

REVIEW

Laparoscopic adrenalectomy: An update

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KEYWORDS

Laparoscopy;
Adrenalectomy;
Adrenal mass;
Malignancy

ABBREVIATIONS

LA, laparoscopic adrenalectomy; ACC, adrenocortical carcinoma; PET, positron-emission tomography; US, ultrasonography; HU, Hounsfield unit; CSI, chemical shift imaging; FDG, ¹⁸F-fluorodeoxyglucose; IVC, inferior vena cava; ACTH, adrenocorticotropic hormone

Abstract Objective: To review the current role and outcome of laparoscopic adrenalectomy (LA) in the management of adrenal tumours.

Methods: A Medline search using the keywords (adrenalectomy, laparoscopy, adrenal masses/tumours) was done for reports published between 1990 and 2011. Key articles were used to find more relevant references on the evaluation and laparoscopic management of adrenal masses.

Results: The hormonal evaluation is not standardised, but initial screening tests are recommended and followed with confirmatory ones when positive, equivocal or the clinical presentation suggest adrenal hyperfunction. The imaging studies had, and continued to, advance, especially computed tomography (CT), magnetic resonance imaging and positron-emission tomography/CT. These advances have increased the accuracy of the diagnosis of adrenal masses, with a reported high sensitivity and specificity of 95–100%. The introduction of laparoscopy has resulted in more adrenal lesions being removed, especially incidental lesions smaller than the 5–6 cm that was previously the indication for surgical excision. The technique has developed and larger lesions of > 6 cm are now considered for LA in the proper setting. The transperitoneal and retroperitoneal approaches are currently widely practised, with minor differences in the outcome. The reported outcome, although mostly retrospective, is excellent and with fewer complications. The role of LA for adrenal malignancy should be considered cautiously. Preoperative imaging signs of invasion into surrounding structures should be considered a contraindication for LA.

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Conclusion: LA is the standard procedure for most adrenal lesions of appropriate size and no signs of surrounding tissue invasion, giving an excellent outcome.

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Introduction

Adrenal surgery was revolutionised by the introduction of laparoscopy in 1992 [1,2]. The adrenal glands are ideal for the use of the technique, as they are small retroperitoneal organs that were traditionally approached through a relatively large abdominal, flank or thoraco-abdominal incision. Laparoscopy enabled surgeons to use safe and effective procedures, and offers patients all the advantages of minimally invasive surgery, with decreased blood loss, less post operative pain, decreased hospital stay and faster recovery [3–6]. Laparoscopy has had an effect on adrenal surgery over the last two decades, with more adrenalectomies being performed, the lesion size as an indication for surgery decreased, and more incidentalomas and benign tumours being resected [7–10].

Evaluation

The primary goals of evaluating adrenal lesions are to determine adrenal hyperfunction and the potential for malignancy. Whether the adrenal mass is found incidentally or with a suggestive clinical presentation, a detailed history and physical examination are the initial steps in the evaluation. Further evaluation of adrenal masses is based on hormonal evaluation and imaging studies.

Hormonal evaluation

There is no agreement on a standard hormonal evaluation of adrenal masses to assess hyperfunction. In patients with asymptomatic incidental adrenal lesion and no hypertension or hypokalaemia, the goal of the hormonal evaluation is to uncover the presence of subclinical Cushing's syndrome or clinically silent pheochromocytoma. It is recommended to start with

screening tests that include measurements of 24-h urine metanephrine and catecholamine levels, plasma-free metanephrines, plasma cortisol and an overnight 1 mg dexamethasone suppression test. In patients with hypertension and or hypokalaemia, the plasma aldosterone concentration and plasma rennin activity are measured. If these tests are negative the focus is directed towards an imaging evaluation. If the screening tests are positive or equivocal, confirmatory tests are done, as in patients with clinical features suggestive of Cushing's disease, pheochromocytoma or primary aldosteronism, as shown in Table 1.

There are variations among endocrinologists in the use of these tests. The issue of false-positive tests should be considered, as well as equivocal results that need cautious interpretation before patients are considered for surgical treatments [11,12]. Sex hormone-secreting adrenal tumours are rare and patients usually present with suggestive clinical features of virilisation or feminisation. It is not warranted to perform routine screening for excess androgens or oestrogens in incidental adrenal tumours.

