Published in final edited form as:

Eur Urol. 2011 July ; 60(1): 118–124. doi:10.1016/j.eururo.2011.03.046.

Robot-Assisted Laparoscopic Partial Adrenalectomy for Pheochromocytoma: The National Cancer Institute Technique

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Abstract

Background—Partial adrenalectomy has recently been advocated to preserve unaffected adrenal tissue during resection of pheochromocytoma.

Objective—To describe a robot-assisted laparoscopic partial adrenalectomy (RALPA) technique and to report on early functional and oncologic outcomes.

Design, setting, and participants—From 2007 to 2010, 15 RALPA were performed on 12 consecutive patients with pheochromocytoma. Follow-up data of >1 yr are available on 11 procedures. Median follow-up for the entire cohort was 17.3 mo (range: 6–45).

Surgical procedure—Positioning and port placement is designed for adequate reach and visualization of the upper retroperitoneum. The plane between the adrenal cortex and pheochromocytoma pseudocapsule is identified visually and with laparoscopic ultrasound. The tumor is dissected away from normal adrenal cortex, preserving normal adrenal tissue.

Measurements—Preoperative, perioperative, pathologic, and functional outcomes data were analyzed.

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Author contributions: Gennady Bratslavsky 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.

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Drafting of the manuscript: Asher, Gupta, Bratslavsky.

Critical revision of the manuscript for important intellectual content: Asher, Gupta, Bratslavsky.

Statistical analysis: Asher, Bratslavsky.

Obtaining funding: Bratslavsky, Linehan.

Administrative, technical, or material support: Gupta.

Supervision: Bratslavsky, Pinto, Linehan.

Other (specify): None.

Financial disclosures: I 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 (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.

The Surgery in Motion video accompanying this article can be found in the online version at <doi to be filled in by typesetter> and via www.europeanurology.com. Subscribers to the printed journal will find the Surgery in Motion DVD enclosed.

Results and limitations—Fourteen of 15 cases were completed robotically. Among 15 procedures, 4 were performed on a solitary adrenal gland. Four cases required resection of multiple tumors (up to six) with two performed in a solitary gland. The mean age of the patients was 30 yr, and the mean body mass index was 27. The mean operative time was 163 min, the median estimated blood loss was 161 ml, and the median tumor size was 2.7 cm (range: 1.3–5.5). There was one conversion to an open procedure in a patient requiring reoperation on a solitary adrenal gland. One patient who underwent RALPA on a solitary adrenal gland required postoperative steroid supplementation at last follow-up. At a median follow-up of 17.3 mo (range: 6–45), there were no recurrences or metastatic events. Study limitations include small sample size and short follow-up.

Conclusions—RALPA for the treatment of pheochromocytoma is feasible and safe and provides encouraging functional and oncologic outcomes, even in patients with a solitary adrenal lesion or multiple ipsilateral lesions.

Keywords

Adrenalectomy; Laparoscopy; Partial adrenalectomy; Pheochromocytoma; Robotic surgery

1. Introduction

Pheochromocytoma is an uncommon tumor with an incidence of approximately one or two per 100 000 adults per year but is much more common in familial cancer syndromes, including von Hippel-Lindau (VHL), multiple endocrine neoplasia (MEN) type 2, and neurofibromatosis type I. Among VHL patients who develop pheochromocytomas, up to 47% will develop bilateral lesions [1]. Traditional surgical treatment for pheochromocytoma has been total adrenalectomy. Recent reports have described adrenal-sparing surgery as a surgical option for patients with hereditary cancer syndromes [2–7]. In addition, adrenal-sparing surgery has also been described for sporadic adrenal masses, since, even in sporadic cases, other pathologic processes may affect the remaining solitary adrenal gland [8–11].

Laparoscopic approaches have become widely used for adrenal lesions [12–14], including several reports describing laparoscopic adrenal-sparing surgery utilizing both the transperitoneal and retroperitoneal approaches [15–17].

