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REVIEW ARTICLE

Adrenalectomy: indications and options for treatment

Giovanni Alemanno[1] · Carlo Bergamini[1] · Paolo Prosperi[1] · Andrea Valeri[1]

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Abstract The history of adrenal surgery is longstanding. Firstly described in 1889 by Thornton, the open adrenalectomy has been for decades the only surgical approach to adrenal diseases. Nowadays, instead, several approaches to adrenal glands have been described in the literature, such as laparoscopic adrenalectomy, robotic-assisted procedure and single-incision technique. Actually, laparoscopic adrenalectomy is considered as the gold standard treatment for adrenal lesions. In fact, all functional tumors, including pheochromocytoma, are candidates for a laparoscopic approach in the absence of other contraindications. In the adrenal gland surgery, it is important to consider that a multidisciplinary approach which comprises surgeons, anesthesiologists, endocrinologists, and oncologists plays an important role in the management of patients and that the success of the procedure is related also to surgeon experience and hospital volume. This review aims to discuss the indications for adrenalectomy and to describe the different techniques options for the adrenal gland surgery.

Keywords Adrenalectomy · Minimally invasive surgery · Laparoscopy · Robotic adrenalectomy

Introduction

The history of adrenal surgery is longstanding; it was, in fact, the 1914 when the first planned adrenalectomy was performed by Perry Sargent [1], while the first flank approach for pheochromocytoma was performed by Charles Mayo in 1927.

In the subsequent years, multiple changes in the surgical approaches to the adrenal gland surgery were proposed, but it was in the 1992 that the first laparoscopic procedure of the adrenal gland was performed and described by Michael Gagner [2]. Since such description there has been a radical change in the management of adrenal tumors because minimally invasive adrenalectomy has been shown to decrease the length of hospital stay, reduce healthcare cost, reduce wound complications and blood loss, and improve the patient's outcome with an earlier patient mobility and faster return to regular activity [3–5]. Actually in the literature, it is surely demonstrated the feasibility and reproducibility of the laparoscopic approach and, in fact, it is considered the ''Gold Standard'' therapy for the majority of adrenal gland tumors. The advent of new technologies and the development of the robot-assisted surgery surely allow new developments and new possibilities of research and application.

This review aims to discuss the indications for adrenalectomy and to describe the different techniques options for the adrenal gland surgery. To lead an extensive analysis, the manuscript describes also the more modern

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✉ Giovanni Alemanno
g.alemannomd@gmail.com

Carlo Bergamini
drcarlobergamini@gmail.com

Paolo Prosperi
paoloprosp@yahoo.it

Andrea Valeri
valeri@aou-careggi.toscana.it

[1] General, Emergency and Minimally Invasive Surgery Unit, Careggi University Hospital, Largo Brambilla 3, 50134 Florence, Italy

attempts at surgical treatment for the adrenal pathology including the latest developments in robotic surgery.

Indications for adrenalectomy

The widespread use in clinical practice of abdominal ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) has created the clinical dilemma of the adrenal incidentaloma [6]. Adrenal masses, in fact, are commonly detected during a radiologic examination performed for indications other than an evaluation for adrenal disease; it is estimated that the prevalence of adrenal incidentaloma at abdominal CT scan is of 4%, while in autopsy is of 8% [7]. The different histotypes of adrenal incidentaloma are reported in Table 1.

The indications for adrenalectomy concern both the presence of a functional tumor associated with hormone secretion and the presence of a non-functional tumor associated with a suspicion of malignancy [8].

It is mandatory that all patients with an adrenal incidentaloma detected during a radiologic examination should have a complete panel of clinical and biochemical evaluation to obtain information on the biological and functional nature of the adrenal mass. The hormone-secreting adrenal tumors in which adrenalectomy is indicated are the followings: Cushing's syndrome, caused by an hypersecretion of glucocorticoids produced in fasciculata adrenal cortex, Conn's syndrome, caused by an hypersecretion of aldosterone produced by glomerulosa adrenal cortex, and Pheochromocytomas that arise from adrenal medulla and produce catecholamines.

