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Robot Assisted Retroperitoneal Lymph-Node Dissection After Adjuvant Therapy: Different Indications

Running head: Robot assisted node dissection after adjuvant therapy

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ABSTRACT

BACKGROUND: Today, access to technology through robotic surgery has allowed urologists to have a valuable tool in order to perform various robot - assisted laparoscopic procedures. Robotic surgery allows reproducing complex techniques such as retroperitoneal or extended pelvic lymphadenectomy. The aim of the study was to report our series of robot assisted retroperitoneal lymphadenectomy and to demonstrate its technical and oncological feasibility.

METHODS: A retrospective analysis on 7 patients (four cases of testicular tumors, one prostate adenocarcinoma, and two bladder urothelial carcinomas), who underwent retroperitoneal para-aortic, interaorto-cava and extended pelvic lymphadenectomy by robot assisted laparoscopic surgery, was conducted. We analyzed demographic, oncologic and operative data (surgical time, blood loss, and hospital stay).

RESULTS: Demographic and operative data showed a mean age of 49 years (18-65), mean BMI of 26.1 kg/m^2(23.7-29.1), mean operative time of198 minutes (180-220), mean estimated blood loss of 88 mL, and mean hospital stay of 3.6 days (3-5). No intraoperative complications occurred. Themean number of dissected nodes was 12 (3-20). Histopathology findings showed one case of post chemotherapy recurrenceof seminoma and six cases of fibrosis.At a mean post-operative follow-up of 39 months (7-75) no patients showed disease recurrence.

CONCLUSIONS: Our case series demonstrated that the robot assisted approach isa feasible and reproducible option in skilled robotic surgical referral centers. The surgeons' experience and the optical magnification, associated to the degree of freedom offered by robotic assisted laparoscopy allow achievinga precise lymph node dissection, also in advanced oncologic patients.

Keywords: Retroperitoneal lymphadenectomy, Chemotherapy, Robot assisted Surgery, Node dissection, Adjuvant Therapy.

Open retroperitoneal lymphadenectomy is the gold standard for staging and treatment of post-chemotherapy (post-CHT) residual masses[1]. To date, the widespread diffusion of minimally invasive surgery supported laparoscopic and robotic approaches, reporting comparable oncologic and functional outcomes[2,3]. The robot-assisted laparoscopic retroperitoneal lymphadenectomy (RA-RPLND) is considered an effective, valuable and reproducible approach[2,3]. The robot-assisted technique requires an utmost experience in robotic surgery and it is highly technically demanding, with limited previous experiences reported in literature[4,5]. At our institution robotic approach has been used since 2006 in selected patients after chemotherapy for different diseases. Herein, we report a case series of patients underwent RA-RPLND (da Vinci Si robotic system, Intuitive Surgical, Sunnyvale, CA) after adjuvant chemotherapy for different urological malignancies.

MATERIALS AND METHODS

Between July 2010 and July 2015 we retrospectively collected data of seven patientsundergoing RA-RPLND and / or pelvic nodes dissectionafter adjuvant chemotherapy.

The study was conducted in accordance with the Declaration of Helsinki and all patients provided written informed consent for participation in the study.

The following data were analyzed: age, size and location of the mass, number of dissected nodes, operative time, mean blood loss,length of hospital stay, and pathological findings.

Before and after chemotherapy, all patients were studied with abdominal CT scans, and in case of doubt underwent PET CT scan. Patients were candidates for resection of retroperitoneal lymph nodes if residual masses were depicted on CT scans obtained after adjuvant therapy. Resection was routinely performed regardless of the size of the mass detected at post adjuvant therapy.

Surgical description

In all cases a transperitoneal approach was preferred. The most of patients (5/7) were placed in lateral modified flank position (45°), the other two were placed as for RA laparoscopic radical prostatectomy (steep Trendelenburg position).In just one patientthe da Vinci robot was docked from the cephalic aspect of the patient (Fig. 1).

