Laparoscopic Adrenalectomy: The Transperitoneal Approach

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Abstract Laparoscopic adrenalectomy (LA) has become the gold standard in the operative approach to tumors of the adrenal gland. It has been 20 years since it was first described in the literature and the technique has afforded improved operative and perioperative outcomes compared to the open approach to the adrenal gland. These include improved cosmesis, less post-operative pain, and reduced morbidity, and have allowed patients to be discharged from hospital earlier and return to normal activity. LA has been proven to be safe and effective when dealing with functioning and non-functioning adrenal incidentalomas, pheochromocytoma, and Cushing's and Conn's syndrome, and has even been used for primary and secondary adrenal malignancies. Here, we describe the laparoscopic transperitoneal approach to the adrenal gland and its evolution since its inception.

Keywords Laparoscopy · Laparoscopic · Minimally invasive surgery · Adrenalectomy · Transperitoneal · Adrenal · Endocrine surgery · Adrenal tumors · Malignancy

Introduction

Since the advent of laparoscopic adrenalectomy (LA) in 1992, the technique has been widely adopted, and is currently the standard of care for resecting small benign adrenal lesions in most countries [1]. Although the indications for LA in Gagner's report were Cushing's syndrome and pheochromocytoma, the list of indications have extended to include most benign adrenal lesions, as well as adrenal metastases. However, the upper limits of size and the suitability of LA for malignant adrenal tumors is still debated. Some of the reported benefits of LA are similar to the benefits of minimal access surgery in general, including reduced post-operative pain and length of stay, reduced blood loss, lower complication rates, as well as better cosmesis [2•]. We seek to present the collective experience of transperitoneal LA in the published literature within the past two decades.

Indications for LA

Adrenal tumors are common, with an estimated prevalence of 5 % in abdominal and chest computed tomographic (CT) exams [3]. With the unprecedented increasing number of cross-sectional imaging studies being performed, the detection of adrenal tumors is rapidly increasing. In the United States, the annual number of adrenalectomies in the Nationwide Inpatient Sample (NIS) database increased from 3,241 in 1998 to 5,019 in 2006 [2•].

Benign, non-functioning lesions smaller than 3 cm may be observed and have sequential imaging whereas larger lesions or functional lesions may be considered for laparoscopic removal. An appropriate endocrine workup is paramount before an operative approach to the adrenal gland is entertained. Serum and urine metabolic parameters

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together with radiological and/or nuclear medical imaging results are important in determining the nature of the adrenal cortical or medullary lesion. Localizing laterality of functional lesions is also of utmost importance.

Current indications for LA include non-functioning incidentalomas, functioning lesions of the adrenal cortex such as aldosteronomas, glucocorticoid and sex-steroid producing adenomas, bilateral functional hyperplasia, pheochromocytoma, Cushing's disease and rarer entities such as adrenal cysts and myelolipomas.

Laparoscopic adrenalectomy for Conn's syndrome has been gaining exponential momentum and many studies have documented successful outcomes [4–11]. These studies demonstrated successful completion of the adrenalectomy laparoscopically with essentially no need for conversion. Our unit has demonstrated a cure rate of 30 % with LA and up to 90 % of patients demonstrating an overall improvement in clinical and biochemical markers [4].

The benefits of LA for Cushing's Syndrome and disease have also been well documented since the late 1990s [12], where Acosta and colleagues compared LA with open adrenalectomy (OA) and declared that there was no discernable difference between the two in terms of cure rate and morbidity.

In the case of pheochromocytoma, preoperative preparation is essential to avoid a hypertensive crisis intraoperatively. Alpha-adrenergic blockade is titrated until the patient is orthostatic. The exact protocol of metyrosine and phenoxybenzamine varies between centers and is dictated by the surgeons' and physicians' preferences and is usually for a course of approximately 2 weeks pre-operatively. Intraoperatively, minimizing tumor manipulation and subsequent spillage is paramount to avoid a catecholamine surge. An experienced anesthetist is essential, as Joris et al. showed that, even during induction of pneumoperitoneum, there is a catecholamine surge and rise in systolic blood pressure. However, the main spike occurs during the procedure, with manipulation of the gland [13]. Nevertheless, the benefits of LA for pheochromocytoma have been underlined by our unit [14] as well as several large studies over the last decade [5, 15, 16].

