 and 5 years, respectively. Nighttime continence rate also improved over time with 40.5% of patients wearing no pad at night at 3 years compared to only 22.8% at 6 months.

Similar studies have been conducted for continence rates after RARC. In a systematic review by Yuh et al. [21], the daytime continence rates range from 40% to 100% over 6 months and 67% to 100% at 12 months. Tyriritizis et
al. [22] reported in a retrospective study of 70 patients, who underwent an orthotopic neobladder, a daytime continence rate of 66% to 88% at 12 months. Nighttime continence appears to have a greater variability, with a range of approximately 11% in a single institution case series of 27 patients by Canda et al. [23] to 66%–81% in Tyriritizis et al. [22]. Of note, the 27 patients in Canda et al. [23], 2 patients had an ileal conduit while 25 underwent an orthotopic neobladder. In a recent retrospective study of 34 patients who underwent a continent cutaneous diversion, daytime and nighttime continence was determined to be 97% at 20-month follow-up [24].

In a more recent study by Satkunasivam et al. [25], continence rates were evaluated after 28 men underwent robotic intracorporeal orthotopic neobladder (iONB) and were compared to a previously characterized cohort of patients who underwent ORC with orthotopic neobladder (ONB). Complete continence rates, which was defined as pad-free, were similar in both the robotic and open cystectomy arms at 17% and 19% respectively (p=0.10). There was no significant difference in the number of pads used by patients in a 24-hour period; however, the robotic group reported use of larger pads during daytime (p<0.0001) and nighttime (p=0.007). There was also a higher degree of daytime pad wetness in the robotic iONB groups compared to the open ONB (p=0.002) with comparable wetness at night (p=0.01) [25]. Several limitations to the study are the retrospective nature, inclusion of only male patients, and relatively small number of patients.

In summary, there is a paucity of literature directly comparing continence rates after RARC to those after ORC. The data that is available often comes from small patient populations with a wide range of follow up and a lack of uniformity in the definition of continence. However, given the available data, it does appear that the continence rates after RARC are equivalent to the continence rates after ORC, regardless of diversion type.

2. Quality of life

Patients are beginning to preferentially choose minimally invasive surgical techniques that purportedly offer a better quality of life [3,4]. Several recent studies have evaluated the health related quality of life between patients undergoing both ORC and RARC. Satkunasivam et al. [25] retrospectively compared 28 men who underwent robotic iONB to a previously established cohort of 79 men who underwent ONB after ORC using 2 validated questionnaires, the Bladder Cancer Index (BCI) and the Short Form Health Survey (SF-36). The study found that there was no significant difference for the urinary function or the urinary bother domains between patients who underwent robotic iONB versus open ONB (p=0.58 and p=0.31, respectively). Overall, there was no significant difference in the mean BCI score and, after multivariate analysis, the technique for ONB construction was not independently associated with the overall BCI score. Several limitations exist for this study, as patients in the RARC arm were compared to a previously established ORC cohort who were enrolled in a clinical trial at the time of surgery, and there was a shorter follow-up time compared to the control arm. In a single center RCT by Khan et al. [11], the quality of life was compared between patients who underwent ORC versus RARC versus laparoscopic RC (LRC) using the Functional Assessment of Cancer Therapy-Bladder scale. Of the 53 of 59 patients who completed the questionnaire, there was no statistically significant difference in quality of life in ORC vs RARC vs LRC. Both of these studies demonstrate that there is no significant difference in the quality of life when comparing ORC vs RARC.

**ONCOLOGIC OUTCOMES**

In order to determine if there is an advantage of RARC over ORC, it is imperative to evaluate the efficacy of RARC in oncologic outcomes. While RARC is often touted for its perioperative benefits, oncologic control after cystectomy remains one of the most important outcomes. We examine RARC vs ORC with respect to positive surgical margins (PSMs), lymph node yields, recurrence rates, and survival outcomes.

1. Positive surgical margins

It has been shown that PSM after RC is an independent predictor of metastatic progression as well as decreased bladder cancer specific survival [3,26]. In an institutional study from Memorial Sloan Kettering Cancer Center by Dotan et al. [26], a PSM after ORC almost doubles the risk of metastatic progression in addition to nearly doubling the risk of bladder cancer death. Therefore, surgical margin status is an important factor in determining the oncologic efficacy of RARC compared to ORC.