Imaging studies

Recent advances in imaging studies have contributed significantly to the accurate diagnosis of adrenal lesions especially in the field of CT, MRI, positron-emission tomography (PET) and PET/CT [13].

Ultrasonography (US) is widely available and free of ionising radiation. However, it is operator-dependent and less accurate in the presence of abdominal gases or in obese patients. The use of contrast-enhanced US was found in a recent study to have a good correlation with CT and MRI findings in differentiating adenomas from malignant lesions, with a sensitivity of 100% and a specificity of 82% [14]. While US has limited use in evaluating

Table 1 Confirmatory tests in patients with clinical features suggestive of Cushing's, pheochromocytoma or primary aldosteronism.

Phaeochromocytoma	Cushing's syndrome	Primary aldosteronism
<i>Screening</i>		
24-h urinary catecholamines metanephrines	Plasma cortisol	Unproved hypokalaemia
Plasma free metanephrines	Low dose dexamethasone suppression test	Plasma aldosterone
<i>Confirmatory</i>		
Clonidine suppression tests	24-h urine cortisol	Urinary aldosterone
Adrenal vein catecholamines	High-dose dexamethasone suppression test	Aldosterone-renin ratio
	Plasma corticotrophin	Postural stimulation test
	Metapyrone stimulation test	Adrenal vein aldosterone
	Petrosal sinus corticotrophin	



Figure 1 A benign adrenal adenoma.

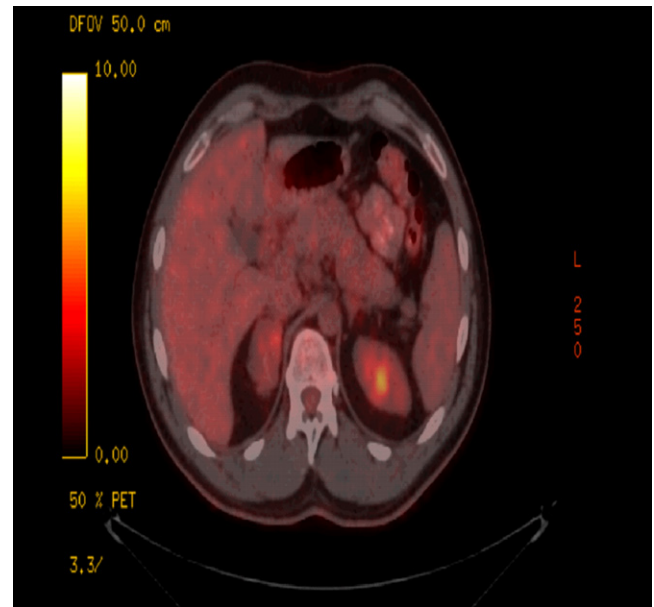


Figure 3 Increased uptake of F-FDG in a right adrenal mass.



Figure 2 A suspect malignant mass, after surgery (ganglioneuroma).

adrenal masses, it can be considered as a follow-up method in selected patients with stable benign lesions, to avoid the risk of ionising radiation and use of contrast agents [11].

CT can adequately assess adrenal lesion size, consistency, contour, complexity, presence of calcification, necrosis, enhancement with contrast medium and involvement of the surrounding structures. Benign lesions are usually small, homogeneous, with a well-defined wall and no signs of infiltration into the surrounding structures (Fig. 1). The high lipid content of these tumours makes the Hounsfield unit (HU) density low (<18). The specificity of the benign nature of adrenal masses can be up to 98% when the HU density is <10 [15]. By contrast, potentially malignant lesions are usually >6 cm, heterogeneous, with an irregular

wall, and can show invasion into the surrounding structures. There are limitations to conventional CT findings using the above features, especially the HU density. The diagnosis of some lesions like myelolipoma with a high fat content might be accurate on CT, but not always conclusive, as many benign incidentalomas can have a poor lipid content in 10–40% of cases [16]. Adrenal metastasis might also be similar to benign adenomas and some patients are not able to have contrast agent due to allergies or impaired renal function. The technique of the CT washout ratio has been reported recently to improve the accuracy in distinguishing suspect masses. Benign adenomas have a 15-min washout ratio of $\geq 40\%$ and lesions with a $<40\%$ washout ratio should be considered suspicious for malignancy [17,18].