At our referral center, the majority of patients have hereditary conditions and may develop bilateral, multifocal adrenal lesions. Additionally, many patients have had prior adrenal surgery and some have multiple adrenal lesions. These patients afforded us a unique opportunity to evaluate robot-assisted, laparoscopic, partial adrenalectomy (RALPA) for pheochromocytoma. Here we describe our surgical technique and report early functional and oncologic outcomes.

2. Patients and methods

We performed 15 RALPA procedures in 12 consecutive patients presenting with pheochromocytoma to the National Cancer Institute, US National Institutes of Health, from June 2007 through August 2010. All patients gave written consent regarding the surgical risks of the procedure and the risk for postoperative steroid replacement. The study protocol was approved by the institutional review board.

2.1. Inclusion and exclusion criteria

All patients with an adrenal mass that had radiographic and biochemical features consistent with adrenal pheochromocytoma were included. Urine and serum catecholamine

measurements, computed tomography scan, magnetic resonance imaging, and metaiodobenzylguanidine scan were obtained to confirm the diagnosis of pheochromocytoma.

Tumors in a solitary adrenal gland or previous adrenal surgery (either ipsilateral or contralateral) did not exclude patients from the RALPA technique.

2.2. Data collection and follow-up

Patients' demographics and perioperative variables, such as operative time, estimated blood loss (EBL), tumor size, and intraoperative blood pressure and pulse were reviewed. All patients had pheochromocytoma on final pathology. Complications were recorded and classified using the Clavien system.

Follow-up consisted of clinic visits at 3 and 12 mo with cross-sectional imaging and biochemical measurements including urine and plasma catecholamine levels to assess for disease recurrence. In the immediate postoperative period, patients with solitary adrenal gland or with signs or symptoms suggestive of adrenal insufficiency were evaluated with an adrenocorticotrophic hormone-based cortisol stimulation test. To assess the long-term functional outcome, we tabulated the clinical need for permanent steroid supplementation. Because of a large number of patients residing far away from our tertiary referral center, telephone follow-up was used in many cases.

2.3. Surgical technique

2.3.1. Patient preparation—Patients were prescribed a 2-wk, preoperative, oral adrenergic blockade consisting of phenoxybenzamine 10 mg twice daily and metyrosine 250 mg three times daily. Patients were encouraged to orally hydrate in the 2 wk prior to surgery. A magnesium-citrate bowel preparation was given the day before surgery. An arterial line was placed for blood pressure monitoring and two large-bore, peripheral intravenous catheters were placed. Blood pressure was carefully monitored intraoperatively to ensure hemodynamic stability during the procedure and specifically during tumor manipulation. We did not observe significant intraoperative blood pressure lability with this regimen, and therefore a central line was not routinely used.

2.3.2. Patient positioning—Two technical modifications are used that distinguish the operative setup for RALPA from typically used robotic configurations for renal surgery. First, the patient is positioned in an extreme flank position, with the axis of the shoulders close to a 90° angle to the operating table. This positioning allows easier access to the adrenal gland, and is particularly important on the right side where pheochromocytoma is typically located retrocavally. Second, the robotic camera axis is placed above and lateral to the umbilicus facilitating better visualization of the upper retroperitoneum (Fig. 1).

2.3.3. Port placement—The port configuration is shown in the Figure 2. In most cases, a single 12-mm assistant port is used between the left robotic trocar and the camera port, but in obese patients, a second assistant port may be added. An additional 5-mm subxyphoid trocar is used for liver retraction in a right-sided case. The robotic cart is then brought in at a 45° angle in relationship to the table over the head of the patient with the working axis of the robot directed at the ipsilateral clavicle (Fig. 2).

2.3.4. Instrumentation—A 30° down lens is utilized throughout the operation. Monopolar scissors are placed in the right robotic arm and bipolar forceps in the left.