To perform RA-RPLND the following instruments were used: monopolar scissors (EndoWrist Hot Shears) in the right robotic arm, and two graspers (EndoWrist Prograsp Forceps) in the other two robotic arms.

Surgical steps for the left-side nodes' template were the identification, isolation, and division of the lumbar vessels with the "split-and-roll" technique, andfull mobilization of the aorta off the posterior abdominal wall and anterior spinous ligament in order to guarantee a complete resection of the lymphatic tissue.

The interaorto-caval lymph nodes were medially dissected just off the inferior vena cava and the aorta with a "split and roll" fashion to the root of the right renal artery, until reaching the inferior mesenteric artery. The lumbar arteries and veins were proximally and distally clipped with Hem-o-lok (Teleflex, Research Triangle Park, NC, USA) before the dissection. At the cranial dissection extent, Weck clips were placed around the lymphatic tissue at the border below the right renal artery.

The extended pelvic node dissection aimed to the bilateral removal of lymph nodes and fibro fatty tissue in the external iliac, hypogastric and obturator regions.The boundaries were represented medially by the lateral border of the external iliac artery, laterally by the hypogastric artery, by the obturator fossa with complete deskeletonization of the obturator nerve caudally up to and including the Cloquets' node, and cranially up to the crossing of the ureter over the common iliac artery. At the end of the extended pelvic lymphadenectomy, the external iliac vein and the hypogastric artery, the obturator nerve and vessels resulted completely cleared of the overlying tissue.

RESULTS

The mean demographic and operative patients data were: age 49 years (18-65), body mass index 26.1 kg/m^2 (23.7-29.1), operating time was 198 min (180-220), estimated blood loss was 88 ml (30-150), number of nodes obtained was 12 (3-20), and hospitalization was 3.6 days (3-5; table 1). CT scan showed in all patients the presence of retroperitoneal residual mass (Fig. 2), and in one case the residual post adjuvant node was detected with fluorine-18 fluorodeoxyglucose[^{18}F] FDG-PET CT scan. The preoperative pathological finding consisted of four cases of testicular tumors (two out four were testicular rhabdo-myo-sarcomas, one teratoma with Yolk sac component tumour, and one seminoma), one prostate adenocarcinoma with Gleason score 6 (3+3), and two bladder urothelial carcinomas. The same skilled surgeon (JP) performed all the RA-RPLND and / or pelvic nodes dissection.

Regarding the nodes localization, in the two patients with residual masses due to primary bladder urothelial carcinoma in both cases a para-aortic, including inter aorto-caval dissection was performed and in the second case a lymphadenectomy was carried out up to the right common iliac vessels. The next two patients with histological diagnosis of primary testicular rhabdo-myo-sarcoma underwent para-caval and pelvic lymph node dissection (Fig. 3).

Two para aortic, inter aorto-caval lymph node dissections were performed for the teratoma with Yolk sac component tumour, and for the seminoma.

The last patient with a prostate cancer node recurrence at iliac level underwent an extended pelvic lymphadenectomy up to iliac common vessels.

The mean dimension of the lymph nodes obtained was 3.8 cm, and the final pathology findings revealed no residual disease in all nodes obtained except for the seminoma case, where the histopathology diagnosed a metastatic node (table 1).

No conversion to open surgery and no intraoperative complications occurred. Post operative complications occurred in two out of seven patients (28.6%) and were graded according to Clavien-Dindo classification[6]. As reported in table 2, all postoperative complications were early (within 30 days after surgery) and low grade (one grade I superficial wound infection and fever; and one grade II bowel ileus). All complications were treated by conservative management. At a mean post-operative follow-up of 39 months (7-75) no patients showed any disease recurrence.