The question of size has been debated with no concrete definition of an appropriate cut-off level. With technical advances, the indication for LA have been successfully expanded from small (<6 cm) benign lesions to tumors >6 cm. Our unit has previously reported that a LA has been considered safe even for larger adrenal neoplasms that have no preoperative or intraoperative evidence of malignancy [17].

Contraindications to LA

Relative contraindications to LA include morbid obesity and multiple previous abdominal operations with known

adhesions. Previous abdominal operations should not be an immediate contraindication as initial laparoscopic assessment and division of adhesions may still provide an appropriate and safe working environment [18]. Laparoscopic abdominal procedures are increasingly common, and Morris and colleagues have shown that prior surgery does not impede nor contraindicate LA and that patients are afforded the same benefits intraoperatively and postoperatively [19].

General contraindications to LA include severe non-correctable coagulopathies, uncontrolled hypertension, severe sepsis, and severe cardiac pathology (severe heart failure, severe aortic stenosis and mitral valve insufficiency) [20].

Absolute contraindications to LA apply in the situation of a lesion with demonstrated local invasion that would require en bloc resection for adequate oncological outcomes. The use of LA to remove primary or secondary malignant adrenal neoplasms continues to be debated but is now no longer considered an absolute contraindication and has been demonstrated to give comparable oncological results in some units [21].

Operative Technique: Lateral Transperitoneal Approach

The adrenals are relatively small organs sitting high in the retroperitoneum requiring a large incision via the anterior approach to obtain access [22]. The trauma caused by the surgical access far exceeds that of the procedure itself. This shortcoming of OA has been entirely eliminated by the advent of LA.

Access: Patient Position and Trochar Placement

The positioning of the patient is vital in LA. A well-positioned patient can facilitate access to the adrenal gland and improve ergonomics for the surgeon, while a poorly positioned patient can limit operative access, cause difficulties in trochar placement and frustration to the surgeon. The keys to the patient positioning are: (1) maximal distraction of the distance between the costal margin and iliac crest in the lateral decubitus position; (2) stable and secure support of the patient to allow table rotation and movement, and avoid loss of position intra-operatively; and (3) adequate protection of all pressure points.

After induction of general anesthesia, the patient is placed in the lateral decubitus position with the side of the adrenal lesion facing up. If a beanbag is used, it should be placed under the patient before induction. Alternatively, the lateral decubitus position can be maintained with side supports. Before securing the patient in that position, the

patient is positioned with the anterior superior iliac spine over the break point of the table and the table flexed in an inverted “V” position to allow maximal distraction of the space between the costal margin and iliac crest. This angle varies between individuals. Once in a satisfactory position, the patient position is secured with the beanbag suctioned or side supports tightened, ensuring that these supports do not encroach into the operative field.

A soft axillary roll, or a liter bag of fluid, should be placed under the axilla to relieve pressure. The lateral malleolus and lateral peroneal nerve of the bottom leg should be padded. A pillow is placed between the legs to support the top leg. Additional tape can be used to further secure the patient to the table, especially to prevent rotation of the upper chest and legs. The shoulder of the uppermost arm should be at least 90° from the torso, and can be rested on a pillow or arm brace.

The first port is placed 2–4 fingerbreadths below the costal margin, along the anterior axillary line. A cut down is performed with entry into the peritoneal cavity under direct vision. A balloon port is used to facilitate a seal. Following pneumoperitoneum at 12–15 mmH₂O with CO₂, the working ports can be inserted under direct vision on either side of the camera port, with at least 5 cm distance between ports to allow adequate triangulation. At least one of these working ports should be a 10-mm port to allow for passage of a vascular stapling device if required. Alternatively, two 5-mm ports can be used with conversion to a 10-mm port as required. A fourth, 12-mm, port is usually required for a liver retractor for a right LA.

