Radical Retropubic Prostatectomy: Comparison of the Open and Robotic Approaches for Treatment of Prostate Cancer

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Radical prostatectomy represents the standard of care for surgical treatment of clinically localized prostate cancer. First described in 1904, the operation became widely performed only after advances in diagnostic and surgical techniques occurred later in the century. Over time, open retropubic radical prostatectomy (RRP) became the most common operation for prostate cancer, and excellent long-term survival outcomes have been reported. More recently, minimally invasive techniques such as the robotic-assisted laparoscopic radical prostatectomy (RALRP) were introduced. Despite a lack of prospectively collected, long-term data supporting its use, RALRP has overtaken RRP as the most frequently performed prostate cancer operation in the United States. This article uses currently available data to compare oncologic, functional, and quality-of-life outcomes associated with both the open and robotic approaches to radical prostatectomy.

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KEY WORDS

Radical retropubic prostatectomy • Prostate cancer • Perioperative outcomes • Robotic-assisted laparoscopic radical prostatectomy

First performed over a century ago, radical prostatectomy was historically associated with significant morbidity and mortality.[1-3] The operation was performed for several years via a perineal approach, until the retropubic approach was introduced in 1948. In the 1980s, development of the nerve-sparing retropubic radical prostatectomy (RRP) [4] by Walsh and colleagues led to reductions in perioperative morbidity, incontinence, and erectile dysfunction.[5-7] RRP ultimately became the gold standard for treatment of prostate cancer.

A minimally invasive approach to prostatectomy was first described in the 1990s. Despite initial successes, laparoscopy proved too technically demanding to gain widespread acceptance.[8-10] The difficulties associated with laparoscopic prostate surgery, however, were greatly reduced when robotic systems became available. The first robotic-assisted laparoscopic radical prostatectomy (RALRP) was performed in 2000, and the procedure has grown in popularity ever since.[11,12]

The rapid growth of RALRP has generated controversy in light of the paucity of long-term follow-up data.[13] Although several large series have demonstrated long-term survival after RRP, similar data for RALRP are simply unavailable due to its recent introduction. Lepor[14] and Finkelstein and colleagues[15] have previously reviewed data comparing RRP and RALRP. Our objective herein is to present an updated review in light of its increased utilization and published data.

Methods

Using PubMed, we searched for original English language studies of RRP and RALRP published through January 2012, with an emphasis on recent data. To provide an inclusive listing of potential reports, the initial search term was *prostatectomy*. The resulting abstracts were evaluated and the most pertinent reports were included in our final assessment.

Within the selected literature, we first examined short-term perioperative outcomes, including perioperative mortality, operative complications, blood loss, transfusion requirements, postoperative pain, and length of hospital stay. In addition, we examined costs and the rates of incontinence and erectile dysfunction associated with each approach.

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Perioperative Outcomes

Perioperative Mortality

Contemporary RRP is associated with minimal risk of perioperative death, both in the United States and abroad.[16-18] In 2008, Gilbert and colleagues examined a 15-year interval within the Nationwide Inpatient Survey and reported a 0.2% perioperative mortality.[19] Similarly, a population-based study from Sweden reported a 30-day mortality rate of 0.11%.[20] Furthermore, studies of RRP have demonstrated minimal risk of mortality in high-risk patients. For example, Pierorazio and associates observed no perioperative mortalities in 386 patients aged 70 years or older.[21]

At the same time, existing data on RALRP reveal minimal risk of perioperative mortality.[22-24] One very large cohort of 2500 RALRP patients reported no perioperative deaths.[25] Perioperative mortality rates reported in smaller series are similarly low, with one institution reporting a single perioperative death in 239 patients (0.4%).[26] Based on consistently low perioperative mortality rates throughout the literature, radical prostatectomy is generally considered to present minimal risk of death, regardless of the surgical approach.

Operative Complications

Assessment of complication rates is limited by substantial disparities in measurement and reporting practices, often leading to a wide range of reported findings. Two population-based analyses provide some insight in this regard.[27,28] In one study, Hu and colleagues[27] assessed complication rates in a national 5% sample of Medicare beneficiaries from 2003 to 2005. After adjustment for age, race, comorbidity, geographic region, and surgeon volume, the overall perioperative complication

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rate was lower in minimally invasive radical prostatectomy (MIRP) as compared with RRP (odds ratio [OR] = 0.73; 95% confidence interval [CI], 0.60-0.90). However, the odds of anastomotic stricture was higher for MIRP (OR, 1.40; 95% CI, 1.04-1.87).