In a prospective RCT by Nix et al. [10] the oncologic and pathologic outcomes were compared for ORC versus RARC in 41 patients. In this study, the rate of PSMs for both groups was zero, demonstrating the non-inferiority of RARC. Similarly, Parekh et al. [6] examined the oncologic efficacy of ORC vs RARC in a prospective RCT of 40 patients, with 20 patients each undergoing ORC or RARC, respectively. There
was one PSM patient in each group with both patients having pathologic T4 disease. Of note, 50% of the patients in the RARC cohort had pT3 disease, demonstrating that even with locally advanced disease, there was no significant difference in PSMs between RARC and ORC [10]. Yuh et al. [21] completed a systematic review of oncologic outcomes in 20 studies comparing RARC to ORC. Their analysis did not show any difference in PSM rates with 5% in RARC and 7% in ORC (p=0.3). In addition, Raza et al. [27] assessed the long term oncologic outcomes after RARC using the International Robotic Cystectomy Consortium database. This database included 702 patients from 11 institutions with ≥5-year follow-up. In this analysis, there was a PSM rate of 8% which is comparable to the PSM rate for ORC (0%–10%) [3,6,21,26,28]. A recent RCT published by Khan et al. [11] found that there was a rate of PSMs in 10% ORC, 15% RARC and 5% in LRC with no statistically significant relationship between the type of surgery and the surgical margin rate. Finally, in a retrospective review by Nguyen et al. [2], 383 consecutive patients underwent ORC (n=120) and RARC (n=263) and had a PSM rate of 13% and 6%, respectively (p=0.03). However, the authors contribute this finding to the unbalanced pathologic stage distribution with 20% of the ORC patients with pT4 disease while only 11% of the patients had pT4 disease in the RARC arm. In summary, there is a strong amount of evidence, including an RCT, that suggests that there is no difference in the PSM rate in RARC compared to ORC.

2. Lymph node yields

Lymphadenectomy demonstrates better oncologic control as well an increase in overall survival in patients undergoing RC [29-31]. Therefore, for equivalent oncologic outcomes, it is imperative for the lymph node (LN) yield to be similar in patients undergoing RARC compared to ORC.

In a prospective RCT, Nix et al. [10] demonstrated non-inferiority for LN yield for RARC compared to ORC on multivariate analysis. In this study, the LN yield for RARC was 1783 and 1914 for ORC (p=0.52). In another prospective RCT, Parekh et al. [6] demonstrated no significant difference between LN yields for RARC vs. ORC with an average of 11 LNs for RARC and 23 LNs for ORC (p=0.135). A retrospective study by Abaza et al. [32] demonstrated the ability to achieve similar LN yield in RARC (n=35) vs. ORC (n=120) if using the same dissection template. LN yield was 369±148 in ORC and 37.5±132 in RARC (p=0.68), demonstrating no significant difference in LN yield based on technique. In a systematic review of 20 studies by Yuh et al. [21], the rate of LN yield for RARC was 19 (range, 3–55), similar to the standard open template of LN dissection with an average yield of 18 LNs. In a RCT comparing LN yield in ORC versus RARC versus LRC, Khan et al. [11] found LN yields of 188, 163, and 155 in ORC, RARC, and LRC, respectively. There was no statistically significant difference in LN yield comparing ORC versus RARC, though there was a statistically significant difference between ORC and RARC. A retrospective study by Nguyen et al. [2] also showed similar LN yields in ORC vs. RARC with LN yields of 20 and 21 for ORC and RARC respectively (p=0.3). The oncologic benefits of lymphadenectomy during cystectomy are well documented, with increasing LN yield corresponding to improved overall survival [30,31]. Therefore, the ability to achieve similar LN yields in RARC compared to the gold standard of ORC is imperative. The recent data demonstrates that RARC achieves similar LN yields and is non-inferior to ORC in lymphadenectomy.