2.3.5. Exposure of adrenal gland

2.3.5.1. Right-sided exposure: Because of the extreme flank positioning, a direct approach to the right adrenal can be performed without bowel mobilization. The triangular liver ligament is divided as cranially as possible to release the liver, and the locking grasper (placed through the subxyphoid trocar) is used as a liver retractor. The posterior peritoneum overlying the upper pole of the adrenal is also divided to release the liver, which is then retracted more superiorly. Superior retraction on the liver is crucial for the right sided approach, as broad exposure of the supra-adrenal cava is essential to avoid hemorrhage and to optimize workspace. Occasionally, short hepatic veins may be divided to gain additional length of the vena cava. The lateral border of the inferior vena cava is identified, the adventitia over the cava is incised, and the dissection is carried until the right adrenal vein is encountered and then clipped and divided. Often, small accessory adrenal veins are identified and controlled with bipolar cautery or clips.

2.3.5.2. Left-sided exposure: The splenic flexure and a portion of the descending colon are mobilized. The lateral attachments of the spleen, as well as splenorenal ligaments, are divided. The spleen, bowel, and the pancreas are mobilized medially until the adrenal gland is clearly visualized. Depending on the location of the pheochromocytoma, the left adrenal veins may or may not be divided.

2.3.6. Identification of pheochromocytoma—Once the adrenal gland has been identified, a laparoscopic ultrasound probe is used to identify the adrenal gland, the upper pole of the kidney, and the pheochromocytoma. On ultrasound, the pheochromocytoma appears as a homogenous, hypoechoic, well-demarcated lesion, distinct from the surrounding normal adrenal. The ultrasound is used to scan the entire adrenal gland to assess for occult multiple masses (Fig. 3).

Once the mass is identified, the Gerota's fascia layer overlying the tumor is incised. Careful, gentle dissection is then used to identify the pheochromocytoma pseudocapsule within the normal adrenal gland. The robotic instruments are particularly helpful with minimizing the handling of normal adrenal tissue, which may help preserve the adrenal blood supply. Dissection of the superior and medial aspects of the adrenal gland is minimized, as these are the sites of arterial blood supply. If, due to the tumor location, superomedial dissection is needed, care must be taken to minimize dissection inferior to the adrenal within Gerota's fascia, as the blood supply from the vasculature in this region is necessary to maintain the viability of the residual unaffected adrenal gland.

Once the mass is clearly visualized, the plane between normal adrenal tissue and pheochromocytoma pseudocapsule can be appreciated (Fig. 4).

2.3.7. Resection of pheochromocytoma—The mass is carefully enucleated, taking great care to keep the tumor pseudocapsule intact and to respect tissue planes. Gentle upward traction is provided with the bipolar forceps and blunt dissection in the proper plane is used to peel the tumor mass away with minimal tissue damage. Dissection into an incorrect plane may produce troublesome bleeding. Locking clips and pinpoint cautery are used for hemostasis. The entire specimen and tumor capsule are inspected to ensure complete resection. The adrenal bed is inspected for residual tumor visually and with laparoscopic ultrasound to ensure adequate hemostasis. A frozen section of the base is not routinely performed (Fig. 5 and 6).

3. Results

A total of 15 RALPAs were performed in 12 patients. Patient characteristics are listed in Table 1. Ten of 12 patients had VHL disease, one patient had neurofibromatosis type 1, and the other had bilateral pheochromocytomas without a known genetic disorder. Median follow-up for the entire cohort was 17.3 mo (range: 6–45), and 11 procedures had >1 yr follow-up. Mean tumor size for the cohort was 2.7 cm.

