

Review Article

An Update on Minimally Invasive Adrenalectomy

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Abstract

Adrenal tumors require careful clinical and biochemical evaluation with appropriate imaging to determine malignancy or functional status. Tumors that are suspicious or confirmed for malignancy or hormone-secreting require adrenalectomy. This review discusses adrenal gland anatomy, physiology, and pathology, indications for adrenalectomy, preoperative management, and an update on surgical approaches with an emphasis on minimally invasive techniques. We describe the transabdominal and retroperitoneoscopic approaches to adrenalectomy and briefly discuss extensions of minimally invasive surgery including robotic-assisted and single portadrenalectomy.

Keywords

- Minimally invasive surgery
- Adrenalectomy
- Laparoscopy
- Posterior retroperitoneoscopic adrenalectomy
- Laparoscopic transabdominal adrenalectomy

ABBREVIATIONS

ACC: Z adrenocortical Carcinoma; PRA: Posterior Retroperitoneoscopic Adrenalectomy; IVC: Inferior Vena Cava; RAA: Robot-Assisted Adrenalectomy; SILS: Single-Incision Laparoscopic Surgery; LESS: Laparoendoscopic Single-Site; LA: Laparoscopic Adrenalectomy

INTRODUCTION

Though surgical approaches to adrenalectomy continue to evolve, minimally invasive laparoscopic adrenalectomy has become the gold standard for resection of adrenal tumors in the last decade. It was first reported in the literature in 1992 and has subsequently changed the management of adrenal tumors [1]. Since then, minimally invasive adrenalectomy has been shown to have decreased length of stay, reduced healthcare cost, fewer wound complications, less blood loss, earlier patient mobility, and faster return to regular activity [2-4]. This review discusses the adrenal gland anatomy, physiology, and pathology, indications for adrenalectomy, preoperative considerations, and surgical approaches.

ANATOMY, PHYSIOLOGY, AND PATHOLOGY OF THE ADRENAL GLAND

The adrenal gland is composed of two distinct units: the outer cortex and inner medulla. The cortex is mesoderm-derived and further divided into three zones: glomerulosa, fasciculata, and reticularis. Mineralocorticoids such as aldosterone are produced in the glomerulosa and play a key role in regulating blood pressure and electrolytes via the renin-angiotensin-aldosterone system. Cortisol, produced in the fasciculata, exerts a variety of systemic roles in metabolism and immune functioning. The deepest layer of the cortex, the reticularis, produces androgens

and sex hormones. The adrenal medulla is derived from the ectoderm layer and produces epinephrine and norepinephrine in direct response to the sympathetic nervous system. Each gland is located in the retroperitoneum, perched atop the superior pole of the kidney. The right adrenal gland is pyramidal in shape and sits between the liver and diaphragm. The left adrenal gland is crescent shaped and lies between the left kidney and aorta. A rich arterial supply to the adrenal gland consists of branches derived segmental from the inferior phrenic artery, the aorta, and the renal artery. Venous drainage is carried from various tributaries into a single adrenal vein. The left adrenal vein is longer than the right and drains into the left renal vein before draining into the inferior vena cava (IVC) while the right main vein is short and drains directly into the IVC.

Dysfunction of the adrenal gland produces various endocrine disorders. Benign lesions of the adrenal cortex include adenomas, lipomas, adrenal cortical hyperplasia and myelolipomas. Malignant tumors of the adrenal cortex include adrenocortical carcinoma (ACC). Tumors of the adrenal medulla consist of benign and malignant pheochromocytoma that may belong to a hereditary disorder such as multiple endocrine neoplasia syndrome type 2, von Hippel-Landau disease, or neurofibromatosis. The rich vascular network of the adrenal gland enables metastases from many primary sources such as the kidney, lung and colon.

INDICATIONS FOR ADRENALECTOMY

With the widespread use of computed tomography (CT) and magnetic resonance imaging (MRI) in clinical practice, the prevalence of incidental adrenal masses has increased such that the term adrenal incidentaloma was coined. Defined as a mass greater than 1 cm in diameter detected during imaging

performed for other indications, adrenal incidentalomas had a prevalence of 4.4% in one prospective study among subjects undergoing CT scans for other indications [5]. Comparably, in autopsy prevalence studies, the mean incidence of adrenal tumors was found to be approximately 6% [5]. Adrenalectomy is indicated for suspected or confirmed malignancy and hormone-secreting adrenal masses [6].