DISCUSSION

In the literature there are few reports on robot assisted retroperitoneal lymphadenectomy, due to the high skillness of robotic expertise required. In the absence of rising tumor markers (α-feto protein, β-hcg, and LDH) surgical excision represents the standard of care. The significant residual mass size criteria on CT scan vary widely from institution to institution. A value of < 20 mm is considered normal by some, while a value of 15 and 10 mm is the standard elsewhere[7]. In one study, a 35% false negative rate was found to exist when the cut off was set to 20 mm, a value accepted as normal in many institutions[8]. This open debate has lead some surgeons to routinely perform RPLNDs on all patients who had post-chemotheraputic residual masses.

The most reports described RA-RPLND in the treatment of metastatic retroperitoneal nodes in non-seminomatous germ cell tumors (NSGCT) after orchiectomy and adjuvant CHT[9-11]. In our case series, two patients with NSGCT (paratesticular rhabdo-myo-sarcoma) underwent left RA-RLPND post-chemotherapy without any postoperative complications compared to the overall rate of complications (32%) reported by a previous post CHT open surgery large case series[9].

Rukstalis et al. reported the first minimally invasive experience of laparoscopic RPLND in 1992. The authors performed a bilateral RPLND for clinical stage 1 testicular cancer, concluding that laparoscopic surgical approach was a technically feasible and reproducible procedure that can remove RPLND from all primary landing sites for testicular metastases with potentially decreased morbidity[10]. Rasswelier et al. reported, in a case series of 26 NSGCTs patients, that laparoscopic node dissection was significantly more difficult in patients with stage II tumors after chemotherapy[11]. In this study the authors concluded recommending laparoscopic RPLND only in stage I patients, and counterindicating in post CHT subjects[12].

In a retrospective review of 7 patients (5 NSGCTs, 1 pure seminoma and 1 epididymal small cell cancer) who underwent laparoscopic RPLND after chemotherapy (multiagent CHT for clinical Stage IIA or higher disease), 5

(71.4%) of 7 patients successfully completed the surgery by laparoscopic approach (2 were converted in open surgery). The overall complication rate was 57.1% (4 of 7), concluding that the technique was challenging and should only be performed at institutions with high laparoscopic expertise[11].

In 2006 Davol and colleagues described the first experience of the RA-RPLND, performed in an 18-year-old Caucasian male with a mixed germ cell tumor, reporting that the da Vinci Surgical System could potentially improve the safety and accuracy RPLND[13].

In our case series, it was possible to perform RA-RPLND with no conversions to open surgery and no intraoperative and perioperative complications occurred and antegrade ejaculation was preserved in all NSGCTs patients. The dissection of the great vessels was optimized due to the three-dimensional vision, with a great magnification of structures (12x) that allowed an accurate and safe dissection of the nodes and the control of vascular side branches (lumbar). Additionally, the degree of freedom offered by the endo-wrist instruments provided an easy and safe access to complex anatomical sites (i.e. interaortocaval node dissection, full mobilization of the aorta off the posterior abdominal wall, etc.).

It was reported an increased rate of peri- and post-operative morbidity after RPLND for seminomatous cancer. The residual masses after advanced seminoma treated with cisplatin-based CHT resulted to be associated with much more extensive fibrosis and they always represented surgical challenge. In one retrospective study outcomes in patients underwent RPLND for seminoma were analyzed, suggesting a higher rate (38%) of additional operative procedures (e.g., inferior vena cava resection, arterial grafting, nephrectomy, and bowel resection) when compared to subjected submitted to the same procedure for NSGCTs (26.8%). Furthermore the rate of postoperative complications resulted greater in the seminoma group when compared to NSGCTs (24.7% vs. 20.3%)[14].

In our series, mean operative time was 230 minutes, lower than those reported by Cheney et al. (311min) with anequal mean amount of nodes dissected. Furthermore in the present study, post chemotherapy patients did not report any increase in operating time or higher blood loss[15].