Four patients underwent RALPA with resection of multiple ipsilateral pheochromocytomas, ranging from two to six lesions. In addition, four patients had a solitary adrenal gland, and of these, two patients had multiple tumors resected (three and six tumors, respectively). Perioperative characteristics are listed in Table 2. Median blood loss was 161 ml. Mean total operative time from skin incision to closure was 163 min (range: 110–357). Intraoperative hypertension or tachycardia was not observed with manipulation of the pheochromocytoma. There was one conversion to open partial adrenalectomy due to severe adhesions to the liver and repeated vena caval injuries requiring initially robotic, and then open repairs. They occurred during medial dissection of the adrenal in a patient with a solitary adrenal gland and prior adrenal surgery on the ipsilateral side. The same patient also had the only operative complication (Clavien grade 3) of the series: a bile leak that required a temporary drain for 5 d. At 16 mo postoperatively, this patient has no evidence of recurrence and does not require steroid supplementation.

Of the total cohort of 15 patients, none had biochemical evidence of recurrent pheochromocytoma and 14 did not require long-term, postoperative, steroid supplementation. One patient, a 44-yr-old woman with a history of bilateral multifocal pheochromocytomas had resection of six masses in a solitary adrenal and has required steroid supplementation since the time of surgery, despite visual preservation of a small portion of unaffected adrenal.

4. Discussion

Pheochromocytoma has traditionally been surgically managed by total adrenalectomy. In this report we describe our technique of RALPA in detail. We have found this technique effective for the management of pheochromocytoma, even with multiple lesions or in the setting of a solitary adrenal gland, with promising functional and oncologic outcomes.

Several technical considerations are important to successfully perform this procedure (Table 3). First, the patient must be positioned in an exaggerated flank position, with the axis of the shoulders almost perpendicular to the operating table. This exaggerated flank position is crucial to easily exposing the adrenal glands. This is in contrast to the robotic renal approach, where the patient is typically positioned in a 45° flank position. Second, the port arrangement should be rotated more laterally and more superiorly, with the camera axis pointed toward the ipsilateral clavicle. Again, this allows better access to the upper retroperitoneum. With these modifications, we typically do not have to mobilize the bowel on the right side and minimize bowel mobilization on the left. Third, on the right side, one must mobilize the liver as cephalad as possible, dividing not only the peritoneal attachments between the upper pole of the kidney and inferior liver surface, but dividing the triangular ligament as superiorly as possible. This allows access to the supra-adrenal vena cava on the right side. This area must be well exposed, as the short hepatic veins enter at this level and may cause hemorrhage if not appreciated. Fourth, the plane between the pheochromocytoma capsule and the surrounding adrenal parenchyma must be clearly visualized. The enhanced visualization of the three-dimensional laparoscopic view and the intraoperative ultrasound facilitate the identification of this plane. Once the correct dissection plane is identified and

entered, the tumor enucleation is straightforward and minimal bleeding is typically encountered. Finally, the advantage of the robotic platform over traditional laparoscopy may best be appreciated during the tumor resection. As the remainder of the unaffected adrenal should be minimally dissected to preserve the blood supply, the articulation of the robotic instruments permits circumferential dissection around the tumor deep within the adrenal with minimal manipulation of the normal adrenal gland.

Laparoscopic partial adrenalectomy has been increasingly utilized in recent years. Walz et al in 2004 reported the largest series in the published literature with 100 laparoscopic adrenal-sparing procedures [17]. Their series used prone patient positioning and a retroperitoneal approach. The median operative time was 79 min and the EBL was 29 ml. At a mean follow-up of 51 mo there were no recurrences. In a subgroup of 15 patients with bilateral adrenal masses and hereditary syndromes (VHL, MEN, succinate dehydrogenase genes), one patient required postoperative steroid supplementation. These findings are similar to our results, in which one of 15 procedures resulted in steroid supplementation. However, 40% (6 of 15) of procedures in our cohort were performed in patients with a solitary gland or multifocal lesions. Patient selection as well as a learning curve can certainly explain our longer operative times. In our most recent RALPA cases, we completed the entire procedure in <60 min, which compares favorably with these reports and with those utilizing laparoscopic or robotic approaches [17,19].