IMAGING

Radiographic imaging is a key to differentiating malignant from benign adrenal lesions. The assessment of tumor size, morphology, CT density, MRI signal characteristics, and enhancement after administration of contrast are critical for diagnostic evaluation and work up. Tumor diameter has been highly correlated with the risk of malignancy: adrenocortical carcinomas are significantly associated with increased size, with 90% being larger than 4 cm in diameter at the time of discovery in one study [7]. However in retrospective review the 4 cm diameter cutoff has a high sensitivity (93%) for malignancy but poor specificity (43%) [8]. Therefore, adrenal incidentalomas greater than 4 cm when discovered are more concerning for malignancy and warrant either close surveillance or resection.

In addition to size, imaging phenotype plays an important role in distinguishing adrenal lesions. Benign adrenal tumors are typically <4 cm in diameter, stable in size over time, homogenous in density, with smooth surfaces and intact planes between organs. Conversely, malignant masses are often >6 cm in size with growth over time and heterogeneous on imaging with irregular borders and lack clear planes [9]. Additionally, adrenal cortical carcinoma has greater density on non-contrast CT, usually >25 HU, and peripheral enhancement on CT post-contrast in comparison to benign masses which are typically <10 HU and demonstrate little to no enhancement [10].

BIOCHEMICAL EVALUATION

Initial evaluation of an adrenal mass requires a combined clinical and biochemical approach in order to evaluate if an adrenal tumor is malignant and/or functional. Biochemical evaluation varies depending on the suspected hormone-secreting adrenal tumors. However, all patients with an adrenal mass on imaging should have a workup including plasma or urinary metanephrines to rule out pheochromocytomas prior to any invasive procedure. A summary of common symptoms and suggested workup for hormone-secreting adrenal tumors is presented in Table (1).

PREOPERATIVE MANAGEMENT

Preoperative management should be tailored to each patient and must take into account the tumor type. For example, patients with a pheochromocytoma are at risk for intraoperative hemodynamic instability. Alpha-adrenergic blockade is typically administered 10-14 days preoperatively to control hypertension. If a patient is tachycardic, then beta-blockade may be added. Concurrently, volume expansion is key prior to resection of a pheochromocytoma. Patients are encouraged to increase their fluid and sodium intake because high levels of catecholamines induce volume contraction and alpha-adrenergic blockade can induce postoperative orthostasis. Patients with cortisol-secreting

tumors, on the other hand, may experience hypotension due to adrenal insufficiency following adrenalectomy. These patients may require intravenous perioperative steroids with transition to an oral taper as an outpatient. In all cases, close collaboration with the anesthesia team is required in order to prepare for intraoperative hemodynamic changes.

MINIMALLY INVASIVE SURGICAL APPROACHES

Various minimally invasive approaches to the adrenal glands have been adopted. The laparoscopic transabdominal approach was first described by Gagner et al., [1], and retroperitoneal by Mercan et al., [11]. The major advantages, disadvantages, and contraindications are listed in Table (2), followed by a summary of the different techniques [12,13].

LAPAROSCOPIC TRANSABDOMINAL APPROACH

Patient positioning

After induction of general anesthesia, the patient is placed in a lateral decubitus position with the side with the adrenal gland

	Symptoms	Workup
Pheochromocytoma	Hypertension Headache Palpitations Sweating	Plasma free metanephrines 24-h urinary fractionated catecholamines and metanephrines
Corticosteroid-Producing Tumors	Centripetal obesity Plethora Moon face Skin atrophy and bruising Hypertension Glucose intolerance Gonadal dysfunction Muscle weakness	24-h urinary free cortisol 1 mg overnight dexamethasone suppression test Midnight salivary cortisol test
Aldosterone-Producing Tumors	Hypertension Headache Arrhythmias Muscle cramps	Serum aldosterone to renin ratio

Table 2: Comparison of laparoscopic transabdominal adrenalectomy and posterior retroperitoneoscopic adrenalectomy.

	Laparoscopic transabdominal adrenalectomy	Posterior retroperitoneoscopic adrenalectomy (PRA)
Advantages	Wide operative field Easy to combine with other transabdominal procedures Easy to convert to open approach	Safer in cases with abdominal adhesions No repositioning needed for bilateral adrenalectomy
Disadvantages	Repositioning required for bilateral adrenalectomy May be challenging in previously operated fields	Small working space limits size of lesions suitable for this approach Not recommended for obese patients
Contraindications	Known or highly suspected malignancy with local invasion	

to be resected facing up. Using the costal arch as a fulcrum, the patient's flank is stretched by lowering the trunk and legs to widen the working space between the costal margin and the iliac crest. The operating surgeon is positioned on the opposite side of the adrenal gland to be removed. First and second assistants are on the same side respectively to the right and to the left of the operating surgeon. The patient should be draped down to the midline of the abdomen, and the costal margin and midline marked. Entry technique of the surgeon's choice may be used to enter the abdominal space and place the first 10 mm trocar (T1) 3 cm under the costal arch at the anterior axillary line. A 30° scope is used with this trocar to later extract the specimen. After insufflating the abdominal cavity to 15 mm Hg, inspection for intra-abdominal adhesions should be performed. Additional trocars may be positioned at least 5 cm to the left (T2 10-12 mm) and right (T3 5 mm) of the initial port and 1-5 cm from the costal arch. A fourth trocar, T4, may be placed in the paraxiphoid area for liver retraction.

