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REVIEW

Minimally invasive techniques in benign and malignant adrenal tumors

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Abstract

Minimally invasive adrenalectomy has become the main treatment modality for most adrenal lesions. Both laparoscopic transabdominal and retroperitoneoscopic approaches are safe and feasible options, each with respective advantages, including better surgical outcomes, fewer complications, and faster recovery over open adrenalectomy. While open surgery remains a valid modality in treatment of adrenocortical cancer in the presence of some findings such as invasion, robotic platforms, and minimally invasive surgery have gained popularity as technology continues to evolve. Organ preservation during adrenalectomy is feasible in some conditions to prevent adrenal insufficiency. Ablative technologies are increasingly utilized in benign and malignant tumors, including the adrenal gland, with various outcomes. A multidisciplinary team, an experienced surgeon, and a high-volume center are recommended for any surgical approaches and management of adrenal lesions. This review article evaluated recent findings and current evidence on minimally invasive adrenalectomy.

Key Words: Adrenalectomy; Laparoscopy; Retroperitoneoscopic; Minimally invasive surgery; Robotic

Core Tip: Minimally invasive adrenalectomy is the standard treatment for most adrenal lesions. Options to approach the adrenal gland include a transabdominal or retroperitoneoscopic route *via* laparoscopy or robotic platform. While each presents their own advantages, all are safe and produce excellent outcomes. Although open surgery for adrenocortical carcinoma remains suitable in some situations, partial adrenalectomy may be appropriate in certain cases to prevent adrenal insufficiency.

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INTRODUCTION

Minimally invasive surgery has become the standard therapy for most adrenal neoplasms, widely accepted since the first laparoscopic adrenalectomy was reported by Wagner *et al*[1]. With its multilayered anatomy and localization, minimally invasive adrenalectomy offers several current surgical options. It can be performed through either a transabdominal or retroperitoneoscopic approach using laparoscopy or robot-assisted surgery. Each route and technique offers remarkable advantages and disadvantages (Table 1)[2].

With the increasing use of diagnostic imaging modalities, adrenal masses are commonly encountered as so-called incidentalomas[3]. Its prevalence varies between 1% and 7% depending on the data source (autopsy *vs* radiology) and population (age, sex), being slightly more common in females[4-7]. While almost equal distribution of incidentalomas on the right and left sides has been reported, bilateral of nodules may present in up to 15% of cases[3,8].

In general, if the nodule is producing excess hormone (functional) or suspected of primary or secondary malignancy, surgery is indicated[9]. Almost all nodules - even malignant in some cases - can be treated with minimally invasive surgical techniques depending on the experience of the surgeon, facilities of the institution, and the patient's and/or tumor's characteristics. Adrenal-sparing surgery has gained popularity for preventing insufficiency in terms of long-term morbidity[10]. In rare situations, thermal ablation may give promising results[11].

This article reviews the findings and controversies of recent studies regarding the minimally invasive techniques for adrenal surgery.

LAPAROSCOPIC TRANSABDOMINAL APPROACH

Since the first laparoscopic transabdominal adrenalectomy (LTA) was performed, multiple studies have been reported on experiences with and consequences of this technique[1,12-14]. As usage spread, LTA became the gold standard[15]. Many surgeons choose the transabdominal approach because it has a larger working space, and surgeons are familiar with the laparoscopic abdominal anatomy and landmarks (Figure 1)[16].

Laparoscopic transabdominal adrenalectomy can be performed in either the lateral decubitus or anterior position. The lateral position allows the gravity of organs for self-retraction, so it is widely used [2]. On the other hand, bilateral adrenalectomy requires repositioning the patient. As the right and left sides present distinct vascular anatomy, surgical techniques and complications differ respectively. Some studies have reported similar or higher complication rates on the left side due to the complexity of the anatomy[17,18]. However, a recent small-sized meta-analysis reported a higher risk of bleeding and conversion rate on the right side[19]. Port positions are similar for both left and right adrenalectomy. After access to the peritoneal cavity using either a Hassan or Veress needle technique nearly 2 cm inferior to the costal margin at the semicircular line, the other two working ports are placed substantially with the lateral one in the mid axillary line[20]. Generally, three trocars are used on the left side and an additional trocar is used for liver retraction on the right side.

The definitive indications or contraindications of LTA remain uncertain. Increasing experience and evolving technology have expanded the size criterion. Some authors reported giant adrenal masses (> 10 cm) resected laparoscopically, especially for rare, benign lesions such as myelolipoma[20-22]. Laparoscopic adrenalectomy is more advantageous *via* the transperitoneal route than the retroperitoneoscopic approach in terms of the larger operating field, but also requires advanced technical skills and expertise. Some parameters and scoring systems can predict the difficulty of laparoscopic adrenalectomy. For example, lesion size is related to longer operating times and higher conversion rates[23,24]. Most studies suggest that a suspicious or malignant adrenal mass smaller than 6 or 8 cm without invasion and suspected malignant lymph nodes can be managed microscopically without disturbing oncological safety. However, high-volume center is emphasized, and the surgeons' experience is of paramount importance[25-27].

