The impact of robotic surgery on pelvic lymph node dissection during radical prostatectomy for localized prostate cancer: the Brown University early robotic experience

Jennifer Yates, MD, George Haleblian, MD, Barry Stein, MD, Joseph Renzulli, MD, Gyan Pareek, MD

Department of Surgery, Division of Urology, Section of Minimally Invasive Urologic Surgery, The Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA

YATES J, HALEBLIAN G, STEIN B, RENZULLI J, PAREEK G. The impact of robotic surgery on pelvic lymph node dissection during radical prostatectomy for localized prostate cancer: the Brown University early robotic experience. The Canadian Journal of Urology. 2009;16(5):4842-4846.

Introduction: *Open pelvic lymph node dissection (PLND) remains the gold standard in patients with intermediate and high-risk prostate cancer undergoing radical retropubic prostatectomy (RRP). Recently, our institution has adopted robotic assistance for performing radical prostatectomy. We sought to determine whether robot-assisted laparoscopic PLND yields comparable numbers of lymph nodes compared to open PLND.*

Methods: *The medical records of patients undergoing open or robot-assisted laparoscopic radical prostatectomy (RALRP) with concurrent pelvic lymph node dissection (PLND) between 2003 and 2008 were reviewed. Demographic factors including age, PSA, and Gleason score were recorded. Pathology reports were reviewed to determine the number of pelvic lymph nodes obtained during PLND. Lymph node yield was further evaluated based on surgeon. Student's t-test was used to compare the number of lymph nodes obtained with each method.*

Results: *A total of 61 patients undergoing open RRP with PLND and 62 patients undergoing RALRP with PLND were included. The mean number of lymph nodes obtained via open PLND was 7.3 while the mean number obtained via robotic PLND was 3.3. These means were significantly different with a p value < 0.001. One patient in the open cohort (1.6%) and two patients in the robotic cohort (3.2%) had micrometastatic disease on PLND.*

Conclusion: *Robot-assisted laparoscopic PLND yielded fewer lymph nodes compared to open PLND at the time of radical prostatectomy for organ confined disease. Patients with higher risk disease may benefit from open prostatectomy with PLND early in a program's robotics experience. These findings may be related to the relative youth of our robotics program and further comparisons as our data mature will be revealing.*

Key Words: robotics, prostatectomy, prostate cancer, lymph nodes

Introduction

In 2009, an estimated 70% of radical prostatectomies will be performed utilizing the da Vinci robotic system. Because of the short period of time that the robotic technique has been in existence, interpretation of outcomes is limited by the lack of large clinical trials comparing robotic prostatectomy with traditional open radical retropubic prostatectomy (RRP). Oncologic outcome definitions differ by study, with some groups finding similar oncologic efficacy when defined as positive surgical margins,[1] and other groups concluding robot-assisted laparoscopic radical prostatectomy (RALRP) may have inferior outcomes if defined by

Accepted for publication July 2009

Address correspondence to Dr. Gyan Pareek, Department of Surgery/Division of Urology, Rhode Island Hospital, 2 Dudley Street, Suite 174, Providence, RI 02905 USA

the need for salvage therapy.[2] The diagnostic utility of pelvic lymph node dissection (PLND) at the time of radical prostatectomy (RP) for organ confined disease is accepted, although the therapeutic effectiveness remains uncertain. The lymph node yield of PLND in open RRP as well as pure laparoscopic RP has been studied, with the number of lymph nodes often used as a surrogate for oncologic efficacy. To our knowledge this parameter has not been well defined in the various published RALRP series. With the recent conversion of our prostate cancer program to the utilization of robotic assistance, we sought to study the impact of this paradigm shift on the number of lymph nodes retrieved during RALRP. Specifically, our goal was to utilize the data observed from this study to help counsel high-risk prostate cancer patients contemplating RALRP versus open RRP.

Materials and methods

Patients undergoing radical prostatectomy with concurrent open or robotic PLND within the last five years were identified (2003-2008). Surgeons performing radical prostatectomies at a single institution were retrospectively reviewed after obtaining institutional review board (IRB) approval. Two surgeons performing open prostatectomies with PLND and two surgeons performing robotic PLND were identified. One surgeon in each group performed PLND on all patients regardless of risk status while the other two surgeons performed PLND only for intermediate and high-risk disease based on the D'Amico Risk Group Classification.[3] Standard pelvic lymph node dissection template was utilized by all surgeons, including the lymph node packets overlying the external iliac vein and extending to the obturator fossa. The PLND was performed with the same configuration of robotic arms as was used for the prostatectomy.