Right flank transabdominal laparoscopic adrenalectomy

The patient is placed right flank up for a right adrenalectomy. The right adrenal gland sits under the right liver lobe, lateral to the inferior vena cava (IVC), inferior to both superior pole of the kidney and the right renal vein. After trocar and scope placement, a liver retractor may be used to mobilize the liver and retract it medially, exposing the adrenal gland and the IVC (Figure 1). Using blunt dissection and electrocautery, a plane is created between the adrenal gland and IVC. The right adrenal vein drains directly into the IVC and can be located by dissecting the gland on its medial border. Once it is clearly separated, the adrenal vein is doubly ligated with clips, and the remaining medial and inferomedial attachments are divided. Once the adrenal gland is lifted, the avascular posterior and lateral attachments may be ligated. The gland is placed in a specimen pouch and removed from the largest port site. The fascia for the extraction trocar site is then closed.

Left flank transabdominal laparoscopic adrenalectomy

The patient is placed left flank up for a left adrenalectomy. Three trocars are inserted in the subcostal space as described

above with an optional fourth inserted 4-5 cm below the first one that can be used for gentle retraction. The lack of major anatomical landmarks like the IVC, smaller size of the left adrenal vein and presence of pancreatic tail in the operative field can make left adrenalectomy challenging. First the splenic flexure is mobilized and the colon is swept inferiorly. Next the splenoparietal ligament is dissected up to the diaphragm for total mobilization of the spleen. Then, the splenorenal ligaments are retracted medially and anteriorly and divided. Careful dissection of the posterior surface of the spleen followed by the tail of the pancreas is performed, maintaining a plane between the pancreas and left kidney. Once the spleen and tail of the pancreas are retracted medially, an additional trocar may be placed for retraction. The adrenal gland should be visualized adjacent to the superior pole of the kidney, and blunt dissection and electrocautery may be used to dissect the medial edge of the adrenal gland from upper to lower pole. During this dissection, the left adrenal vein, which drains into the left renal vein, is isolated, doubly clipped and divided. Lifting the adrenal gland up exposes its posterior aspect, allowing for dissection of the remaining attachments at the posterolateral edge. Once the gland is mobilized it is removed via extraction bag.

Posterior Retroperitoneoscopic Approach

After induction of general anesthetic, the patient is placed in the prone, jack-knife position with all pressure points padded, in order to maximize space between the posterior costal margin and the posterior iliac crest. The surgical team is positioned on the same side as the adrenal lesion. Important landmarks are the 12th rib and iliac crest. A 1.5 cm transverse incision is made below the tip of the 12th rib, and blunt and sharp dissection is used to reach the retroperitoneal space. Using finger guidance, two 5-10 mm trocars are placed 4-5 cm in the mid axillary line and sacrospinalis muscle, respectively. A blunt trocar with inflatable balloon and adjustable sleeve is then placed in the initial incisional site to insufflate retroperitoneal space to 20-25 mmHg. A 5-10 mm 30° endoscope is introduced into the first trocar and used for retroperitoneoscopy while the lateral two ports are used by the operating surgeon.

The Zuckerkandl's fascia is then opened using blunt and sharp dissection to access the retroperitoneum. The first and most important landmark in PRA is exposure and dissection of the upper pole of the kidney. The operative field is thus demarcated by the kidney upper pole caudally, the diaphragm cranially, the peritoneum laterally, and the spine medially. Dissection of the kidney upper pole exposes the inferior edge of the adrenal gland. By lifting the adrenal gland, the surgeon can identify the adrenal vein. For a right adrenalectomy, lifting the gland exposes the IVC which drains the short right adrenal vein. After dissecting free the adrenal vein, it is divided between clips. In a left adrenalectomy, it is possible to use the diaphragmatic vein joining the main left adrenal vein between the adrenal gland and the diaphragmatic branch as a landmark to identify the left adrenal vein. Once dissected, the left adrenal vein can then be sectioned between clips. The remaining adrenal attachments are then dissected, and the resected adrenal gland may be extracted via specimen bag in the middle port.