While obesity is considered a risk factor for complications in most surgeries, LTA is feasible for obese or morbidly obese patients[28]. This is because although obesity is associated with a longer operation time, it is not associated with morbidity or conversion in LTA[29,30]. Conversely, the retroperitoneal approach is adversely affected by obesity or periadrenal fat due to limited working space[31,32].

Table 1 Comparison of key features of different approaches for adrenal surgery

Therapeutic approach	Advantages	Disadvantages
Laparoscopic transabdominal approach	Familiarity for surgeons, larger working space, suitable for larger lesions	Repositioning for bilateral surgery, learning curve
Retroperitoneoscopic approach	Less pain and time, fewer adhesion-related problems	Inability to fully explore abdomen
Transabdominal robotic adrenalectomy	Improved vision, articulating instruments, and surgeon's comfort	Cost, learning curve
Single-port adrenalectomy	Better cosmesis, less pain, faster recovery	Special instruments
Open adrenalectomy	Vascular/organ invasion, large malignant tumors	Postoperative pain, longer recovery, large wound with risk of infection
Ablative therapies	Better for poor surgical candidates	Hypertensive crisis, lack of evidence

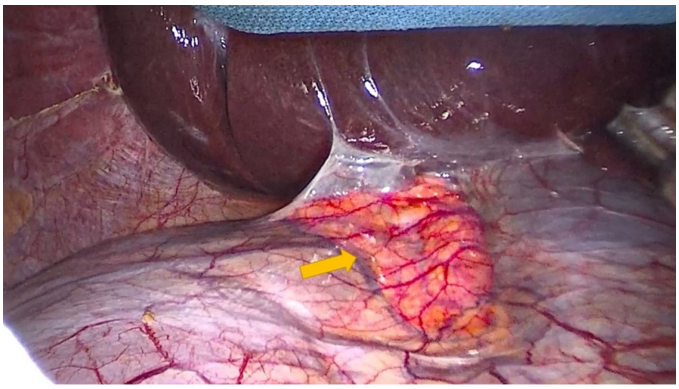

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Figure 1 Laparoscopic transabdominal view of the right adrenal gland (arrow), which is familiar to most surgeons.

Concomitant surgery is sometimes needed. If the necessity of any other intraabdominal surgery arises, the transabdominal approach may be a viable option[33,34].

Minimally invasive adrenal surgery in children has been adopted in many centers[35,36]. The most common adrenal pathology is neuroblastomas in childhood. Due to the tendency of this tumor to adhere to vascular structures, a relatively small number of neuroblastomas patients are managed laparoscopically[37]. The transabdominal route is used most commonly in this subset of patients[38].

Retroperitoneoscopic approach

Posterior retroperitoneoscopic adrenalectomy (PRA) became widespread after it was first introduced to the surgical world[39]. This technique approaches the adrenal glands directly without entering the abdomen, and thus avoids dissection or mobilization of intraabdominal organs such as the liver and colon. It has distinctive features compared to the transperitoneal approach, including the prevention of complications that may occur during entry into the abdominal cavity (bowel injury, *etc*). Previous surgery-related adhesions are not problematic. In addition, both adrenal glands can be reached in the same position, as repositioning may prolong operation time. The patient is placed in a modified prone position for maximizing the distance between the costal margin and iliac crest. The first trocar is placed at the tip of the 12th rib. The other two trocars are inserted approximately 4 cm medial and lateral to the first middle trocar below the rib cage. Higher insufflation pressure (up to 25 mm Hg) is required to create working space when compared to the LTA approach. This pressure results in less blood loss, as it compresses small vessels. Nevertheless, rare but fatal air embolism complications associated with vena cava injury may be encountered during surgery[40]. Also, higher carbon dioxide insufflation causes some physiological changes such as acidosis and greater end-tidal values[41]. Accordingly, the anesthesiology team must be aware of and manage these parameters.

Several studies compared the two approaches. Most have shown that PRA offers distinctive advantages over LTA, including less estimated blood loss, shorter time to oral food intake, less operative time, and a shorter hospital stay[42-44]. However, these lesser complications may be related to the smaller tumor size in the PRA group[44,45], and thus should be carefully evaluated in the light of additional data such as the experience of the surgeon and the center. Moreover, the learning curve is longer and another possible drawback of this approach[46]. Finally, capsular disruption, which is an important problem when operating for malignancy, may be higher in PRA[16]. Overall, both approaches are safe and have similar outcomes in experienced hands.

