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Open Versus Laparoscopic Retroperitoneal Lymph Node Dissection: Assessing Adequacy of Dissection in a Porcine Model

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Abstract

Background and Purpose: Laparoscopic retroperitoneal lymph node dissection (L-RPLND) is emerging as a viable alternative to traditional open retroperitoneal lymph node dissection (O-RPLND). Despite numerous reports confirming clinical oncologic equivalency between the two approaches, however, concerns still remain over the adequacy of laparoscopic dissection. We therefore sought to compare the completeness of dissection between O-RPLND and L-RPLND in a porcine model.

Materials and Methods: Fourteen domestic swine were divided into two equivalent groups. Both groups underwent bilateral retroperitoneal lymph node dissection, approximating templates used in human dissection. In one group, the procedure was performed through an open midline incision, while the other group underwent completely laparoscopic dissection. Tissue was independently analyzed by a pathologist, who recorded lymph node yield based on microscopic evaluation.

Results: All animals in the L-RPLND group underwent successful procedures, without the need for conversion. Two open procedures were aborted because of hemorrhage. Mean lymph node yield from O-RPLND was 32, while the mean yield for L-RPLND was 29. This difference was not statistically significant ($P = 0.65$).

Conclusions: In the porcine model, L-RPLND is capable of providing a quality of dissection equivalent to that of O-RPLND, in terms of absolute lymph node yield on microscopic examination. The applicability of this data to human patients, however, may be limited by significant anatomic differences between the human and the pig. Further prospective comparison in human patients is critically needed.

Introduction

Despite numerous advances in minimally invasive urologic oncology, open retroperitoneal lymph node dissection (O-RPLND) remains the gold standard for the surgical management of low-stage nonseminomatous germ-cell tumors.[1] Recent reports, however, indicate that laparoscopic retroperitoneal lymph node dissection (L-RPLND) may be a viable alternative to the open approach.[2–10]

One of the major concerns surrounding L-RPLND has been its adequacy as a stand-alone procedure that does not require the use of adjuvant chemotherapy in the instance of incomplete dissection.[11,12] Indeed, while initial long-term studies have demonstrated oncologic outcomes equivalent to an open approach,[2,3,5,8,10] there is a paucity of literature directly comparing the lymph node yield between L-RPLND and O-RPLND, with one recent direct comparison suggesting that node counts are significantly less with the laparoscopic approach,[9] while another meta-analysis suggests that node counts may be the same between the two approaches at high-volume centers.[8]

To further explore this critical and controversial aspect of the advanced surgical management of testis cancer, we sought to explore the adequacy and completeness of dissection of L-RPLND, compared to O-RPLND, using an animal model.

Materials and Methods

After approval from our institutional animal care and use committee, 14 domestic swine were divided into two equivalent groups consisting of seven animals each. Group A underwent O-RPLND, while group B underwent transperitoneal

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L-RPLND. Both underwent bilateral lymph node dissection, approximating modified template dissections previously described by Donohue and associates.[13,14] Briefly, the boundaries of dissection were defined by the renal vessels superiorly, the ureters laterally, and the common iliac arteries inferiorly. Nerve-sparing procedures were not attempted in this animal model.

For the open approach, the pigs were placed in a supine position, and a midline laparotomy incision was made. The peritoneum was incised along the white line of Toldt, and the bowel was reflected cephalad to expose the retroperitoneum. Full dissection was performed, using a "split-and-roll" technique to obtain lymph node tissue circumferentially.

For the laparoscopic approach, a transperitoneal technique similar to that described by Janetschek and colleagues[15] was used. The pig was placed initially in a right lateral decubitus position for left-sided dissection. Three ports were arranged in a triangular configuration, with additional ports placed as necessary for bowel retraction. After completion of the left side, the animal was repositioned in the left lateral decubitus position for right-sided dissection. Again, a split-and-roll technique was used to ensure a complete dissection.

A combination of sharp and blunt dissection as well as Bovie electrocautery was used in all open cases, while energy was delivered with a LigaSure device (ValleyLab, Boulder, CO) during the laparoscopic procedures. At the conclusion of each procedure, the animals were humanely sacrificed according to institutional protocol.