This group subsequently evaluated Medicare-linked Surveillance, Epidemiology, and End Results (SEER) data from 2003 to 2007.[28] In 8837 men, the unadjusted rate of overall complications was similar between MIRP (21.9%) and RRP (23.4%; $P = .31$). Propensity scores were then used to control for differences in age, race/ethnicity, income, education, region, population density, marital status, pathologic grade, and stage. After adjustment, the overall complication rates remained similar between the groups ($P = .58$). In contrast to their previous findings, this analysis revealed decreased odds of anastomotic stricture in those who underwent MIRP (OR, 0.38; $P < .001$). Notably, the definition of MIRP employed in these studies included traditional laparoscopy, although the vast majority of cases were in fact RALRP.

A more recent assessment by Trinh and colleagues compared outcomes after RRP and RALRP using the Nationwide Inpatient Sample.[29] In multivariate logistic regression analysis of populations matched by propensity score, patients who underwent RALRP were less likely to experience an intraoperative (OR 0.47; 95% CI, 0.31-0.71) or postoperative complication (OR 0.86; 95% CI, 0.77-0.96).

Blood Loss and Transfusions

A number of studies have demonstrated lower blood loss in RALRP. One comprehensive review reported blood loss ranging from 142 to 230 mL versus 790 to 820 mL in robotic and open series, respectively.[15] Similarly, a comparative study by Rocco and colleagues noted significant differences in median blood loss, favoring RALRP (200 vs 800; $P < .001$).[30] Despite observing a difference in total blood loss, Farnham and associates[31] found no significant difference in the need for transfusion after RALRP (0.5%) and RRP (2.9%; $P = .14$); notably, very few patients required transfusion in either group.

More recently, a 2010 study of 1244 patients found significantly lower blood loss and less decrease in hematocrit associated with RALRP.[32] Furthermore, transfusion was required in a significantly lower proportion of patients undergoing RALRP (0.8% vs 3.4%; $P = .002$). These findings were consistent with the 2009 study from Hu and colleagues, in which MIRP had a strong protective relationship against transfusion (OR 0.11; 95% CI, 0.06-0.17).[28] The recent findings of Trinh and associates also revealed that patients undergoing RALRP were significantly less likely to receive a blood transfusion (OR 0.34; 95% CI, 0.28-0.40).[29]

Length of Stay

Several studies have demonstrated shorter length of stay (LOS) after RALRP as compared with RRP. For example, Bolenz and colleagues observed mean LOS of 1.56 days for RALRP and 2.51 days for RRP, although formal statistical comparisons were not reported.[33] The SEER-linked Medicare data revealed median hospital stay of 2 days after MIRP versus 3 days after RRP (OR 0.67; 95% CI, 0.58-0.72),[28] and Rocco and associates reported median stay of 3 days for RALRP and 6 days for RRP.[30]

On the other hand, a study from Vanderbilt University (Nashville, TN)[34] reported equivalence between the approaches, with a mean LOS of 1.17 days after RALRP and 1.25 days after RRP ($P = .27$). This practice is in conjunction with current practice at Johns Hopkins University (Baltimore, MD), wherein patients are managed on the same clinical care pathway irrespective of surgical approach. The variation in LOS at different institutions may reflect differences in surgical volume, era, or patient characteristics.

Pain

It is often assumed that minimally invasive surgery is associated with less pain than conventional open procedures. Indeed, studies from robotic centers have consistently reported favorable pain scores.[35] Webster and colleagues compared postoperative pain in a radical prostatectomy population by measuring narcotic use and by self-assessment using a Likert scale.[36] Narcotic use was low in both the RALRP and RRP groups, and there was no significant difference between them. Although pain perception scores were low across the study population, scores were significantly lower in the RALRP cohort (2.05 vs 2.60; $P = .027$) on the day of surgery. However, equivalent pain scores were reported on postoperative days 1 (1.76 vs 1.73; $P = .88$) and 14 (2.51 vs 2.42; $P = .72$).

Narcotic use was low in both the RALRP and RRP groups, and there was no significant difference between them. Although pain perception scores were low across the study population, scores were significantly lower in the RALRP cohort (2.05 vs 2.60, P = .027) on the day of surgery.