Robotic adrenalectomy

Robot-assisted surgery is currently used in all surgical disciplines, and considered the standard approach in some types of surgery. In adrenal surgery, robot-assisted adrenalectomies began to be reported in the early 2000s[47,48]. The general advantages of robotic systems include three-dimensional magnified image, stable and tremor-free image and intervention, articulated arms, and the comfort for the surgeon.

Although many studies have compared the robotic and laparoscopic approaches in adrenal surgery, none have demonstrated a clinically meaningful superiority of one over the other. One small-sized, randomized prospective trial that was previously published compared both methods, concluding that as the perioperative morbidity is higher in the robotic group, the laparoscopic approach is therefore superior to robot-assisted adrenalectomy[49]. However, increasing experience with robotic technology have improved perioperative outcomes. Recent studies and meta-analyses reveal that robotic adrenalectomy results in shorter hospital stays, less estimated blood loss, and similar postoperative complications compared to laparoscopic adrenalectomy[50-52]. Operative times differ between studies as the docking step may add extra operative time[53,54]. The robotic approach may offer an advantage for obese patients and larger and left-sided lesions[55-57]. A robotic platform may be advantageous when used in combination with indocyanine green in cases of partial adrenalectomy[58]. However, the studies are on a case-by-case basis, and there is no study comparing robotic and laparoscopic partial adrenalectomy.

Cost-effectiveness is an important drawback of robotic adrenalectomy, even in high-volume centers. The robotic approach doubles or triples the cost at $900 per case, although for subgroups where more benefits are expected for the robotic approach, such as larger and more difficult lesions, may reduce this cost[59,60]. In addition, a learning curve is needed in about 20 cases to achieve comparable results, even for the experienced laparoscopic surgeon[54]. Overall, robotic adrenalectomy is a safe and acceptable method compared to laparoscopic adrenalectomy in terms of postoperative outcomes.

Single-port adrenalectomy

Single-port (single incision, reduced port) surgery has been introduced in the last 20 years for numerous surgical types. In adrenal surgery, the first cases and series were published with different routes and instruments[61,62]. Single-port surgery aims to reduce incisions and pain and improve cosmetics. It is applicable *via* numerous instruments (articulating or straight) and port systems[63-65]. Even a handmade "glove port" can be used to reduce the cost[66,67].

Many studies have compared multiport and single-port adrenalectomy with different routes (retroperitoneal or transabdominal) on different platforms (robotic or laparoscopic). There are five meta-analyses for laparoscopic single port *vs* multiport adrenalectomy[68-72]. Laparoscopic single-port adrenalectomy is better in postoperative pain, hospitalization days, and recovery, but requires longer operative time. However, most of the included studies are retrospective, small-sized, and heterogeneous in terms of the route (transabdominal-retroperitoneal) and the devices[72]. Robotic single-incision adrenalectomy may overcome the disadvantages of laparoscopy through articulation of the instruments and surgeons' comfort. Retrospective studies reveal robotic single-port adrenalectomy as a safe and potentially feasible alternative to the multiport approach, but cost-effectiveness and risk of incisional hernia remain a matter of debate[73-75].

Partial adrenalectomy in benign conditions

The philosophy behind preserving endocrine organs comes from the prevention of lifelong hormone replacement therapy. For instance, thyroid lobectomy is an established option to avoid lifelong levothyroxine replacement therapy, which is related to lower quality of life[76]. Similarly, preserving healthy adrenal tissue especially for bilateral conditions may avoid steroid dependence. Partial adrenalectomy (sometimes called cortical sparing adrenalectomy) is more difficult and needs meticulous dissection. In technical aspects, it is crucial to understand the anatomy and landmarks of the nodule in preoperative imaging and vascular supply of remnant tissue. Recently, indocyanine green has been used intraoperatively to check the remnant gland's vascularity[77]. During partial adrenalectomy, intraoperative bleeding and blood loss may be higher than in total adrenalectomy, as it is a highly vascular gland[78,79]. Even so, partial adrenalectomy is safe and offers similar or better postoperative surgical outcomes, including shorter hospital stay and operative time when compared to total adrenalectomy[80,81].

After partial adrenalectomy for hormonally active lesions, the requirement of hormone supplementation and recurrence also must be considered. Although studies are heterogeneous, most of the patients remain steroid-independent after partial adrenalectomy[82-85]. However, bilateral disease and resection may decrease this success. In most series, tumor recurrence due to hereditary conditions or multinodularity is low (< 10%) or acceptable when compared to total adrenalectomy[86,87].