Lymph node packets were then analyzed by a single pathologist (PAH), who recorded the overall size of each lymph node packet, as well as the total gross number of nodes collected from each dissection. In addition, microscopic examination and confirmation of node count was performed after paraffin embedding and sectioning, along with hematoxylin and eosin staining. Statistical comparison of lymph node counts between O-RPLND and L-RPLND was then performed using a two-tailed Student's *t*-test, after normality of distribution and equal variance of our samples was confirmed with a Shapiro-Wilk test, and an F test, respectively.

Results

Histologic data are summarized in Table 1. Mean size of the animals was 41 kg and was equivalent between the two groups. O-RPLND was completed in five animals; two of the animals in the O-RPLND group experienced major operative misadventures resulting in exsanguination before lymph node dissection could be completed. This occurred early in the laboratory experience. In the L-RPLND group, the procedure was completed in all seven animals without intraoperative complications or the need for open conversion.

Pathologic evaluation revealed a mean aggregate packet size of 4.3×4.1 cm for O-RPLND, and 4.7×4.8 cm for L-RPLND. Mean aggregate lymph node yield for O-RPLND was 32 lymph nodes (range 16–49), and 29 lymph nodes for L-RPLND (range 18–40). The aggregate lymph node yield was equivalent between the two approaches ($P = 0.65$).

Subset analysis evaluating the adequacy of dissection for both left- and right-sided dissections, based on the boundaries of modified unilateral templates, revealed no difference in mean lymph node yield for left- and right-sided dissections for O-RPLND (16.8 *v* 15.0, respectively, $P = 0.7$). For L-RPLND, however, significantly more nodes were obtained during left-sided dissection, compared with the right-sided dissection (19.4 *v* 9.6, respectively, $P = 0.005$). When comparing the left- and right-sided yield between both open and laparoscopic approaches, the difference in unilateral lymph node yield for both sides was not statistically different between the two modalities.

Discussion

Testis cancer is currently the most common genitourinary malignancy affecting young postpubertal males. Fortunately, advances in the understanding of the natural history of the disease, along with refinements in surgical and medical therapy, have resulted in a drastic decrease in cancer-related deaths over the past 40 years.[11,16–18]

For patients with low-stage nonseminomatous testis tumors, retroperitoneal lymph node dissection remains one viable option for secondary management after orchiectomy, along with chemotherapy or active surveillance. RPLND is perhaps unique among the three strategies in that it is able to provide accurate pathologic staging of the disease in addition to the potential for eradication of metastatic disease to the retroperitoneum,[1–3,5,7,11] which is found in approximately 30% of patients with low-stage nonseminomatous disease.[1,19]

Table 1. Comparison of Microscopic Lymph Node Count for Open and Laparoscopic Retroperitoneal Lymph Node Dissection

	O-RPLND			*L-RPLND*		
Subject	*Left*	*Right*	*Total*	*Left*	*Right*	*Total*
1	13	15	28	14	4	18
2	12	14	26	25	15	40
3	8	8	16	24	0	24
4	26	23	49	15	12	27
5	25	15	40	15	13	28
6	N/A	N/A	N/A	19	8	27
7	N/A	N/A	N/A	24	15	39
Mean count	16.8	15.0	31.8	19.4	9.6	29.0

O-RPLND = open retroperitoneal lymph node dissection; L-RPLND = laparoscopic retroperitoneal lymph node dissection.

L-RPLND was first described by Rukstalis and Chodak[20] in 1992, for a 19-year-old man with low-stage nonseminomatous disease. While their report demonstrated the feasibility of a laparoscopic approach, the authors were unable to perform a complete dissection that included tissue posterior to the great vessels, thus raising concerns over the adequacy of dissection via a laparoscopic approach.

In the ensuing years, advancements in technique and minimally invasive technology have allowed surgeons to more adequately replicate the open technique.[4,21,22] Indeed, recent reports of long-term outcomes of L-RPLND indicate that oncologic efficacy in terms of disease-free and disease-specific survival is equivalent to that of O-RPLND.[2,3,5–8,10,23]

In addition, high-volume centers report that, in experienced hands, L-RPLND is associated with less morbidity, shorter hospital stays, and fewer overall complications compared with O-RPLND, while demonstrating inferiority only in terms of increased operative time and slightly increased overall costs.[3,5,8–10,21,24–26] Furthermore, L-RPLND has been demonstrated to be associated with less bother from postoperative pain compared with O-RPLND, as well as faster return to normal daily activities and improved quality of life scores on validated questionnaires.[24]