MRI is an alternative method that can show anatomical details in addition to information on tissue characteristics (Fig. 2). The normal adrenal has a low-to-intermediate signal on T1- and T2-weighted imaging. Adrenal adenomas usually show relatively uniform enhancement on immediate gadolinium-enhanced images [19]. Pheochromocytoma typically has high signal intensity on T2-weighted images, although this finding is not universal. Chemical shift imaging (CSI) is the mainstay of the MR evaluation of solid adrenal masses [13]. MRI identifies intracellular lipid because of the different resonant frequencies of fat and water. The sensitivity and specificity of CSI are 81–100% and 94–100%, respectively, in differentiating adrenal adenoma from non-adenomatous lesions [20–22]. The inherited limitation of MRI is the inconvenience of being a long motionless procedure, and the potential for gadolinium toxicity.

PET is based on the concept of increased glucose uptake by malignant lesions using ^{18}F -fluorodeoxyglucose (FDG), with a high sensitivity and specificity. The use of PET/CT offers accurate anatomical localisation of any FDG focal uptake (Fig. 3). The combination of PET/CT can raise the sensitivity and specificity for indeterminate lesions on CT or MRI to 95% [17,18].

The use of fine-needle aspiration and biopsy has been mostly replaced by the current imaging methods (CT washout, MRI and PET/CT), and thus rarely indicated. It is essential to exclude pheochromocytoma before considering the procedure, and to be aware of the potential risk of tumour seeding in adrenocortical carcinoma (ACC).

Indications and contraindications for laparoscopic adrenalectomy (LA)

Surgical excision is indicated for all functioning adrenal lesions and those with imaging findings suspicious of malignancy. Tumour size as an indication for surgery in adrenal incidentalomas has previously been lesions of >5–6 cm, due to the high likelihood of malignancy.

The indication for LA has been expanding over the last two decades. Currently the main absolute contraindication is a malignant adrenal tumour with imaging signs of local invasion. The size upper limit to consider LA has been increased progressively from 6 cm, to 8 cm and to 10–12 cm, depending on the proficiency of the surgical team [23]. While LA for larger lesions can be safe, surgeons should note that laparoscopy is an approach offered to patients. If the principles of an optimal oncological procedure or patient safety are compromised by laparoscopy, alternative open surgery should be offered. It is also true that adrenal tumours of >5–6 cm are potentially more malignant and more technically difficult to treat, and this is important to consider when using LA in practice (Table 2).

Technique

LA is an established procedure and can be done using a transperitoneal or retroperitoneal approach. While each

approach has its relative advantages and potential limitations, comparative studies showed no significant differences in outcome [24–27]. The recent wide adoption of the robotic surgical system, especially among urologists, has found its way into LA [28,29]. Single-port surgery is the latest addition to the techniques used for LA, as progress is being made in skills, instruments and technology [30]. The principle of LA is to perform gentle and delicate dissection of the surrounding tissues away from the adrenal mass, to avoid tumour rupture or excessive release of catecholamines during aggressive manipulation. Another principle of this procedure is the early control of the main adrenal vein to avoid an intraoperative hypertensive crisis secondary to catecholamine release.

Transperitoneal

The transperitoneal approach is the most common for LA [23]. Two approaches have been described, the lateral and the anterior. The anterior approach is done with the patient supine and requires additional working ports for dissection and retraction, and is being less practised and reported.

For the lateral transperitoneal approach, the patient is positioned with the operative side up at 45–70°. Pneumoperitoneum is established with a Veress needle or an open technique. Port placement takes into account the patient's body habitus and weight. The camera port is usually placed in the peri-umbilical area in thin patients or lateral to the rectus muscle at the midclavicular line, 2–4 cm above the umbilical level. Additional working ports are inserted under vision after pneumoperitoneum is established. The working ports can be 5–10 mm depending on the instruments used, and are usually placed at the anterior axillary line at the iliac fossa and the other in the midclavicular line \approx 4 cm below the costal margin. On the right side a 5-mm fourth port is placed in the midline for liver retraction. On the left

Table 2 Indications and contraindications for LA.

