



Platinum Priority – Brief Correspondence

Editorial by James Porter, Scott Eggener, Erik Castle and Phillip Pierorazio on pp. 610–611 of this issue

Adverse Surgical Outcomes Associated with Robotic Retroperitoneal Lymph Node Dissection Among Patients with Testicular Cancer

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Article info

Article history:

Accepted May 21, 2019

Associate Editor:

Giacomo Novara

Keywords:

Testis cancer
Retroperitoneal lymph node dissection
Robotic surgery
Recurrences

Abstract

Surgery for metastatic testicular disease has been an essential factor in the long-term cure rates for men with testicular germ cell tumors. Robotic approaches to retroperitoneal lymph node dissection (R-RPLND) have been proposed as an alternative to open surgery with few if any adverse events reported. We report the clinical course for five recent patients referred to our center for recurrences after R-RPLND, focusing on recurrence patterns, treatment burden, and treatment-related morbidity and mortality. The median time to recurrence after R-RPLND was 259 d. The recurrence patterns after R-RPLND were aberrant from our past experience in managing recurrences after open RPLND. One man experienced an in-field recurrence located in close proximity to an undivided lumbar vessel. Four patients had out-of-field recurrence in abnormal locations: pericolic space invading the sigmoid colon, peritoneal carcinomatosis with a perinephric mass, large-volume liver lesions with suprahepatic disease extending into the retrocrural space, and lymph nodes in the celiac axis. The treatment burden was high: the five men were subjected to 12 different chemotherapy regimens and three underwent additional surgeries. Three patients developed significant cisplatin-induced toxicity. One patient died due to progression of testicular cancer after failing all chemotherapy and surgical options.

Patient summary: We report our initial experience in managing patients with testicular cancer referred to our institution after robotic retroperitoneal lymph node dissection (RPLND). We found that the recurrences were highly variable and in unusual locations and were associated with a high treatment burden. We conclude that further investigation into the safety and long-term oncologic efficacy of robotic RPLND is necessary before widespread implementation.

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In 2017, Pearce and colleagues [1] published a multi-institutional retrospective cohort study evaluating early clinical outcomes for 47 men who underwent robotic

retroperitoneal lymph node dissection (R-RPLND) for low-stage nonseminomatous germ cell tumors (GCTs). The authors should be congratulated for their collaborative



effort and exceptional outcomes. However, two areas for criticism that hamper an understanding of the true benefit of a robotic approach are the short follow-up period and the lack of a control group. Nevertheless, with only one reported recurrence, the authors suggest early oncologic equivalence when compared to the standard open surgical procedure [1].

In the 2 yr since this publication, we have observed a trend for referral to our institution for management of unusual retroperitoneal and/or diffuse metastatic recurrences following R-RPLND. Here we describe the clinical course for five men to communicate events not previously described in the literature. The importance of our observations is bolstered by recent high-impact publications describing inferior recurrence and survival outcomes among women treated with minimally invasive hysterectomy compared to open surgery for the management of early-stage cervical cancer [2,3]. We believe that it is reasonable to assume that these discrepancies in recurrence and survival may occur in patients with other malignancies, which is especially concerning for men undergoing RPLND for GCT given the high expected cure rates and long-term survival for men treated with open surgery [4].

The median age at initial presentation of these five patients was 34 yr (range 32–39). All patients presented with nonseminomatous good-risk ($n = 4$) or intermediate-risk ($n = 1$) disease. Three patients underwent a primary RPLND (2 patients with clinical stage I disease and one with a 1.4-cm lymph node) and two patients previously underwent standard platinum-based chemotherapy followed by postchemotherapy R-RPLND. The residual mass size in these two patients was 2.9 cm and 3 cm, respectively. Four of the procedures were performed at academic centers by physicians with significant oncologic experience and one surgery was performed in the community. Serum tumor

markers were negative before R-RPLND in all cases. RPLND specimens were negative in three of these men. The median time to recurrence from the initial RPLND was 259 d (range 92–503). Initial recurrence patterns included one in-field recurrence (Fig. 1A). Four patients had out-of-field recurrence in unusual locations: pericolic space with invasion into the colon, peritoneal carcinomatosis in addition to a perinephric mass, large volume liver lesions with suprahilar disease extending in the retrocrural space (Fig. 1B–D), and lymph nodes in the celiac axis.

All patients were treated with chemotherapy at the time of initial recurrence. Overall, these five patients were treated with a total of 12 different chemotherapy regimens after their R-RPLND. Four of these patients ultimately underwent high-dose chemotherapy with stem cell support (HD-CT), with one of these patients undergoing two distinct HD-CT regimens. Three patients had significant chemotherapy toxicities. Two had cisplatin-related ototoxicity and two had significant peripheral neuropathy.

Three patients underwent further operations after the time of initial recurrence. Two patients required repeat open RPLNDs for persistent disease after chemotherapy (Fig. 1A and B). One of these patients required a colectomy during the operation, with pathology confirming that embryonal carcinoma had invaded the wall of the sigmoid colon (Fig. 1B). The third patient underwent two thoracic resections but continued to relapse after surgery in the chest and retroperitoneum despite multiple lines of chemotherapy. These relapses ultimately resulted in the death of the patient. Two other patients are currently undergoing HD-CT with the potential for postchemotherapy surgery.