Despite the numerous potential advantages of L-RPLND, the technique has struggled to make inroads as the preferred modality for intervention at many high-volume centers,[22] based primarily on the concern that L-RPLND is incapable of providing an equivalent dissection to O-RPLND.[11,12] Indeed, while clinical oncologic outcomes may be similar, few studies have directly compared institutional experiences with L-RPLND and O-RPLND, with emphasis on objective measurement of the technical adequacy of dissection. While a meta-analysis of results from high-volume centers did note equivalency between the open and laparoscopic approaches in terms of lymph node yield,[8] one retrospective single-institution series demonstrated nearly double the lymph node count for O-RPLND, compared with L-RPLND (33 *v* 17, respectively, $P = 0.005$).[9]

To our knowledge, however, no prospective comparison of the adequacy of dissection offered by O-RPLND and L-RPLND has been described in the literature. We therefore sought to evaluate lymph node yield with both open and laparoscopic RPLND using an animal model.

Our results demonstrate that, for bilateral retroperitoneal lymphadenectomy, L-RPLND is capable of providing lymph node yields equivalent to the open approach in a porcine model. In fact, while there was no significant difference between the two approaches in terms of overall tissue mass excised, there was a trend toward larger specimens in the L-RPLND group, indicating little difficultly in extracting whole, intact tissue packets via a minimally invasive approach.

There are potential limitations to our present study, some of which may limit the applicability of our results to the treatment of human patients with low-stage nonseminomatous disease. Sample sizes in our experimental investigation were admittedly small. Furthermore, in the open group, two procedures had to be aborted because of exsanguination, which further limited the size of the open cohort. While statistical analysis was able to be successfully performed, it is nevertheless possible that our study was underpowered.

Furthermore, we are unable to clearly identify the factors that contributed to the noted discrepancy between lymph node yield for left- and right-sided dissections in our L-RPLND experience, a difference that was not noted in the O-RPLND cohort. Potential explanations include the possibility of increased technical challenge for right-sided dissections via a laparoscopic approach, or erroneous inclusion of right-sided lymph node tissue in the packets obtained from the left-sided dissections. That said, when comparing the adequacy of unilateral dissection, no statistical difference could be identified between the open and laparoscopic approaches for either side, and thus the practical implications of this discrepancy remain unclear.

In addition, the RPLND procedures performed in this experimental model were on animals with no pathologic diagnosis, and presumably normal lymph node tissue. Our dissections were carried out with the intent of providing as complete a dissection as technically possible in both arms of the study. Nevertheless, our experimental model may inadequately replicate dissections that are performed on pathologically abnormal nodal tissue, or in postchemotherapy patients.

Finally, we must acknowledge that there are significant anatomic differences between humans and pigs in terms of retroperitoneal lymph node distribution, and that these differences may limit the applicability of our results to a human model. In the pig, we noted that the bulk of the lymphatic tissue was found in the region of the renal pedicle, and along the iliac vessels, while the interaortocaval region—a territory rich with tissue in the human—was relatively devoid of lymphatic tissue in the pig. That said, our study was intended simply as a preliminary experimental investigation before undertaking direct prospective comparison of techniques in human patients. In this regard, our reported experimental model is similar to other published investigational studies, which have also used a porcine model,[15,27–29] often with successful transition thereafter to human studies.[27,29] Indeed, investigation of the efficacy and long-term outcomes of L-RPLND in humans at our institution is currently underway,[6] although reports of long-term prospective comparison of lymph node yields between the open and laparoscopic approaches in humans is currently lacking.

Conclusions

Despite early concerns over its efficacy as a curative procedure, L-RPLND continues to establish itself as a viable alternative to O-RPLND, offering less morbidity and increased patient satisfaction, while providing equivalent oncologic outcomes in the hands of experienced surgeons. In the porcine model, L-RPLND is capable of providing lymph node yields equivalent to O-RPLND, further supporting the potential for oncologic equivalency via a minimally invasive approach.

Disclosure Statement

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Abbreviations Used

L-RPLND = laparoscopic retroperitoneal lymph node dissection
O-RPLND = open retroperitoneal lymph node dissection
RPLND = retroperitoneal lymph node dissection