Right LA

The right lobe of the liver is mobilized by dividing the right triangular ligament and the liver retracted medially with a fan or paddle retractor via an epigastric port. Care should be taken to avoid avulsion of hepatic accessory veins draining from the caudate lobe directly into the IVC [23, 24]. With the right hepatic lobe retracted, the IVC, adrenal lesion and right kidney should be identified before proceeding.

The plane between the medial edge of the adrenal gland and the lateral edge of the IVC is developed, and it is within this plane that the right adrenal vein is expected to be encountered. The plane is developed along the entire medial border of the gland, as posteriorly as the psoas muscle. Anatomical variations such as drainage into accessory hepatic veins or duplicate right adrenal veins have been reported in 13 % of autopsy series, and therefore care should still be taken in dissecting this plane after division of a right adrenal vein [23, 24]. The vein can be ligated by a variety of methods including an energy-sealing device, clips and vascular stapler, depending on the size

[25]. As the dissection of this plane proceeds inferiorly, an accessory branch of the renal artery may be seen heading toward the superior renal pole. It should be preserved to avoid infarction of the renal pole. The inferior limb of the adrenal gland may extend as far inferior as the renal hilum and therefore inadvertent injury to the hilar vessels must be avoided during dissection of a low lying limb.

Once the medial adrenal border is defined, dissection can be continued laterally by separating the inferior adrenal border from the superior renal pole, and superiorly by lifting the adrenal gland off the psoas muscle. Separating the gland from the lateral and superior attachments completes the dissection. This part of the dissection is best done with an energy sealing device as the arteries feed into the adrenal gland from its periphery [25].

Left LA

The left LA begins with defusing the spleen by dissecting the small peritoneal attachments from the greater omentum. The plane between the splenic flexure, mesocolon and the kidney is developed and the spleen is mobilized by dividing the lienorenal ligament, and continuing the dissection onto the posterior surface of the pancreatic tail and splenic vessels. The diaphragmatic attachments of the spleen are divided superiorly until the fundus of the stomach is in view, and the spleen medially rotated without retraction. The retroperitoneum is opened along the medial border of the adrenal gland, and the left adrenal vein identified. A guide to this vein is the inferior phrenic vein, which drains into the left adrenal vein before it drains into the left renal vein. Alternatively, the left renal vein could be a guide to the adrenal vein.

Once the adrenal vein has been ligated, the gland can be dissected off its attachments from the superior renal pole and psoas muscle in a medial-to-lateral and inferior-to-superior manner, with an energy-sealing device.

Special Considerations

While observing the standard principles of LA as described above, additional technical pointers may further facilitate excision of particular types of lesions. When excising a pheochromocytoma, it is useful to “dissect the patient away from the tumor”, and avoid handling the tumor directly. Excessive pressure on the tumor may cause a surge of catecholamine release into the circulation resulting in hemodynamic lability. The gland should never be grasped; if necessary, periadrenal fat, the disconnected vein or retroperitoneal fascia may be used as “handles” to gently retract the tumor. Early ligation of the adrenal vein also helps minimize catecholamine release.

In resections of metastatic deposits in adrenal glands, it is important to observe the oncological principle of en bloc resection to include the peri-adrenal fat [26•]. Not only is it oncologically sound, an en bloc resection also avoids having to dissect the gland through malignancy-induced inflammatory adhesions. Although it is usually desirable to control the adrenal vein early in the procedure and start the dissection on the medial side, it may be difficult to do so with large tumors. In such cases, mobilization of the lateral and inferior borders of the gland may facilitate access to the medial border for ligation of the adrenal vein. In cases of large spleens, a fourth port may be required for additional retraction.

Surgical Outcomes

Complications

There is a large body of evidence to support laparoscopic adrenalectomy as the gold standard for surgery to remove the adrenal gland. Indeed, benefits such as reduced pain, reduced ileus, reduced perioperative morbidity, less blood loss, earlier return to full activity and improved cosmesis are all clearly seen with the laparoscopic approach compared with the open approach in adrenal surgery.