A comprehensive literature review of partial adrenalectomy was performed by Kaye et al, reporting on 417 patients, including 319 laparoscopic partial adrenalectomies performed via a variety of approaches. Thirty-seven percent of these procedures were performed for pheochromocytoma. Mean operative time was 130 min and mean EBL was 72 ml. In the laparoscopic group, complications occurred in 7.3% of patients. Six of 133 (4.5%) patients required long-term steroid supplementation in this review [18]. These numbers are comparable to the findings of our series, despite our more challenging patient cohort, as described earlier. Recently, there have been several case reports of RALPA in the literature. Narmada et al reported on four patients undergoing partial adrenalectomy for pheochromocytoma using a transperitoneal, four- or five-port technique [19]. Their report, similar to our experience, emphasized the exaggerated flank positioning as a key operative step. They reported a mean blood loss of 97 ml and mean operative time of 77 min. All patients had a single lesion in this cohort and none had multifocal lesions. Kumar et al described a transperitoneal, robotic, partial adrenalectomy in a left-sided adrenal metastasis in a patient with renal-cell carcinoma and a previous right adrenalectomy [20]. The operative time was 90 min and blood loss was 50 ml. We also recently reported on a cohort of patients treated with transperitoneal RALPA for adrenal masses [21]. The present report focuses on our surgical technique for pheochromocytoma. In our cohort, EBL was slightly higher (161 ml) and operative times were longer (163 min) than in these other laparoscopic series. As mentioned above, these findings may be explained in part by patient selection as well as a learning curve, as the cases are frequently performed by the fellows in training.

A strength of our study is the follow-up on functional outcomes. Only one of 15 patients in our cohort has required postoperative steroid supplementation. This is an encouraging result considering our challenging patient population and its propensity to developing bilateral, multifocal pheochromocytomas potentially requiring bilateral adrenalectomy. Three patients in this series had bilateral lesions at presentation and, after staged bilateral RALPA, each of these patients has no evidence of residual tumor and none require steroid supplementation. Finally, of four patients with a solitary adrenal gland, three patients did not require long-term treatment with steroid replacement after RALPA, indicating that the residual adrenal gland after RALPA was able to provide physiologic levels of endogenous steroids. These results are consistent with the findings of Sanford et al, evaluating outcomes of patients

requiring adrenal surgery on a solitary adrenal [22]. Given the risks associated with bilateral adrenalectomy and uncertain dosing with exogenous steroids, it appears that adrenal-sparing surgery offers these patients a significant benefit. Our described technique of robotic assistance may facilitate and allow for a wider acceptance of adrenal-sparing surgery, while conferring the benefits of a minimally invasive laparoscopic approach [23].

In general, our results are consistent with other published, laparoscopic, partial adrenalectomy series. In our experience, we have found that while the perioperative outcomes may not yet be significantly different than those of published laparoscopic series, the procedure may be technically easier to perform. Other studies have demonstrated that laparoscopic approaches for adrenal surgery are associated with decreased blood loss, shortened convalescent time, and decreased need for postoperative analgesia, as compared with open adrenalectomy, and we have observed the same benefits in the current series compared with our open experience [24]. The enhanced visualization and articulating dissecting instruments allow for a controlled, accurate enucleation, and use of a two-handed technique with assistance afforded by the robotic platform. The robotic approach is particularly well-suited for laparoscopic surgery that requires very precise dissection in a small space. Additionally, in our experience, the RALPA technique has been easily learned by urologic oncology fellows.

There are several inherent limitations in the current study. It is retrospective and the sample size is small. The follow-up is limited and the long-term oncologic outcomes are not yet available. While this current report describing our technique does not yet demonstrate long-term oncologic efficacy, recent evidence suggests that partial adrenalectomy for pheochromocytoma may provide excellent, long-term, oncologic and functional outcomes [4]. Additionally, Kaye's review also demonstrates an evolving role for adrenal-sparing surgery [18]. The patients in this series have hereditary syndromes predisposing to the development of bilateral, multifocal adrenal pheochromocytomas, which may affect our perioperative outcome measures. Finally, our surgical team has significant experience in both open and laparoscopic partial adrenalectomy, which may have contributed to our perioperative outcomes in this series.