Open vs laparoscopic/robotic adrenalectomy for malignancy

Although minimally invasive adrenalectomy is the first choice in many cases, open surgery plays an important role in malignant adrenal tumors such as adrenocortical carcinoma (ACC). General surgical

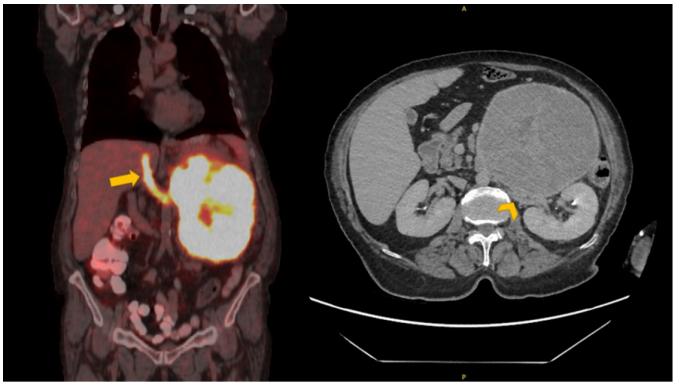

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Figure 2 Computerized tomography and positron emission tomography scan of adrenocortical carcinoma. Since tumor thrombus (arrow) and vascular invasion (arrowhead) are obvious, open surgery is necessary.

principles for localized ACC are en bloc resection (including invaded structure or organ) together with locoregional (periadrenal, renal hilum) lymphadenectomy[88]. ACC may invade the kidney, liver, pancreas, or spleen, and tumor thrombus or vena cava extension may also occur, which are conditions that mandate open surgery (Figure 2)[89]. Preoperative evaluation and imaging for the presence of these findings are crucial. Intraoperative tumor rupture/spillage and violation of the capsule are associated with poorer survival[26].

No randomized studies have compared the two methods. A laparoscopic approach without evidence of invasion should be performed by only an experienced surgeon. The described oncological principles must be followed during laparoscopy. Most endocrine and endocrine surgery societies accept a cutoff of 6 cm for size criterion[25,88]. A retrospective study comparing open and laparoscopic adrenalectomy for < 10 cm ACC revealed similar oncological outcomes but a higher peritoneal recurrence in the laparoscopy group than in open adrenalectomy[90]. In choosing laparoscopy, the transabdominal approach is recommended, as there is more experience with this approach. In addition, this route is more suitable for intra-abdominal exploration in terms of metastasis, invasion, and carcinomatosis[25]. The role of the robotic approach for ACC remains unclear. A recently published article comparing robotic and laparoscopic adrenalectomy for malignancy found higher conversion rates tied to poorer survival in the laparoscopy group. However, this dataset lacks detail about the reason for conversion and data for the rupture of tumor capsule[91]. More comparative studies are needed for this situation.

For adrenal metastatic diseases, a minimally invasive approach may be preferred. There is no difference in local recurrence and margin status between the laparoscopic and open approaches. However, tumor size and radiological evaluation for the invasion are of paramount importance in this group[92].

Ablative therapies for adrenal tumors

Adrenal gland tumors are typically operated/resected using the techniques outlined above. Ablative technologies such as radiofrequency ablation, microwave ablation, cryoablation, and laser ablation are currently in use for many tumors, including liver, lung, bone, or kidney[93-95]. Its use in endocrine tumors such as benign or malignant thyroid tumors is increasingly discussed in the literature[96].

Supporting literature draws on small series or cases of adrenal tumors. For functional adenomas (aldosterone or cortisol producing, pheochromocytoma), short-term outcomes and biochemical cure rates are satisfactory[97,98]. Planned future studies may address questions on this issue[99]. Additionally, hypertensive crisis is a critical and frequent complication of adrenal ablation to be considered [100].

Adrenal metastases are ablated more rarely than functional adenomas. Outcomes depend on the primary tumors' characteristics and size. The effect on survival is unknown because of the heterogenity of primary malignancies[11]. Adrenocortical carcinoma can be managed with ablative options in addition to surgery for advanced cases[25,88]. In general, adrenal ablation may be an alternative for poor candidates for adrenalectomy[101,102].

CONCLUSION

Minimally invasive adrenalectomy is well established and effective for most adrenal lesions. It may be performed *via* transabdominal or retroperitoneal route using laparoscopy or a robotic platform. Each approach has its pros and cons. The most preferred method is laparoscopic transabdominal adrenalectomy, as it is familiar to most surgeons. The cost is the leading disadvantage of robotic

surgery. Malignant adrenal tumors that are greater in size and invade adjacent structures warrant open surgery. Whichever approach is used, the contribution of an experienced endocrine surgeon is indisputable. Partial adrenalectomy may be a suitable option in some conditions such as hereditary or bilateral diseases. Ablative therapies are still in their infancy and further studies are needed.

FOOTNOTES

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