The clinical course for the only patient in our cohort who did not require HD-CT is worth mentioning. This man underwent primary R-RPLND that revealed zero out of

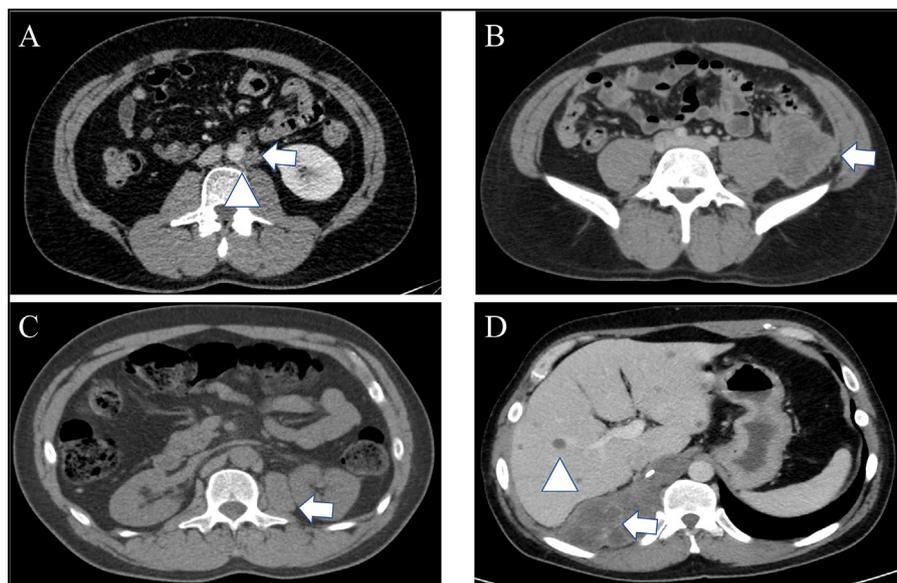


Fig. 1 – Representative computed tomography images at the time of recurrence after robotic retroperitoneal lymph node dissection. (A) In-field recurrence in the periaortic space (arrow) in close proximity to an intact lumbar vessel (arrowhead). (B) Out-of-field recurrence in the pericolic space (arrow) with extension into the descending colon. (C) Out-of-field recurrence in the perinephric space (arrow). This patient had diffuse carcinomatosis in the mesentery and pelvis (not shown). (D) Out-of-field recurrence with diffuse liver metastasis (arrowhead) and a large suprahilar mass extending into the retrocrural space (arrow).

21 lymph nodes as positive. Some 3 mo later, an in-field recurrence with elevated tumor markers was noted that was adjacent to an undivided lumbar vessel (Fig. 1A). Our group previously reported that incomplete lumbar division was one of only two significant factors for local recurrence after initial RPLND [5], suggesting that an incomplete initial dissection was performed. After three cycles of BEP x 3 with normalization of his tumor markers, the persistent retroperitoneal mass was resected using an open approach. The pathology of the residual mass was teratoma. Although this patient is likely to be cured of his disease, he was subjected to full-dose induction chemotherapy and repeat RPLND as a cost of his initial poor outcome. The ultimate fate of the other three living patients is unknown.

The patterns of recurrences described here are new to our experience in managing patients with GCTs. The reasons for this are unclear. Potential explanations include poor patient selection, poor operative technique, or surgical technology. In this series, we believe that patient selection was appropriate. No patient who underwent R-RPLND had elevated markers and the size of the residual mass in the postchemotherapy setting was small and manageable. Operative technique was poor in at least one of the cases in our series, as referenced above (undivided lumbar vessels). It is unknown if the oncologic surgery tenets for testicular GCTs such as complete vascular mobilization and minimal disruption of lymphatic tissue were followed in the remaining four cases. We argue that surgeons should not perform these operations (open or minimally invasive) if these principles cannot be followed and consider referral to experienced centers. The use of robotic technology should not replace the appropriate assessment, multidisciplinary care, and fundamental surgical principles well established by years of published experience in the management of testicular cancer.

We believe that the clinical scenarios for these five patients should serve as a word of caution with regard to the widespread implementation of robotic operative approaches for men with GCTs. The true incidence of these poor outcomes after R-RPLND is unknown. We acknowledge that the number of patients who had active disease and were successfully treated with R-RPLND is unknown. However, we also believe that our report under-represents the scope of this problem as our institution is not the only center that receives national referrals for testicular cancer. For context, our center performs approximately 150 RPLNDs annually, with the majority being postchemotherapy. During the 2-yr presentation period for these patients we performed ten repeat RPLNDs, including the two patients described here. Recent gynecologic oncology publications suggest that the operative approach may

impact recurrence and overall survival among women with cervical cancer [2,3]. Our small case series described here suggests that widespread implementation of the robotic approach without strict adherence to the established principles and practice for testis cancer management may result in similar outcomes. Men with metastatic GCT have excellent long-term survival so any deviation from standard management must maintain the current standard of care.

Author contributions: Adam C. Calaway had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Calaway, Einhorn, Foster, Cary.

Acquisition of data: Calaway, Cary.

Analysis and interpretation of data: Calaway, Cary.

Drafting of the manuscript: Calaway, Einhorn, Foster, Cary.

Critical revision of the manuscript for important intellectual content: Einhorn, Foster, Masterson, Cary.

Statistical analysis: Calaway, Cary.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: None.

Other: None.

Financial disclosures: Adam C. Calaway certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

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