3. Recurrence rates and survival outcomes

Recurrence rates as well as disease specific and overall survival for patients who have undergone RARC are difficult to assess due to the relatively recent emergence and lack of long-term follow-up of this surgical approach. Five-year recurrence outcomes, for example, are just now beginning to be published for RARC. By contrast, ORC has relatively mature survival outcomes, with longer follow-up data.

Khan et al. [11] reported equivalent 12-month oncologic outcomes of disease recurrence, cancer-specific survival and overall survival between patients who underwent ORC versus RARC (p=0.5, p=0.1, and p=0.1, respectively). In a systematic review by Yuh et al. [21] in 2014, 18 series were assessed for survival outcomes after RARC. The mean follow-up for the series was 6–84 months though only 6 of the 18 series had mean follow-up>36 months. The recurrence free survival at 1, 2, 3, and 5 years was 79%–96%, 67%–81%, 67%–76%, and 53%–74%, respectively; cancer specific survival was 88%–94%, 75%–89%, 68%–83%, and 66%–80%, respectively; overall survival was 82%–90%, 54%–89%, 61%–80%, and 39%–66%, respectively. In a single institution review of 99 patients who underwent RARC, Raza et al. [27] reported a 5-year recurrence free survival of 53%, a 5-year cancer specific survival of 68% and an overall survival of 42% at median follow up of 73 months. These rates are similar to those seen in ORC with a 5-year recurrence free survival of 67%–68%; cancer specific survival 71%; overall survival 66% [3,26].

Nguyen et al. [2] reported oncologic outcomes and recurrence patterns for 383 consecutive patients who underwent
ORC (n=120) and RARC (n=263) at a single institution. This retrospective review found no statistical difference in the median time to recurrence after ORC (30 months) or RARC (23 months) (p=0.6). The study also demonstrated a similar number of local and distant recurrences within two years for patients who underwent ORC and RARC. For local recurrence, there was 15 of 65 (23%) in the ORC arm versus 24 of 136 (18%) in the RARC arm while for the distant recurrences, there was 26 of 73 (36%) for the ORC arm and 43 of 147 (29%) for the RARC arm [2]. However, interestingly, the study found that the sites of distant recurrences were different depending on the surgical technique. While the most frequent locations of distant recurrences were consistent across surgical technique, both extrapelvic lymph node (EPLN) locations and peritoneal carcinomatosis were more frequently found in RARC than ORC (23% vs. 15% for EPLN in RARC vs. ORC; 21% vs. 8% for peritoneal carcinomatosis in RARC and ORC respectively) [2]. Pathologic stage does not account for the differences in distribution as there was a higher proportion of patients with pT4 disease who underwent ORC compared to RARC. LN yield also does not contribute as there was no difference in LN yields across both techniques and all of the recurrences were outside of the extended pelvic lymph node dissection template. The authors suggest an alteration in the lymphatic dissemination or an effect of pneumoperitoneum as possible explanations for these phenomena. However, they do stress that the EPLNs were outside the extended pelvic lymph node template and the patients with peritoneal carcinomatosis had pathologic stage >T3 which could be a reflection of disease biology as opposed to surgical technique. Therefore, while the rate of recurrence does not appear to be dependent upon the surgical technique, there may be a predilection for distant metastases in the EPLNs and in the peritoneum for patients who have undergone RARC compared to ORC.

CONCLUSIONS

RARC is increasing in popularity, consistent with the rising trend towards MIS. Few studies have compared RARC to ORC with regards to perioperative, functional, and oncologic outcomes. Preliminary data suggests that RARC offers perioperative benefits over ORC, such as lower EBL and transfusion rates. In contrast, ORC is less expensive and associated with a shorter OR time. Recent studies have not shown a difference in continence and quality of life between RARC and ORC. In terms of oncologic outcomes, RARC appears to be noninferior to ORC with respect to negative surgical margins, LN yield, survival and recurrence rates. Patients undergoing RARC, however, may be more likely to have distant metastases in the EPLNs and peritoneum. Ultimately, as more surgeons are trained in robotic surgery, it is imperative to continue comparing RARC and ORC to provide the best patient care and satisfaction.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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