Cost

In 2010, Bolenz and colleagues[33] directly compared the cost of

robotic, laparoscopic (LRP), and open prostatectomy in 643 consecutive patients (262 RALRP, 220 LRP, 161 RRP). Importantly, there were no significant differences in disease characteristics across the groups. Although mean LOS was shorter, the median cost of RALRP was significantly higher than LRP or RRP ($6752 vs $5687 vs $4437; $P < .001$). Considering the cost of purchase and maintenance of the robot, the use of RALRP increased costs by $2698 per patient (using a benchmark of 126 cases per year). Another study similarly estimated a cost advantage of $1726 for RRP as compared with RALRP.[37] Because a significant proportion of this cost relates to purchase and start-up of the robotic system, the financial burden of a single robotic operation decreases as operative volume increases. As such, one recent analysis demonstrated that costs equivalent to RRP may be achieved at high-volume centers performing 10 or more robotic procedures per week.[38]

Follow-Up Outcomes

Potency

Although the nerve-sparing procedure has led to improvements in potency, there remains significant variation in potency rates among surgeons and institutions.[39,40] Case mix is an important contributing factor because potency after radical prostatectomy has been strongly associated with patient characteristics, even after adjustment for baseline potency.[27] Thus, data on potency must be interpreted carefully in the context of patient-specific factors.

The 2009 study from Hu and colleagues reported 1.4 times greater odds of erectile dysfunction after RALRP (OR 1.40; 95% CI, 1.14-1.72) after adjustment for patient factors and stage of disease.[28] However, the literature has described a poor correlation between claims data and patient-reported assessments of functional outcomes,[41] suggesting that these findings should be interpreted with caution. More recently, Barry and associates addressed this limitation by comparing sexual function in Medicare patients using a patient survey.[42] Completed surveys were obtained from 685 (86%) of 797 eligible subjects at a median of 14 months after surgery. In logistic regression models adjusted for age and education, robotic prostatectomy was associated with similar odds of a moderate or big problem with sexual function (OR 0.87; 95% CI, 0.51-1.49).

In another study, Malcolm and colleagues[43] compared postoperative sexual function using the validated University of California, Los Angeles Prostate Cancer Index (UCLA-PCI). Over 3 years of follow-up, sexual function was slightly better in patients who underwent RRP, although formal statistical comparisons were not reported. In a direct comparison of subjects matched by patient and disease criteria, Krambeck and colleagues[44] reported a trend toward higher potency after RALRP, although it was not statistically significant (70% vs 62.8%; $P = .081$). Similarly, Di Perro and associates[45] reported greater recovery of erectile function after RALRP (55% vs 26%; $P = .009$), but this study began with only 150 patients and was limited by 41% attrition in the RALRP group. Overall, there is little evidence that potency outcomes are significantly impacted by surgical approach.

Continence

Several large series from the 1990s demonstrated restoration of continence in over 95% of patients after RRP,[46-48] and recent data from robotic series have revealed similarly high rates of continence. A few studies have reported significant differences in continence by approach, although there were notable limitations. For example, in the SEER-Medicare cohort, minimally invasive procedures were associated with a higher rate of incontinence than RRP (15.9 vs 12.2 per 100 person-years; $P = .02$).[28] Again, the drawbacks of using claims data for functional outcomes should be considered.[41] It is also notable that the overall incontinence rates are higher in this population compared with others. Meanwhile, Di Pierro and colleagues found higher continence rates at 3 months after RALRP ($P = .003$), although this difference was no longer significant after 1 year of follow-up ($P = .092$).[45]

Direct comparisons have failed to demonstrate significant differences in continence based on surgical approach. Notably, the overall rates of continence in comparative studies have varied greatly, likely due to differences in patient population and manner of data ascertainment. Based on postoperative surveys, Barry and colleagues found that 31.1% of Medicare patients reported a moderate or big problem with continence after prostatectomy. In multivariate models, men who responded that they underwent a robotic prostatectomy were more likely to report problems with continence.[42] Krambeck and associates reported continence rates in excess of 90%, and this cohort demonstrated no significant difference based on surgical approach (RALRP 91.8% vs RRP 93.7%; $P = .344$).[44] Similarly, using the UCLA-PCI, Malcolm and colleagues reported nearly equivalent urinary function scores between the two groups.[43]

Oncologic Control

Regardless of surgical approach, the primary goal of radical

prostatectomy is oncologic cure. Because prostate-specific antigen (PSA)-detected prostate cancers have a long natural history from presentation to death,[49] long-term data are needed to assess cancer-specific mortality.[50] Studies of RALRP, however, have limited follow-up, such that surrogate endpoints have been used to estimate cancer control. Here, we review oncologic outcomes based on three such endpoints (surgical margin status, biochemical recurrence, and need for salvage therapy), with the caveat that these measures are imperfect proxies for long-term survival outcomes.