For non-functional adrenal tumors, instead, the indication for surgery is the risk of malignancy that is related to the size of the lesion. If the lesions are smaller than 4 cm, the risk of malignancy is approximately 2%, for lesions of 4–6 cm the risk of malignancy is 6%, while for lesions of 6 cm the risk of malignancy is 25% [9]. Adrenalectomy, furthermore, may also be indicated for the resection of adrenal metastases from primary lesions of the lung, kidney, breast, melanoma and the Gastro-intestinal tract [10] and in selected patients with oligometastatic disease [11].

Table 1 Histotypes of adrenal incidentaloma

Diagnosis	Frequency (%)
Non-functional adenoma	75
Myelolipomas	3
Cyst	2
Functional tumor	
Pheochromocytoma	4
Cushing's syndrome	9
Aldosteronoma	1.5
Ganglioneuroma	1.5
Adrenal carcinoma	4
Metastasis	<1

Options for treatment

Several different techniques have been proposed for the treatment of adrenal gland tumors. The evolution of the surgical technique has been remarkable over the years; indeed, it is important to consider that if the open adrenalectomy has been the gold standard treatment for adrenal disease in the past, from the advent of laparoscopic surgery applied to adrenal tumors in 1992, this status is completely changed and actually minimally invasive adrenalectomy has replaced open adrenalectomy. This is due to the fact that minimally invasive adrenalectomy results in less blood loss, earlier ambulation, shorter hospital stay, faster return to normal activity and similar long-term outcomes as compared with open surgery [12–16].

With the advent of robotic surgery, robotic-assisted adrenalectomy has become an alternative to conventional laparoscopic adrenalectomy, but actually the evidences on the possible advantages and drawbacks of this technique remain limited.

According to the Sages guidelines for minimally invasive treatment of adrenal pathology, surgeons should choose the approach they are most familiar with, have had training in, and have the best patient outcomes with [17].

Selection of patients for laparoscopic and open adrenalectomy

Actually laparoscopic adrenalectomy is considered as the gold standard treatment for adrenal lesions [18]; in fact, all functional tumors, including pheochromocytoma, are candidates for a laparoscopic approach in the absence of other contraindications. Conversely, the open approach is recommended in patients with evidence at preoperative imaging studies of malignancy with local invasion of adjacent structures, thus facilitating lymph-node dissection and en-bloc resection of adjacent structures to achieve negative margins. The size of the tumor should be considered in the operative planning, but is not an absolute contraindication to a laparoscopic resection; in fact, if in the past a tumor of 6 cm was considered a contraindication to laparoscopy, actually tumor size greater than 6 cm is not an absolute contraindication to laparoscopy [19, 20]. It is mandatory to consider that surgeon experience, hospital volume and a multidisciplinary approach to patients, which comprises surgeons, anesthesiologists, endocrinologists, are three important parameters in the selection of patients. Contraindications to laparoscopic adrenalectomy are reported in Table 2.

Laparoscopic adrenalectomy

Since the introduction of laparoscopic adrenalectomy in 1992 [21], different endoscopic approaches have been described, such as the anterior approach (with patient in supine position), the lateral approach (with patient in lateral position) and a retroperitoneoscopic approach (with patient in prone or lateral position) [22–25].

The anterior trans-abdominal adrenalectomy consists in a sub-mesocolic approach to the adrenal glands. This is the least common of the techniques employed for adrenalectomy because of the conventional abdominal laparoscopic view of the abdomen that leads to longer operatory times and greater number of ports utilized [26, 27].

The lateral trans-abdominal approach is actually the most widely practised since it provides a good exposure of the adrenal gland and surrounding structures, and provides to surgeon precise anatomic landmark with a safe control to vascular structures. Moreover, it allows to treat other abdominal pathologies simultaneously [22, 23].

The posterior retroperitoneoscopic approach, instead, allows a direct access to the adrenal glands with a minimal dissection of the surrounding structures and facilitates the surgical procedure in case of peritoneal adhesions and bilateral adrenalectomy, but has an important limitation that consists in the small working space and for this reason a large tumor size is indicated as the main limitation of this technique [28].