By far the most common intraoperative complication is hemorrhage. The cumulative rate is up to 40 % of overall complications [27]. Laparoscopic control of this can range from increasing insufflation pressures, simple electrocautery and placement of endoscopic clips and ligatures, but in some rare cases, conversion to an open laparotomy is required. Conversion to open surgery was documented to be as high as 6 % in some early studies [28] during the evolution of the technique to a low of only 0.6 % in a recent large study by Kulis and colleagues [29•].

Other intraoperative morbidity that arises includes injury to viscera and solid organs including the kidney, liver and spleen [30]. Assalia and Gagner [27] quoted a intraoperative complication rate of 9.5 % in their review of the literature in 2004, although the accuracy of this figure was difficult to ascertain due to a lack of a standardized definition.

Although both LA and OA are reported to have low mortality rates, the mortality rate associated with LA was significantly lower (0.6 vs. 1.3 %, $p < 0.0001$) [2•]. Similarly, LA has been consistently found to have a lower morbidity rate than OA (4.5 vs. 7.8 %, $p < 0.0001$), and shorter length of stay (3.2 vs. 5.2 days, $p < 0.0001$) [2•, 31, 32].

Outcomes Comparison Between Open and Laparoscopic Adrenalectomy

To date, no prospective randomized controlled trials comparing LA with OA. Nevertheless, the trend in the last

20 years has been undisputedly in favor of LA. Multiple retrospective studies that have analyzed the safety, efficiency and outcomes of LA versus open adrenal surgery (Table 1). Despite blood loss being a significant complication in LA, it still remains lower than the estimated blood loss that was measured in an OA. As a reflection of this, the requirement for postoperative blood transfusions is also higher for the OA group.

The one aspect of LA that was variable between studies was that of total operative time. There is a trend towards a longer operative time in the laparoscopic approach compared to the open approach amongst early adopters of the technique. However, with the advancement of technology and modernization of laparoscopy together with experience and familiarity with the procedure, the trend has shifted to a shorter operative time [21], and in a recent case series of 306 patients by Kulis and colleagues [29•], the operative time has been slashed to <100 min.

In the comparative studies of LA and OA, LA patients also benefited from an earlier discharge from hospital compared to OA patients and has the clear advantage of a earlier return to a normal diet [33] and earlier resumption of normal activity [34]. The benefit of a laparoscopic approach was further underlined in the comparative studies that measured analgesic requirements, showing LA patients requiring far less analgesics compared to their OA counterparts [35–37].

The long-term operative morbidity is indeed also lower for LA patients, no doubt benefiting from much smaller wounds. In series which had long-term follow-up, the finding was that patients underwent OA for various reasons had a much higher wound complication rate, up to 54 % in a posterior OA group [36]. This finding is supported by data from Imai et al. [35], with a late wound complication rate of 47.5 % in the OA group compared to zero in the LA group.

The lateral transperitoneal approach is our preferred method of LA. It affords familiar anatomical landmarks and provides a larger working space [17, 38, 39].

Outcomes Analysis for Malignant Adrenal Masses

Primary Adrenal Malignancy

The adoption of LA for malignant neoplasms of the adrenal gland has been met with mixed reviews. The main concern lies with gland rupture and subsequent locoregional as well as port-site recurrence [12, 40, 41].

The debate on whether LA is oncologically adequate for resection of adrenocortical cancer (ACC), considering the impact of resection margin status on recurrence and survival, is ongoing. There is currently insufficient published data to settle this debate. Of the available literature,

methodological flaws such as selection bias, small numbers, and short follow-up periods make interpretation difficult [42•].

A relatively large recent study looking at 152 patients with ACC and comparing LA ($n = 35$) and OA ($n = 117$) demonstrated that, for smaller lesions (≤ 10 cm), a patient under going LA had similar oncological outcomes compared to having an OA [43•]. They found similar outcomes with regards to disease-specific survival, disease-free survival, tumor capsule violation or peritoneal carcinomatosis. However, in an attempt to standardize patient groups, this study suffered from selection bias.

A similar study has also been conducted in the past, examining the laparoscopic approach to the adrenal gland for both primary adrenal and secondary tumors. Porpiglia and colleagues [44] found comparable outcomes with 18 cases of LA and 25 cases of OA in patients with Stage I and II ACC, with comparable disease-free survival [42•, 44].