Surgical Margin Status

Positive surgical margins (PSMs) are associated with increased risk of local and biochemical recurrence.[51-53] However, some studies have found that margin status is not independently associated with cancer-specific or overall mortality,[52] highlighting the limitations of evaluating this endpoint. Nonetheless, margin status is often used to provide a preliminary assessment of cancer control after prostatectomy.[54]

In 2007, Smith and colleagues[55] reported significantly lower PSM rates after RALRP as compared with RRP (15% vs 35%; $P < .001$). However, RALRP patients had more favorable pathological stage and Gleason score. In stratified analyses, significantly lower positive margin rates persisted for RALRP in patients with stage pT2 disease (9.4% vs 24.1%; $P = .001$) and a Gleason score ≤ 6 (9.0% vs 30%; $P < .001$), but differences were not significant in other strata. In 2009, Krambeck and associates frequency-matched 294 RALRP and 588 RRP men based on year of surgery, age, baseline PSA, clinical stage, and biopsy Gleason score.[44] Their analysis revealed no significant difference in positive margin rates based on surgical approach (RALRP, 15.6%; RRP, 17.0%; $P = .608$).

A more recent study limited its comparison to high-volume surgeons[56] in order to minimize confounding by surgeon experience. The RALRP and RRP groups had similar preoperative characteristics and disease burden in this study. Positive surgical margins were identified in 18% of RALRP and 16% of RRP cases (OR 1.30; 95% CI, 0.83-2.04; $P = .25$). A 2011 study by Magheli and colleagues examined 522 men who underwent RALRP and an equal number of men who underwent RRP and LRP,[57] using propensity scores to adjust for age, race, PSA, biopsy Gleason score, and clinical stage. Overall, they observed higher PSM rates after RALRP (19.5%) than RRP (14.4%) and LRP (13.0%; $P = .01$). When stratified by pathological stage of disease, this pattern persisted in T3 disease (RALRP 48.5%, RRP 32.1%, LRP 43.8%; $P = .013$) but was not statistically significant in the T2 group (RALRP 9.3%, RRP 6.6%, LRP 6.7%; $P = .264$).

Single-surgeon comparative studies may also provide value in comparing techniques that are affected by experience. A recent report from Masterson and colleagues examined margin status in 357 RRP and 669 RALRP performed by an experienced surgeon.[58] When stratified by stage of disease, the incidence of positive surgical margins did not differ based on surgical approach in men with organ-confined disease. Another recent study investigated 950 patients treated by a single surgeon between 2005 and 2008.[59] After adjustment for year of surgery, body mass index, use of nerve sparing, and age, RALRP patients were significantly more likely to have a positive surgical margin when compared with those who underwent open RRP (adjusted OR, 1.9; $P = .0095$). There was also a significant interaction between surgical approach and nerve-sparing status. With nerve sparing, the RALRP cohort had a higher rate of PSM than the RRP cohort (13.5% vs 7.6%; $P = .007$), despite a trend toward lower rates in the absence of nerve-sparing ($P = .09$). These findings suggested that cancer control and preservation of potency may be more difficult to attain simultaneously using the robotic approach.

Biochemical Recurrence

Preliminary observations of biochemical recurrence after RALRP demonstrated adequate short-term cancer control. However, data describing biochemical recurrence-free survival (BRFS) have been limited by follow-up. As such, few studies have attempted to compare this outcome directly.

One comparative study reported 3-year recurrence-free survival rates of 83.5% after RRP and 84.0% after RALRP ($P = .19$).[24] Accordingly, survival analysis showed no significant differences in BRFS when subjects were stratified by tumor stage, margin status, and pathological Gleason score. On multivariate analysis, BRFS was not significantly associated with surgical approach (RALRP vs RRP, hazard ratio [HR] 1.01; 95% CI, 0.72-1.41). Nevertheless, the median time to recurrence was 24 months but the median follow-up was only 10 months, which was likely insufficient to identify all patients who would eventually recur. Furthermore, follow-up after RRP was significantly longer than after RALRP (median 17 vs 8 months; $P < .01$).

Krambeck and colleagues also observed no significant difference in 3-year recurrence-free survival between RALRP (92.4%) and RRP (92.2%; $P = .69$), although this study was similarly limited by a

small number of patients with sufficient follow-up (median follow-up, 1.3 years).[44] In addition, the single-surgeon report from Masterson and colleagues demonstrated nearly identical rates of BRFS after 24 months (RRP 87% vs RALRP 87%) and 60 months (RRP 71% vs RALRP 73%) of follow-up ($P = .97$; log-rank test).[58] Other comparisons have suggested similar recurrence-free survival rates between treatment groups,[45,57] but these studies also have significant limitations. Additional follow-up should allow for a more definitive assessment of oncologic outcomes.