The lateral retroperitoneoscopic adrenalectomy is commonly used by urologic surgeon due to the familiarity of this technique with the laparoscopic nephrectomy. This technique has the advantage of avoiding the peritoneal cavity that facilitates the surgical procedure also in case of peritoneal adhesions but has important limitations in tumor size, in longer operating times and in the requiring of more ports [29–31].

Anterior trans-abdominal adrenalectomy

The patient is placed in a supine position, the first entry in the abdominal cavity is performed in the umbilicus and three other additional trocars are placed in various configurations. The operatory time of this procedure comprises for the left adrenalectomy the elevation of the transverse mesocolon, the identification of the ligament of Treitz and the inferior mesenteric vein and the opening of the posterior retroperitoneum. Subsequently, the dissection proceeds inferiorly till to elevate the pancreas and indentifying the left renal vein and the left adrenal vein. Then, the dissection proceeds with the mobilization of the gland inferiorly, medially, superiorly and laterally.

Table 2 Contraindications to laparoscopic adrenalectomy

Absolute	Coagulopathy
	Malignancy
	Large size tumors over 12 cm in diameter
	Cardiopulmonary high risk patients
Relative	Large size tumors
	Obesity
	Previous abdominal surgery

Lateral trans-abdominal adrenalectomy—right flank

After performing anesthesia, the patient is placed in a left lateral ''decubitus'' position at a 50–60 angle to the operatory room bed with a cushion under the left flank. The patient's flank is stretched using the electric operating room beds by lowering the trunk and then the legs using the costal arch as a fulcrum. In this way, the area of the adrenal gland acquires a wider and more accessible surface area [32].

The first trocar of 10 mm is positioned 3 cm under the costal arch at the level of the right anterior axillary line and 10 cm laterally with respect to the umbilical incision. The second (10–12 mm) and third (5 mm) trocars are, respectively, positioned about 4–5 cm to the right and left of the first trocar and 1–5 cm from the costal arch. The fourth trocar is positioned in the paraxiphoid area and is used to retract the liver.

After the exploration of the abdominal cavity, in order to maximize the dissection of the adrenal area, it is necessary to mobilize the right liver with the resection of the right triangular ligament. The first step consists of resecting the posterior parietal peritoneum identifying the adrenal mass and the inferior vena cava (IVC). Using blunt dissection and electrocautery, the dissection proceeds creating a plane between the adrenal gland and IVC and then proceeds inferiorly until encountering the renal vein. The next steps consist in the Ligation of the Medial Vein, the Dissection of the Superior and Inferior Poles and the Posterior-Lateral Dissection. In this way, the dissected gland could be inserted into the laparoscopic sac and extracted through the orifice of first trocar. Then, the hemostasis is performed and a capillary drain is positioned in the adrenal area. After removing the trocars under laparoscopic vision, the fascia for the extraction trocar site is then closed [33, 34].

Lateral trans-abdominal adrenalectomy—left flank

After performing anesthesia, the patient is placed in a lateral right decubitus position with the help of a cushion that is placed under the right flank. The operatory bed is then angled to maximize the exposure of the space between the costal margin and the iliac crest. The left arm is extended and suspended.

The first trocar of 10-mm is inserted in the subcostal space at the anterior axillary line, the second and the third ones, of 10 mm, are inserted about 7 cm on each side of the first trocar below the costal margin. An optional fourth trocar could be inserted below the first one, at a distance of 4–5 cm.

First of all, the mobilization of the splenic flexure to move down the colon and the dissection of the splenoparietal ligament to obtain a total mobilization of the spleen are mandatory. It is important to dissect the posterior surface of the spleen followed by the tail of the pancreas in order to retract them medially. The medial reflection of the spleen and pancreas exposes the upper pole of the kidney and the adrenal area. Using blunt dissection and electrocautery, the medial edge of the adrenal gland is dissected from upper to lower pole. During this phase, the left adrenal vein is isolated, clipped and divided. Then, all the remaining attachments at the posterolateral edge are dissected; in this way, the gland is mobilized and inserted in a laparoscopic sac for the extraction through the incision of the first trocar. Usually a drain tube is placed in the adrenal area and the port site is closed.