5. Conclusions

RALPA for pheochromocytoma is a safe, technically feasible procedure that provides excellent short-term functional and oncologic outcomes. Our technique for RALPA may be used for patients with adrenal pheochromocytoma, including multifocal lesions, and is especially well suited to those with a solitary adrenal gland. The procedure may be applicable for other type of adrenal lesions. Longer follow-up is needed to assess long-term functional and oncologic outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Lateral and superior port placement. The camera port and the robotic axis are rotated superiorly and laterally to access the adrenal gland in the posterior retroperitoneum.

Fig. 2.

Port placement for robot-assisted laparoscopic partial adrenalectomy. This case was performed on an obese patient. In addition to the 5-mm trocar used between the camera port and right robotic port, another assistant port is placed between the camera and the left robotic port in patients with extreme obesity. A 5-mm subxyphoid port is used for liver retraction. Note the axis of the camera port directed at the ipsilateral clavicle.

Fig. 3. Laparoscopic ultrasound aids in identifying pheochromocytoma. The pheochromocytoma appears as a well-demarcated, homogenous, dark mass that is distinct from the surrounding normal adrenal cortex.

Fig. 4. Identification of the plane between normal adrenal cortex and pheochromocytoma. The enhanced visualization allows identification of the plane between tumor tissue and adjacent normal adrenal cortex. A plane of dissection can then be developed.

Fig. 5. Dissection of tumor from uninvolved adrenal cortex. By following the pseudocapsule of the lesion, the pheochromocytoma is carefully enucleated. Locking laparoscopic clips are used to control small perforating vessels.

Fig. 6. Minimal handling of normal adrenal tissue. The dissection is performed to maximize the separation of tumor tissue from the underlying uninvolved adrenal bed. The precise movements of the robotic instruments allow for minimal handling of normal adrenal tissue, which may help preserve blood supply and minimize long-term damage to normal healthy adrenal cortical tissue.

Table 1

Demographic and preoperative data

Patients, No.	12
RAPLA, No.	15
RAPLA with planned staged procedures, No.	3
RAPLA performed on right side, No. (%)	9 (60)
Patient age, yr, mean (range)	30.0 (15.9–61.9)
Follow-up, mo, median (range)	17.3 (6–45)
BMI, kg/m ² , mean (range)	27 (20–48)
Procedures for multifocal lesions, No. (%)	4 (26)
Procedures on solitary adrenal gland, No. (%)	4 (26)

RAPLA = robot-assisted laparoscopic partial adrenalectomy; BMI = body mass index.

Table 2

Perioperative, postoperative, and functional outcomes

Perioperative	
Operative time, min, median (range)	163 (110–357)
EBL, ml, median (range)	161 (50–300)
RAPLA requiring transfusion, No.	1 (7.5)
Conversions to open procedure, No. (%)	1 (7.5)
Intraoperative hypertension/tachycardia episodes, No.	0
Postoperative	
Largest tumor size, cm, median (range)	2.7 (1.3–5.5)
Local or distant recurrence, No.	0
Functional	
RAPLA requiring steroid replacement postoperatively, No. (%)	1 (7.5)

EBL = estimated blood loss; RAPLA = robot-assisted laparoscopic partial adrenalectomy.

Table 3

Technical keys to success with robot-assisted laparoscopic partial adrenalectomy

1. Thorough preoperative blockade with phenoxybenzamine and metyrosine
2. Extreme flank positioning
3. Axis of robotic ports directed at ipsilateral clavicle
4. Identify adrenal vein and ligate if there is potential for injury
5. Identify adrenal pheochromocytoma visually and with laparoscopic ultrasound
6. Establish plane between pseudocapsule of lesion and normal adrenal
7. Minimize handling of tissue and use of cautery to preserve blood supply
8. Resect the mass along the pseudocapsule plane