Although the conclusion that LA is oncologically not inferior to OA in localized ACC under 10 cm, the authors stated that LA is justified for potentially malignant adrenal incidentalomas and selected cases of Stage I and II ACC. However, again, this needs to be interpreted with caution as the patients were recruited from a national registry involving many treating centers and surgeons [42•].

Given the variability in the results from the literature, we would favor not undertaking LA for a patient with a high suspicion of ACC even if the lesion is small (< 6 cm) [45, 46].

Secondary Adrenal Malignancy

Non-small cell lung cancer, gastrointestinal, renal and melanoma are known to metastasize to the adrenal glands [47]. Kebebew and colleagues [45] concluded that a laparoscopic approach to suspected malignant adrenal lesions may be of potential diagnostic and therapeutic potential. The same study also concluded that LA for unsuspected ACC is associated with higher recurrence, likely due to possible tumor spillage or incomplete resection. Moinzadeh and Gill concluded in their series of 31 patients that LA for small, organ-confined adrenal metastases provided acceptable perioperative and oncological outcomes.

A larger study by Strong et al. [21] compared both OA and LA for isolated adrenal metastases. They found no difference in terms of margin status, local recurrence and overall survival, but LA provided better intraoperative and perioperative outcomes.

In summary, it seems that the benefits of LA are quite variable for selected cases of primary and secondary adrenal malignancy. Therefore, before more conclusive evidence becomes available, the choice of operative approach for potentially malignant or malignant adrenal tumors should depend on surgeon and center experience, likelihood of malignancy and local invasion, and tumor size. If LA is the chosen approach, a low threshold for conversion should be adopted if there are concerns regarding a satisfactory oncological resection and before

Table 1 Outcomes comparison between open and laparoscopic adrenalectomy

Series and year	Number of patients	Tumour size (cm)	Operative time (min)	Estimated blood loss (cc)	Length of stay (days)	Morbidity (%)	Time to regular diet (days)	Time to return to normal activity
Strong et al. [21]	31 Lap	NR	175 $\pm$ 9	106 (78–134)	2.8 $\pm$ 0.4	0	NR	NR
	63 Open	NR	208 $\pm$ 13	749 $\pm$ 108	8.0 $\pm$ 0.5	11	NR	NR
Ramachandran et al. [39]	22 Lap	3.3 $\pm$ 0.56	199.7 $\pm$ 14.3	NR	3.95 $\pm$ 0.32	14	NR	NR
	23 Open	2.4 $\pm$ 0.40	143.7 $\pm$ 5.9	NR	10.16 $\pm$ 0.83	39	NR	NR
Haveran et al. [61]	45 Lap	4.3 (0.5–11)	171 (90–375)	96 (10–500)	2.5 (2–8)	4	1.9 (0–4)	NR
	19 Open	5.5 (1–10)	229 (100–550)	371 (5–1,200)	5.8 (3–12)	47	4.4 (1–7)	NR
Prager et al. [62]	102 Lap	3.8 (3.0–10.0)	NR	NR	NR	9	NR	NR
	48 Open	6.8 (2.0–16.0)	NR	NR	NR	21	NR	NR
Barreca et al. [34]	79 Lap	3.9 (1.5–9.0)	168.6 (60–400)	208 (50–700)	4.2 (2–15)	5	NR	18.8 (7–28) days
	93 Open	3.8 (1.5–9.0)	132.3 (60–305)	269 (50–700)	10 (3–30)	10	NR	29.4 (14–67) days
Hazzan et al. [37]	28 Lap	3.6 (0.5–8)	188	NR	4	16	2	2.2 weeks
	24 Open	2.9 (0.5–7)	139	NR	7.5	39	3.9	5.2 weeks
Imai et al. [35]	40 Lap	2.8 $\pm$ 1.7	180	40	12	5	1.3	NR
	40 Open	2.7 $\pm$ 1.4	127	162	18	50	1.3	NR
Thompson et al. [36]	60 Lap	2.9	167	NR	4.1	6	NR	3.8 weeks
	50 Open	2.9	127	NR	5.7	18	NR	7 weeks
Brunt et al. [31]	24 Lap	2.7 $\pm$ 1.4	183 $\pm$ 35	104	3.2 $\pm$ 0.9	NR	NR	NR
	25 Open	3.4 $\pm$ 1.4	142 $\pm$ 38	408	8.7 $\pm$ 4.5	NR	NR	NR

NR not recorded

the occurrence of irreversible events such as violation of tumor capsule.