Posterior retroperitoneoscopic adrenalectomy

The patient is in the prone position with the chest and the abdomen supported by the Wilson frame that allows the abdominal contents to be full anteriorly. A 1.5 cm transverse incision is performed 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. The retroperitoneal space is insufflated with 20–25 mmHg of CO_2 with a balloon trocar in place in the middle port. The main landmarks that surgeon have to identify are the superior pole of kidney caudally, the paraspinous muscles medially, and the posterior surface of liver (right) or spleen (left) laterally. The adrenal gland must be mobilized, the adrenal vein must be identified and ligated in a medial or inferomedial position with clips or a hemostatic device and the dissection can proceed laterally between the diaphragm and the psoas.

Finally, the resected gland is extracted by means of endoscopic specimen bags through the central trocar port.

Lateral retroperitoneoscopic adrenalectomy

The position of the patient is in a 60–90 degree angle with tumor side up and with the table flexed as in the lateral trans-abdominal approach. This technique involves the use of 4–5 trocars. Anatomic landmarks that surgeons should identify are the superior pole of the kidney, the parietal peritoneum, diaphragm, retroperitoneal fold, posterior renal fascia, and psoas muscle. For this technique, the operation is then performed in the same way as the posterior retroperitoneoscopic adrenalectomy.

Robotic adrenalectomy

Due to the normal limits of laparoscopy such as the two-dimensional view, an unsteady camera, the lack of a good ergonomic setting and rigid instruments, the introduction of robot-assisted surgery seems to overcome these limitations, so much so that, actually, robotic-assisted adrenalectomy has become an alternative to conventional laparoscopic adrenalectomy. It was the 2001 when the first robotic adrenalectomy was described by Horgan et al. [35], and since then many studies reported the advantages of this techniques mostly in obese patients and large tumors [36]. Conversely, it is important to consider the disadvantages of this technique addressed by most authors to longer operatory time, higher costs and the learning curve of the entire surgical team [36–38].

Right robotic adrenalectomy

The patient is positioned supine with 20° tilting on the left side. The pneumoperitoneum can be performed using a Verres needle technique. This technique needs 5 trocars: the first one for the optical camera is positioned on the lateral side of the para-rectal line, above the umbilical transverse line; three robotic ports then are placed along a concave line and focused on the adrenal area. Another auxiliary trocar is placed near the umbilicus. The main step of this procedure comprises the mobilization of the right colonic flexure and the dissection of the second portion of the duodenum from the vena cava. The fourth robotic arm is used to mobilize the right lobe of the liver for a better exposure of the vena cava.

The gland is then mobilized with the help of bipolar, hook or harmonic scalpel and the adrenal vein is dissected with clips or stitches. The arterial vessels that go to the adrenal gland are controlled with clips. The adrenal gland is removed through an endobag and finally the robotic cart is removed and the port sites are closed.

Left robotic adrenalectomy

The patient is positioned supine tilted at 20° on the right side. The pneumoperitoneum can be performed using a Verres needle technique. The trocar for the camera is placed in the left upper quadrant, the second one laterally in the left side, the third one in subcostal right and the fourth one in approximately midline. Another auxiliary

trocar is placed between the optical trocar and the left lateral arm. The main step of this procedure comprises the mobilization of the left colonic flexure, the exposure of the retro cavity and the mobilization of the pancreatic tail. The fourth robotic arm is used to gently lift the spleen for the exposure of the adrenal area. The gland is then mobilized with the help of bipolar, hook or harmonic scalpel and the adrenal vein dissected with clips or stitches. Therefore, the adrenal gland is detached from the fat of the renal capsule and dissected by controlling the arterial adrenal branches.

The adrenal gland is removed through an endobag and finally the robotic cart is removed and the port sites are closed.

Single port adrenalectomy

Technically a trans-abdominal single port adrenalectomy requires a 2–3 cm incision at the umbilicus for the placement of a multiport device and the utilization of extra-long instruments able to reach the adrenal gland. The right adrenalectomy needs the help of an additional 2 mm needlescopic port for the liver retraction.

Several authors reported the outcomes with single-incision adrenalectomy [39–43] and some studies compared the conventional laparoscopic approach with single port adrenalectomy demonstrating no significant differences in patient length of stay or morbidity and a small benefit in cosmesis and postoperative pain but longer operative times with single port laparoscopy [44–46]. Actually, data on this approach remain limited and further researches are necessary.