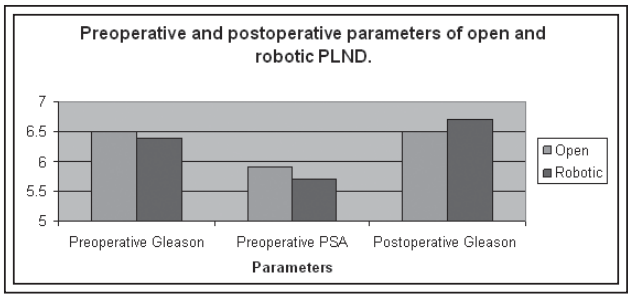

Figure 1. Comparison of preoperative (i.e. biopsy) Gleason scores, preoperative PSA, and pathologic Gleason scores in the open and robotic cohorts.

Patients receiving neoadjuvant chemotherapy, hormone therapy, or radiation were excluded. Preoperative age, biopsy Gleason score, and preoperative PSA were recorded. Pathology records were reviewed to determine the number of lymph nodes obtained with each PLND and surgical Gleason score. All pathologic specimens were reviewed by pathologists at a single institution. Statistical analysis was performed using Student's t-test.

Results

A total of 61 patients undergoing open RRP with PLND and 62 patients undergoing RALRP with PLND were included. Mean patient age was 59.9 years and 59.8 years in the open and robotic cohort, respectively. The mean preoperative PSA was 5.9 and 5.7, mean preoperative Gleason score 6.5 and 6.4, and mean pathological Gleason score 6.5 and 6.7 in the open and robotic groups, respectively, as shown in Figure 1.

The mean number of lymph nodes obtained via open PLND was 7.3 while the mean number obtained via robotic PLND was 3.3 as depicted in Figure 1. These means were significantly different with a p value < 0.001. The mean number of lymph nodes obtained

TABLE 1. **Descriptive characteristics of the three patients with micrometastatic disease on LND**

	Age	**Number LN's retrieved**	**Preoperative PSA**	**Biopsy Gleason score**	**Stage**
Open cohort patient	64	9	5.3	7	Gleason 4+3 pT2a N1
Laparoscopic cohort patient #1	53	3	8	7	Gleason 4+3 pT3a N1
Laparoscopic cohort patient #2	65	2	9.3	8	Gleason 3+4 pT3b N1

by each surgeon was reviewed; in the open cohort the individual lymph node yields were 9.7 and 6.9. In the robotic cohort, the individual yields were 3.5 and 1.5.

One patient in the open cohort (1.6%) and two patients in the robotic cohort (3.2%) had micrometastatic disease on PLND; all three of these patients had biopsy and final pathologic Gleason 7 with PSA less than 10. These patients are further described in Table 1.

Discussion

Prostate cancer remains the second leading cause of cancer death in the United States,[4] with an expanding array of treatment modalities available to the patient and physician. These include watchful waiting, cryosurgery, high frequency ultrasound, radiation therapy, open radical prostatectomy, and robotic or laparoscopic radical prostatectomy. Over the last several years, the latter procedures (pure laparoscopic prostatectomy and RALRP) have gained a tremendous amount of momentum as primary treatment modalities. In a recent review of Medicare beneficiaries undergoing radical prostatectomy, Hu et al found that RALRP increased from 12.2% of all radical prostatectomies in 2003 to 31.4% in 2005.[2] The basis for this increase remains controversial, with recent non-published data supporting the notion that increased procedures are performed due to patient demand. The latter has been attributed to marketing and parties with great financial interest promoting RALRP. Ultimately, a treatment modality may be influenced by all these parameters, but its durability will be defined by the safety and efficacy of the procedure. Certainly, 6 years following FDA approval, studies have revealed that the da Vinci prostatectomy offers several key advantages when compared to open surgery. Short and longer term outcomes are reported on patients undergoing RALRP, with the majority of studies consistently finding hospitalization time and estimated blood loss to be less with RALRP.[1,2] Outcomes such as PSA recurrence, disease free survival, and overall survival are difficult to compare as RALRP patients generally have a shorter follow up time period. Surrogate measures of oncologic outcomes such as positive margin rates and numbers of lymph nodes obtained are used in reporting oncologic efficacy.