Other Considerations

Single Port Access Laparoscopic Adrenalectomy

Evolving technology has allowed the evolution of single incision laparoscopic surgery (SILS) to be employed in various procedures. Articulated instruments and a specialized laparoscope introduced through a single, albeit larger, laparoscopic port are used. Post-operative benefits include reduced analgesic requirements and improved cosmesis with a single scar [48, 49]. However, the downsides include spatial unfamiliarity, the requirement and subsequent cost for specialized instruments as well as port-site congestion despite the use of articulated instruments to prevent operator and assistant interference.

In the case of SILS adrenalectomy, the technique was first described by Castellucci and colleagues in 2008 [50]. There have been several subsequent reports and series examining the efficacy of SILS in adrenalectomy. In most instances, an additional port is sometimes required to aid in organ retraction. Rane et al. [51] reviewed the available literature and examined the outcomes in SILS adrenalectomy versus the conventional laparoscopic approach. They concluded that operative time was longer in SILS compared to the conventional laparoscopic approach, but analgesic requirements were reduced post-operatively. One significant hurdle was the longer mean operative time, a reflection of multiple factors both at the operator and instrument level, factors that may improve with familiarity and newer technology.

Laparoscopic Retroperitoneal Adrenalectomy

Given the normal location of the adrenal glands in the upper retroperitoneal space, a laparoscopic retroperitoneal (LR) approach has been viewed by some as an evolution of the traditional transperitoneal LA approach. Certainly, a direct retroperitoneal approach confers faster operative access without the need to traverse the peritoneal cavity and avoiding intra-peritoneal organs. Without the need to enter the peritoneal cavity and irritate abdominal viscera, the risk of ileus and need for analgesia is potentially further diminished.

A large series of 560 procedures by Walz et al. [52] demonstrated that, in experienced hands, LR adrenalectomy is safe and potentially faster than a trans-peritoneal approach. Lee and colleagues [53] demonstrated that a LR approach elevated the peri-operative benefits initially demonstrated with the advent of transperitoneal LA versus OA. Indeed, LR adrenalectomy has also been shown to be

effective in Conn's adenomas and hyperplasia [54] and in pheochromocytoma [55, 56].

Robotic Adrenalectomy

The advent of robotic surgery and its purported benefits with a tremor-free three-dimensional imaging, improved operator ergonomics, improved instrument manoeuvrability and improved cosmesis compared to conventional open surgery have been documented since being described in the early 2000s [57, 58]. Disadvantages compared to traditional laparoscopic surgery include the lack of tactile feedback, especially when approaching a fragile organ such as the adrenals, longer operating times, and the significant cost associated with robotic surgery. Brunaud and colleagues [59] compared the advantages and disadvantages of robotic adrenalectomy (RA) with the traditional transperitoneal LA. In a large series of 109 patients, with 50 undergoing RA and 59 undergoing LA, they found that RA was associated with lower blood loss and longer operating times which ceased to be significant once a learning curve had been overcome. They found that RA was approximately 2.3 times more costly than traditional LA but, like other studies, the cost-benefit ratio may improve with multi-specialty use of the robot and sharing of expenses at larger centers [59, 60].

Conclusions

The evolution of the laparoscopic transperitoneal approach to adrenal surgery has been significant in the last 20 years. It has proven to be a reproducible and safe procedure with identical or improved operative and perioperative outcomes when compared to OA. LA has virtually replaced OA in nearly all aspects of adrenalectomy. Undoubtedly, we will see further adaptation of LA as technology continues to improve and outcomes analysis of newer approaches to LA come to hand.

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