Open adrenalectomy

First described in 1889 by Thornton, the open adrenalectomy has been for decades the only surgical approach to adrenal diseases. Actually open adrenalectomy still remains a possible technique in the presence of general or specific contraindications to laparoscopy (a patient's inability to undergo pneumoperitoneum is an absolute contraindication to laparoscopy) or when specific features of the adrenal tumor require a safer procedure such as the presence of large lesions (12 cm in diameter) or the presence of malignant tumor with the invasion of adjacent structures.

Open adrenalectomy could be performed in different possible accesses, by a transperitoneal approach (anterior, median, transverse, subcostal), by an extrapleural–extraperitoneal approach (lateral, posterior) and by a transpleural–transdiaphragmatic approach (trans-thoraco-abdominal).

Table 3 Comparison of different techniques for adrenalectomy

	Laparoscopic				Robotic	Single port	Open
	Anterior trans-abdominal	Lateral trans-abdominal	Posterior retroperitoneoscopic	Lateral retroperitoneoscopic			
Advantages	Conventional laparoscopic view of abdomen	Good exposure of adrenal glands Precise anatomic landmark Safe control to vascular structures	Safe in case of abdominal adhesions No repositioning needed for bilateral adrenalectomy	Safe in case of abdominal adhesions	3D vision Seven degrees of freedom that allows precise movements in limited working spaces Major surgeon's comfort intraoperatively	Benefit in cosmesis Lower postoperative pain	Allows treatment of large adrenal lesions >12 cm in diameter Allows treatment of adrenal malignancy with local invasion
Disadvantages	Longer operatory times Greater number of ports utilized	May be challenging in previously operated fields	Small working space Large tumor size is the main limitation Not recommended for obese patients	Limitation in tumor size Longer operating times Require more ports	Longer operatory times Higher costs Surgical team learning curve	Longer operative times	Post-operative ileus Greater Post-operative pain Laxity in flank muscles and flank numbness for extraperitoneal approaches
Contraindications	Malignancy with local invasion—large size tumors—general contraindications to laparoscopy						

The choice of approach will depend on size, location, possibility of malignancy, and surgeon experience with the different techniques. Also the outcomes and morbidity of open adrenalectomy vary with the pathology of the disease and with the approach chosen. All approaches that limit the access to the peritoneum decrease the rates of postoperative ileus, while the extraperitoneal approaches are associated with high rates of neuromuscular morbidity including chronic pain (14%), laxity in flank muscles (30%), and flank numbness (10%) [47].

Conclusions

In the adrenal gland surgery, it is important to consider that a multidisciplinary approach which comprises surgeons, anesthesiologists, endocrinologists, and oncologists plays an important role in the management of patients and that the success of the procedure is related also to surgeon experience and hospital volume. Several approaches to adrenal glands have been described in the literature, starting from open adrenalectomy till laparoscopic adrenalectomy and including robotic-assisted and single-incision technique, and surgeons should choose the approach they are most familiar with (Table 3).

Many studies confirmed that laparoscopic adrenalectomy is safe, effective, decreases hospital stays, operative blood loss, and wound complications and have similar long-term outcomes if compared with open surgery; actually, in fact, is considered the gold standard for adrenal diseases requiring surgery. The learning curve for laparoscopic adrenalectomy may be difficult due to the paucity of these cases in general practice. Robotic adrenalectomy may offer advantages if compared to laparoscopic adrenalectomy for large tumors and in morbidly obese patients, but the real benefits of this technique are not really clear considering the high costs and longer operative times of robotic procedure. In the same way, single port adrenalectomy is technically feasible and safe in experienced hands but offers little if any advantage over other standard laparoscopic approaches to adrenalectomy.

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Compliance with ethical standards

Conflict of interest The authors certify that there is no actual or potential conflict of interest in relation to this article and they state that there are no financial interests or connections, direct or indirect, or other situations that might raise the question of bias in the work reported or the conclusions, implications, or opinions stated—including pertinent commercial or other sources of funding for the individual author(s) or for the associated department(s) or organization(s), personal relationships, or direct academic competition.

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