Lymph node dissection during radical prostatectomy, open or robotic, continues to be of uncertain significance. Oncologic purists would argue that lymph node retrieval during radical prostatectomy offers tremendous data, allowing maximum information in order to offer the patient a disease free survival. Contrarians would argue that lymph node dissection in patients with low risk parameters such as PSA < 10 and predominant Gleason 6 pattern have no benefit from LND. The argument for LND is less controversial in high-risk patients, those with a PSA > 10, Gleason 7 or higher pattern on diagnosing prostate biopsy. The incentive for studying PLD during robotic prostatectomy is influenced by this latter subpopulation of prostate cancer patients. As mentioned previously, the technologic influence of robotics has overwhelmed the urologic world. In our view, the oncologic efficacy must be maintained irrespective of the surgical method employed during radical prostatectomy. Therefore, we evaluated the impact of robotic surgery on lymph node dissection at our program since the inception of the robotics technique. Comparison to the gold standard open radical prostatectomy was made and. the preliminary data appears to favor an open surgical approach to patients with high-risk prostate cancer.

The practice of performing PLND at the time of radical prostatectomy is not standardized, with limits of dissection as well as patient selection varying by surgeon and institution. In a recent review of CaPSURE data, the authors found a decrease in the number of patients undergoing PLND over time.[5] Variables other than patient risk status also affect whether a patient undergoes PLND. Prasad et al found in reviewing a contemporary cohort (2003-2005) of Medicare beneficiaries minimally invasive radical prostatectomy, advanced age, and multiple comorbidities predicted omission of PLND; interestingly, high-volume minimally invasive prostatectomy centers were more likely to perform PLND.[6] The selection bias of patients for PLND is likely to continue until firm evidence-based guidelines are established.

The significance of lymph node volume rests with both the diagnostic and possibly therapeutic applications of PLND. Extending the lymphadenectomy template beyond a limited dissection improves cancer detection and thus staging in open RRP.[7] This may also be true in patients who traditionally would not be considered higher risk based on PSA criteria. Schumacher et al showed that extended PLND in men with a PSA less than 10 yielded an 11% positive lymph node rate with a median of 20 lymph nodes analyzed in each patient. The extended PLND was well-tolerated, with a 2% rate of symptomatic lymphocele requiring drainage. This suggests that extending PLND could provide additional prognostic information.[8]

In men with negative lymph nodes, the number of lymph nodes obtained correlates with increased biochemical recurrence-free survival.[9] Similarly, in reviewing the SEER database, Joslyn and Konety[10] found that patients undergoing PLND yielding at

least 4 nodes –whether the patients had positive or negative nodes – lowered the risk of prostate cancer-specific death. They also found that patients with lymph node involvement had a significantly greater number of lymph nodes removed. Acknowledging the role of PLND in prostate cancer staging, the next logical question is whether we can offer our patients the same oncological outcomes with a robotic PLND as compared to open PLND.

While there is a paucity of data addressing robotic PLND, pure laparoscopic PLND can provide some insight into the efficacy of minimally invasive LND. Wyler et al performed laparoscopic PLND and obtained 21 LNs with a complication rate of 4%.[11] Several authors have shown the safety and efficacy of an extending PLND, thus increasing the node positivity rate. Touijer et al found that the odds for node positivity were 7.15 times higher for standard PLND as compared to a limited PLND. The number of lymph nodes obtained via limited laparoscopic PLND was 9, compared to 14 nodes with standard PLND.[12] This LN volume is comparable to open PLND series, with one group retrieving 11.6 nodes from a standard PLND and 8.9 nodes from a more limited dissection.[13]