Indications	Contraindications
<i>Established/accepted</i>	Tumours with invasion on imaging
Functioning adenoma \leq 6 cm	Metastatic pheochromocytoma
Incidentaloma 3–6 cm*	ACC with local invasion
Solitary metastasis \leq 6 cm	Tumours > 12 cm
<i>Optional/relative</i> [†]	
Functioning adenoma 6–12 cm	
Incidentaloma 6–12 cm	
Solitary metastasis 6–12 cm	

* Young healthy patients.

[†] Depending on surgeon expertise and proficiency.

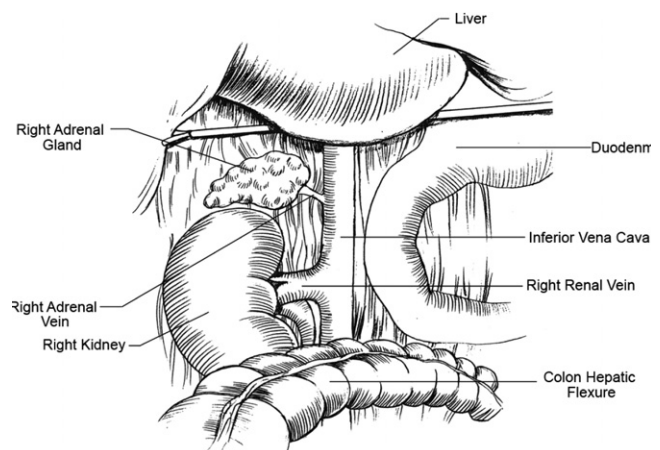


Figure 4 Transperitoneal view for right LA.

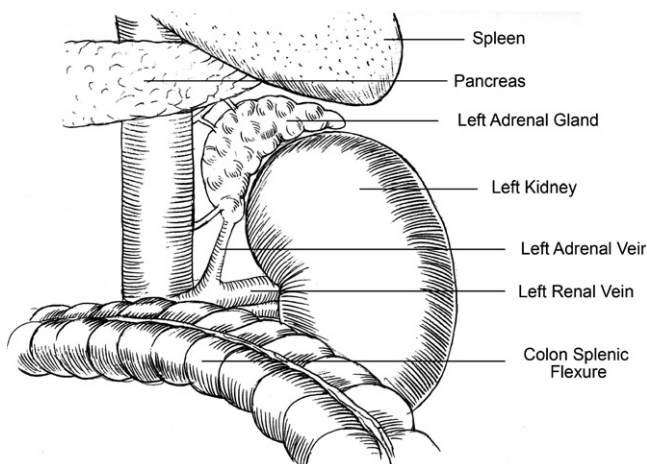


Figure 5 Transperitoneal view for left LA.

side a fourth port is sometimes needed in the mid-axillary line to help retraction of the colon splenic flexure, pancreas or spleen.

On the right side the liver is retracted upwards to expose the posterior peritoneum, which is incised lateral to the inferior vena cava (IVC). The triangular ligament of the liver is incised to help further upward retraction of the liver to expose the upper IVC. Occasionally the colon hepatic flexure might need to be mobilised medially and downwards to expose the duodenum that is mobilised medially to expose the IVC and the right renal vein (Fig. 4). Careful dissection is done lateral to the IVC, starting from the right renal vein upwards to find the main adrenal vein. This vein is usually short and commonly found at the upper medial part of the gland [31]. This part of the procedure is very critical to avoid bleeding or rupture of the adrenal tumour. When the adrenal vein is identified, it is clipped and divided. Alternatively, the adrenal vein can be controlled with an energy-based device like the LigaSure™ (Covidien, Mansfield, MA, USA). Occasionally veins draining into the hepatic veins are encountered and controlled. The tumour is then dissected off the upper pole of the kidney, with care taken to control veins draining into the right renal vein. Arteries are usually small and controlled with electrocautery, LigaSure or ultrasonic shears. The last to be freed are the posterior and lateral attachments from the diaphragm. The specimen is placed in an endobag and placed above the liver. The operative site is inspected at low intraperitoneal pressure for haemostasis.