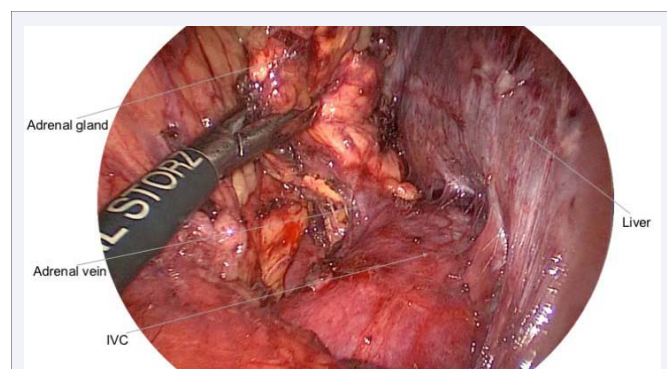


Figure 1 Right adrenalectomy exposing the right adrenal vein draining into the inferior vena cava (IVC).

OTHER APPROACHES

Robotic-Assisted Adrenalectomy (RAA)

As advances in minimally invasive procedures continue to be made, surgeons have explored the use of RAA. First described in 2001, RAA has now been used in both PRA and transabdominal adrenalectomy [14]. Proponents of this technique cite the two-dimensional view and poor ergonomics for the surgeon in laparoscopic adrenalectomy (LA) as reasons for using RAA to perform more precise surgery. The literature reports similar effectiveness and short-term outcomes in RAA and LA [15,16]. While others have described significantly longer operative times with RAA than LA [17,18], other authors showed that operative time improves with increased experience after the initial learning curve [19,20]. Finally, many authors report no difference in morbidity and mortality between RAA and LA [15–18,20,21]. RAA may be preferred in cases of bilateral adrenalectomy to perform cortical sparing adrenalectomy to avoid steroid dependence and for PRA it may be useful in patients with glands above the 12th rib [22].

Single port technique

Single-incision minimally invasive surgery known as single-incision laparoscopic surgery (SILS)/laparoendoscopic single-site (LESS) adrenalectomy is also of interest for addressing adrenal pathology. Although LA is less morbid and offers superior cosmetic results to open adrenalectomy, it still requires multiple incisions, each of which carries risk of pain, port-site complications, and scarring. SILS/LESS adrenalectomy has been developed to address these points and has been used in both PRA and transabdominal cases. The most recent meta-analysis by Wu et al., in 2016 concluded that LESS adrenalectomy is a safe alternative to LA with shorter hospital stay and better post-operative pain scores in certain patients [23]. Similar to older reports [24,25], Wu et al did not find significant differences in operative time, perioperative complications, and estimated blood loss. Data on this approach remains limited and further research is necessary to better understand its limitations and benefits.

Open Approach

Although LA is now the gold standard for adrenalectomy, the open approach is still required for certain indications. More often, tumor characteristics make open adrenalectomy preferable over a laparoscopic approach. Historically, tumor size >6 cm and significant risk of ACC were seen as contraindications to a minimally invasive approach. Newer data makes the case that size exceeding 6 cm is not an absolute contraindication, especially in the absence of local invasion [26]. An open approach is the current recommendation for patients with evidence of malignancy and local invasion on preoperative imaging studies to allow for complete resection, lymph node dissection, and en bloc resection of adjacent structures.

DISCUSSION & CONCLUSION

Adrenal tumors discovered incidentally or otherwise, should have appropriate biochemical evaluation and imaging as part of work up to determine malignancy and functional status. Suspected or confirmed malignancy and hormone-secreting

adrenal tumors should be treated with adrenalectomy. Minimally invasive adrenalectomy is effective, safe, and decreases hospital stays, operative blood loss, and wound complications. Since its introduction, it has become the standard of care for resecting adrenal tumors. Both the transabdominal and posterior retroperitoneoscopic approaches are appropriate for most adrenal pathology. Traditionally, the transabdominal approach has been the standard method although PRA has demonstrated increasing popularity amongst surgeons. Two recent studies, including a systematic review of eight studies comparing PRA to transabdominal adrenalectomy [27], and a randomized clinical trial of PRA versus transabdominal adrenalectomy [28], found PRA to be superior or at least comparable to the transabdominal approach in blood loss, operative time, pain score, length of stay, and return to activity. The feasibility of minimally invasive adrenalectomy as an ambulatory procedure remains uncertain, with one study reporting an 100% success rate in 22 cases [29] and other studies using perioperative variables to identify candidates for early discharge [30]. More recently, extensions of minimally invasive adrenalectomy have been explored, including robotic-assisted adrenalectomy and single-incision technique, with promising results. An open approach is still recommended for known or highly suspicious malignancy with local invasion.

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