About advanced prostate cancer patients no relevant data have been published on the impact of RPLND. A retrospective study by Busch et al. reported 6 patients with nodes metastases from advanced prostate cancer underwent a retroperitoneal LND. In these subjects primary therapy was represented by radical prostatectomy (3 pts.), radiation therapy (2 pts.), and androgen deprivation (one case). The Authors concluded that RPLND in advanced prostate cancer patients could be safely performed withasignificant postoperative PSA decrease, and a delay of toxic systemic therapies up to 12 months[16].

A recent study by Suardi et al. analyzed 59 patients affected by biochemical recurrence with 11 C-choline PET/CT scan showing pathologic nodes' activity. In these subjects salvage lymph node dissection represented the treatment of choice for nodal recurrence after radical prostatectomy. The best candidates for this approach seemed to be patients with low volume and limited pelvic areas recurrent nodal disease. Although most patients progressed to biochemical recurrence after salvage LND, approximately 40% of patients did not show any clinical recurrence at 8 years of median follow-up[17].

RA - RPLND is a challenging but feasible procedure. The published results are comparable to open surgery in terms of oncological outcomes[18-20]. In expert hands, it can be performed with minimal morbidity compared to the open approach.

The present study main limitations were represented by the small number of patients (even if in line with the most case series studies in literature), and the retrospective study design. The strength points of this study were the challenging post CHT patients enrolled, all the interventions performed by the same skilled surgeon, and the mean number of nodes dissected, supporting the RA-RPLND role in advanced oncologic patients.

CONCLUSIONS

The approach to residual masses by robot assisted surgery results as an excellent choice in high volume robotic centers with dedicated skilled surgeons: the da Vinci System improved the optical magnification and the

endowrist technology provided an outstanding degree of freedom, resulting in a more accurate and detailed RPLND, in patients already treated with CHT or RT. Moreover, patients undergoing the RA-RPLND reported an overall low complication rate, with a shorter hospital stay and prompt resumption of all daily life activities. Further prospective, randomized studies are needed to definitively establish the role of minimally invasive robotic assisted in the post-CHT RPLND.

Disclosure Statement

No competing financial interests exist.

Conflict of interest statement

All authors certify that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (e.g., employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

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ABLE 1. Demographic, operative and pathology data

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	65	18	24	36	60	55	49
BMI (kg/m2)	25.6	23.7	26.1	26.1	26.2	26.3	29.1
a Vinci docking position	Lateral	Lateral	Lateral	Lateral	Steep trend position (as for RALRP) plus cephalic	Steep trend position (as for RALRP)	Lateral
Operative time (minutes)	185	180	200	210	200	180	220
spital stay (no. of days)	5	3	4	5	3	3	4
imated blood loss (mL)	50	120	70	150	90	70	30
tology of primary tumour	Urothelial carcinoma	Rhabdo-myosarcoma	Teratoma + Yolk	Rhabdo-myosarcoma	Urothelial carcinoma	Prostate Cancer Gleason 6 (3+3)	Seminoma
ymph Vascular Invasion	No	No	No	No	No	No	Yes
ximum nodes size (cm)	3x2x2, 3x1, 12x1	6x4x2,0.5x0.3x0.3	6x4x4	3X4X2	3x2x2	2x9x2	5x1.5x5, 5x4x4
adjuvant therapy	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lymph node issection areas	Para-aortic, interaortocaval	Para-caval /Pelvic	Para-aortic, interaortocaval	Para-caval / Pelvic	Right Common Iliac	Pelvic Extended	Para-aortic, Interaortocaval
Tumor side (no. of nodes)	Right (9)	Right (16)	Left (9)	Right (8)	Right (7)	Right (20)	Left (3)
RPLND Pathology findings	Negative	Negative	Negative	Negative	Negative	Negative	Yes, Seminoma

TABLE 2. Post-operative complications according to Clavien-Dindo classification [6]

COMPLICATIONS	no. (%)	MANAGEMENT
No. complications	5 (71.4%)	Antibiotics and bedside management
I (superficial wound infection and fever)	1 (14.3 %)	
II (Bowel ileus)	1 (14.3%)	Conservative