In the left side the splenic flexure is mobilised medially and downwards by dividing the splenocolic and lienorenal ligaments. Dissection is carried cranially and lateral to the diaphragm to help the spleen and the tail of the pancreas to drop medially. The upper pole of the left kidney is identified and followed medially to find

the left renal vein. The upper edge of the left renal vein is carefully dissected to find the main left adrenal vein draining into its superior aspect. The adrenal vein is mobilised, clipped and divided or controlled with an energy-based device like the LigaSure. Medial dissection is done carefully to separate the mass from the pancreas, and some veins might be encountered medially and superiorly draining into the phrenic vein that needs to be controlled. The adrenal tumour is separated from the upper pole of the left kidney and from the spleen and diaphragm by finding the avascular plane, using gentle dissection to avoid injury to the splenic vein, diaphragm or tail of the pancreas (Fig. 5). The specimen is placed in an endobag and placed above the spleen. The operative site is inspected for haemostasis under low intraperitoneal pressure.

Retroperitoneal

The retroperitoneal approach has the advantage of avoiding potential peritoneal adhesions from previous surgery, potential visceral injury and bowel complications. Its main limitations are the unfamiliar anatomical landmarks and the small and narrow surgical field that might be confusing to less experienced surgeons. It might be further compromised in obese patients, making operation on relatively larger tumours more challenging [23].

There are two approaches reported, the lateral (flank) approach and the posterior approach. The lateral retroperitoneal approach is more common among urologists, who are more familiar with it when performing laparoscopic renal surgery. The patient is placed in the full flank position with mild flexion of the table at the iliac bone. The access is made using an open technique that will be the site of the camera port. A 1.5–2 cm incision is made below the tip of the 12th rib at the mid-axillary line. It is deepened until the lumbodorsal fascia is reached and incised. The retroperitoneum is entered and blunt finger dissection is used to feel the psoas muscle and create enough space for balloon dilatation. The retroperitoneal balloon dilatation is a matter of surgeon's preference and availability of resources. Care should be taken to dilate anterior to the psoas muscle and posterior to the Gerota's fascia. After creating enough space an additional working 5–10 mm port is placed under finger guidance between the paraspinus muscle and the 12th rib at the posterior axillary line. Some blunt dissection might be needed to sweep the peritoneum medially and another 5-mm port is placed at the anterior axillary line medial to the camera part. A fourth port might be placed caudally and used for additional retraction or suction.

On the right side, the landmarks to find are the psoas muscle and the right ureter. By lifting the kidney upwards the IVC and gonadal vein are usually identified. The right ureter can be used as a guide to find the right

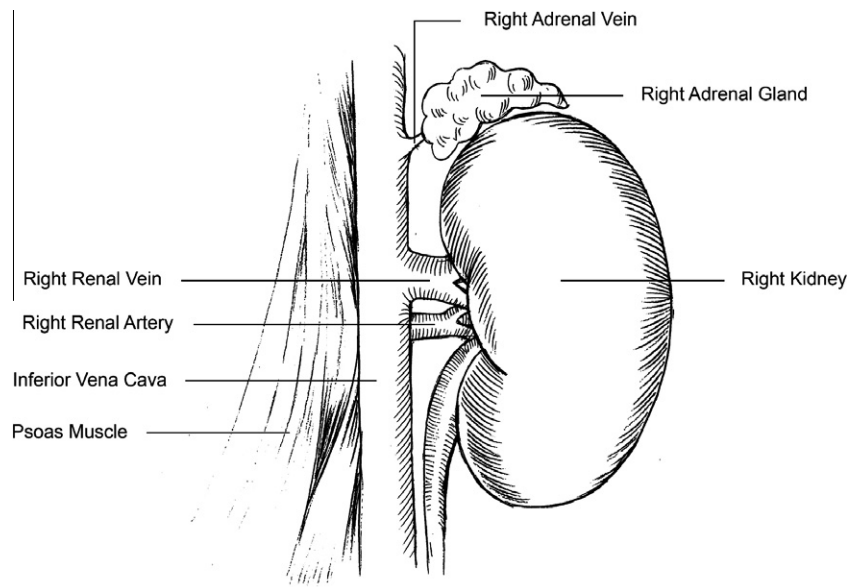


Figure 6 Retroperitoneal view for right LA.