Need for Salvage Therapy

In 2008, Hu and colleagues reported re-treatment rates of 9.1% after RRP and 27.8% within 6 months after MIRP.[27] The adjusted OR for early secondary therapy was 3.67 for MIRP vs RRP (95% CI, 2.81-4.81). These findings suggested that MIRP may fail to achieve oncologic cure more frequently. In a subsequent study, these authors found that rates of additional cancer therapies did not differ by surgical approach (MIRP 8.2 vs RRP 6.9 per 100 person-years; $P = .35$).[28] Similarly, Lowrance and associates[60] found no difference in rate of salvage therapy based on surgical approach (LRP 9.2%, RRP 11.6%). It is worth noting that these studies were limited to older men, and additional therapy was assessed during only 1 year of follow-up.

Discussion

Any attempt to truly compare the open and robotic approaches must consider a large number of factors. On a most basic level, study methodology must be valid and consistent. Ideally, operations would be performed at a single institution with uniform surgical technique, grading of complications, and pathological assessment. Validated questionnaires should be used to assess functional outcomes such as potency and continence. Furthermore, consistent clinical criteria should be used for decision making, such as the need for transfusion and the appropriate time for discharge. One European group has designed a protocol to standardize the collection of such data,[61] but it may take several years until outcomes at these centers can be assessed.

Given the heterogeneity of patient populations, surgeon experience, clinical care pathways, and outcome reporting, comparisons of open and robotic prostatectomy have been difficult to perform and interpret. As has been pointed out, the majority of RALRP data have emerged from a small number of institutions and is not of high quality.[62] Although some smaller studies reveal significant differences based on surgical approach, reports from high-volume centers less frequently observed differences, with the exception of lower blood loss in RALRP. Similarly, at Johns Hopkins University all prostatectomy patients are treated according to the same clinical care pathway, with a similar postoperative course in uncomplicated cases. This observation raises the possibility that the robotic approach offers perioperative benefits to low-volume centers, but that such advantages diminish when surgeon experience and institutional volume are higher.

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Functional and quality-of-life outcomes generally appeared to be more heavily influenced by patient-specific factors than surgical approach. In the case of continence, both procedures frequently reported excellent results. The analysis of Hu and associates provides the strongest support in favor of RRP, as well as the largest volume of data.[28] However, it is difficult to draw definitive conclusions based on the nature of these data. On the other hand, comparative studies favoring RALRP[30,45] also have significant limitations. One significant concern is that patients undergoing robotic procedures may have greater, potentially unrealistic expectations of postoperative function.[63] In counseling these patients it is important to address any such perceptions that are not supported by the available data.

The superior approach for achieving oncological cure is ultimately unclear. From a conservative standpoint, the traditional open procedure should remain the standard of care, given there are long-term data supporting its effectiveness. Although recent observations from experienced robotic centers are encouraging,[64] longer follow-up, including diverse practice settings, is needed.

Conclusions

Most data suggest that, in the hands of an experienced surgeon, cure can be feasibly achieved with either an open or robotic approach to radical prostatectomy. Perhaps surgical approach is not a critical determinant of subsequent patient outcomes. On the other hand, in the current context of healthcare reform, existing data do not demonstrate an unambiguous improvement associated with RALRP to help justify its considerable increase in cost. Ultimately, the accrual of longer follow-up in contemporary

RALRP series, combined with additional comparative studies, will shed further light on this debate. ■

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MAIN POINTS

- The rapid growth of robotic-assisted laparoscopic radical prostatectomy (RALRP) has generated controversy in light of the minimal availability of long-term follow-up data. Although several large series have demonstrated excellent long-term survival after retropubic radical prostatectomy (RRP), similar data for RALRP are simply unavailable due to its recent introduction.
- Studies of RRP and RALRP have demonstrated minimal risk of perioperative mortality. Based on consistently low perioperative mortality rates throughout the literature, radical prostatectomy is generally considered to present minimal risk of death, regardless of the surgical approach.
- The majority of RALRP data has emerged from a small number of institutions and is not of high quality. Although some smaller studies reveal significant differences based on surgical approach, reports from high-volume centers less frequently observed differences, with the exception of lower blood loss in RALRP.
- Functional and quality-of-life outcomes generally appeared to be more heavily influenced by patient-specific factors than surgical approach. In the case of continence, both procedures frequently reported excellent results.
- The best approach for achieving oncological cure remains unclear. From a conservative standpoint, the traditional open procedure should remain the standard of care, given there are long-term data supporting its effectiveness. Although recent observations from experienced robotic centers are encouraging, longer follow-up, including diverse practice settings, is needed.

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