To our knowledge no study has compared the number of lymph nodes obtained via open PLND and robotic PLND. In our relatively new robotics program, we found that the number of lymph nodes obtained via robotic PLND was significantly less than open PLND. We can find several explanations for this finding. First, robotic LND can be technically more limiting than laparoscopic PLND as trocars are placed in a configuration to maximize prostatic dissection. This placement is in a relatively caudal position and thus access to the pelvic sidewall is more difficult. This could be overcome by altering trocar placement. Second, this finding could represent a learning curve as the robotics program at our institution as with many institutions is relatively young. Perhaps more experience with robotic PLND will yield higher lymph node volume; this is a question we plan to pursue as our program matures. Third, while the pathologic specimens were processed and analyzed by a single group of pathologists at a single institution, this group did not include a dedicated urologic pathologist. With the recent addition of a urologic pathologist to our institution, continuing this study in a prospective fashion with all specimens analyzed by this single pathologist may alter our findings. Finally, the difference in lymph node yield may simply be a function of surgeon technique. This is a less likely explanation as two surgeons were included in each group. To overcome this limitation, a randomized study in which individual surgeons performed both open and robotic PLND would be necessary; as RALRP and robotic LND becomes more prevalent a study such as this would be difficult to execute. With this honest retrospective assessment of lymph node outcomes, we may also find that individual robotic surgeons make a concerted effort to perform a more thorough PLND and over time and with more experience the volume of tissue increases.

Conclusions

Current data suggests that PLND is an important staging and perhaps therapeutic tool in the treatment of prostate cancer. Robotic prostatectomy appears to offer comparable oncologic outcomes when positive surgical margin rate is compared to open prostatectomy. However, in our program's early experience, robotic PLND may not yield as many lymph nodes as open PLND. Further study of the impact of increasing case volume will help determine whether robotic PLND can yield the same number of lymph nodes as open PLND. This data suggests that in the early experience of a robotics program, patients at high-risk of metastatic disease should be managed with open PLND. In addition, meticulous attention to anatomic and technical aspects of robotic PLND is important to improve lymph node yield. □

References

1. Berryhill R, Jhaveri J, Yadav R et al. Robotic prostatectomy: A review of outcomes compared with laparoscopic and open approaches. *Urology* 2008;72(1):15-23.
2. Hu JC, Wang Q, Pashos CL et al. Utilization and outcomes of minimally invasive radical prostatectomy. *J Clin Oncol* 2008;26(14):2278-2284.
3. D'Amico AV, Whittington R, Malkowicz SP et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998;280(11):969.
4. Jemal A, Siegel R, Ward , et al. Cancer statistics, 2007. *CA Cancer J Clin* 2007;57(1):43-66.
5. Kawakami J, Maxwell V, Sadetsky N et al. Changing patterns of pelvic lymphadenectomy for prostate cancer: Results from CaPSURE. *J Urol* 2006;176(4part1):1382-1386.
6. Prasad SM, Keating NL, Wang Q et al. Variations in surgeon volume and use of pelvic lymph node dissection with open and minimally invasive radical prostatectomy. *Urology* 2008;72(3):647-652.

7. Bader P, Burkhard FC, Markwalder R et al. Is a limited lymph node dissection an adequate staging procedure for prostate cancer? *J Urol* 2002;168(2):518.
8. Schumacker MC, Burkhard FC, Thalmann GN et al. Is pelvic lymph node dissection necessary in patients with a serum PSA <10ng/ml undergoing radical prostatectomy for prostate cancer? *European Urology* 2006;50(2):272-279.
9. Masterson TA, Bianco FJ, Vickers AJ et al. The association between total and positive lymph node counts and disease progression in clinically localized prostate cancer. *J Urol* 2006;175(4):1324-1325.
10. Joslyn SA, Konety BR. Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. *Urology* 2006;68(1):121-125.
11. Wyler SF, Sulser T, Seifert H-H et al. Laparoscopic extended pelvic lymph node dissection for high-risk prostate cancer. *Urology* 2006;68(4):883-887.
12. Touijer K, Rabbani F, Otero JR et al. Standard versus limited pelvic lymph node dissection for prostate cancer in patients with a predicted probability of nodal metastasis greater than 1%. *J Urol* 2007;178(1):120-124.
13. Allaf ME, Palapattu GS, Trock BJ et al. Anatomical extent of lymph node dissection:impact on men with clinically localized prostate cancer. *J Urol* 2004;172(5Part1):1840.