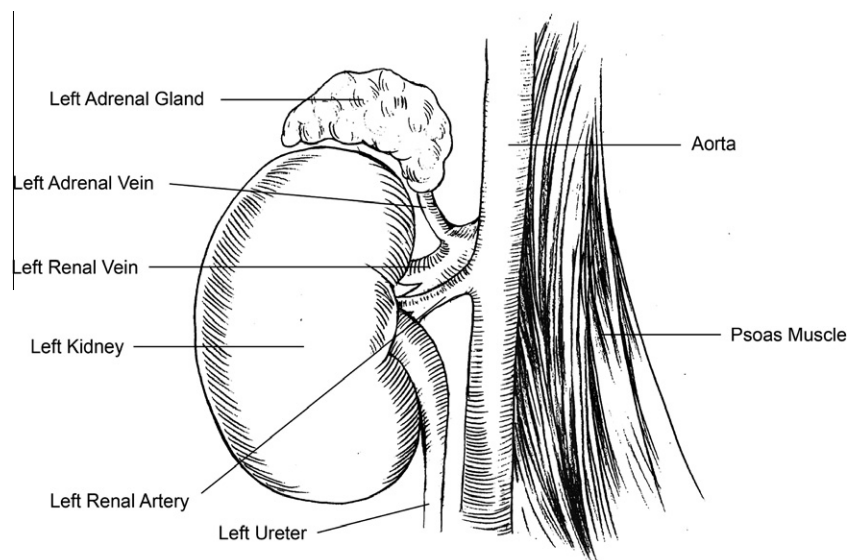


Figure 7 Retroperitoneal view of left LA.

renal hilum. Dissection is carried out cranially to further expose the upper IVC to find the right adrenal vein (Fig. 6). In patients with excessive perirenal fat, it is helpful to open Gerota's fascia and expose the upper pole of the right kidney. Careful dissection is done on the lateral aspect of the IVC until the adrenal vein is identified, clipped and divided or controlled with LigaSure. Inferior, medial and posterior dissection is done to free the mass from upper pole of the kidney, IVC and diaphragm, taking care to control additional veins as needed. The superior and lateral attachments are then freed and the tumour is placed in an endobag. The field is inspected for haemostasis and the specimen is removed by enlarging the initial camera port while the camera is placed in the 10 mm posterior working port.

On the left side the landmarks to find are the psoas muscle and the left ureter that are followed cranially to find the left renal hilum and upper pole of the left kidney (Fig. 7). As in the right side, opening Gerota's fascia might help in exposing the upper pole and the left renal vein to find the left adrenal vein. The vein is freed, clipped and divided or controlled with LigaSure. The mass is dissected carefully from the left renal upper pole and pancreas, as additional veins draining to the phrenic vein should be controlled as found. Dissection is then finished in the avascular plane to free the mass from the diaphragm and peritoneal attachment. The mass is placed in an endobag and the field is inspected for haemostasis.

The posterior retroperitoneal approach has been recently popularised mainly by endocrine surgeons [32–

34]. It has the advantage of performing bilateral adrenalectomy when needed with no need for further patient positioning. Patients are positioned prone on a Wilson table. The main disadvantage of this approach is the limited working space and unfamiliar anatomical landmarks, making operating on obese patients with larger tumours more challenging.

Robotic-assisted

The robotic surgical system has become common in most urological centres performing radical prostatectomy. It gives superior three-dimensional vision at the operating console, in addition to wide-range tremor-free movements at the tip of the surgical instruments. These give the operating surgeon the leverage to work more comfortably in small areas with difficult angles. The potential technical limitation is the absence of tactile sensation that can result in tissue tearing during dissection. This point is crucial during adrenal surgery, to avoid tumour rupture, especially in potentially malignant lesions.

The robotic-assisted LA has been used with both the transperitoneal and the retroperitoneal approach [28,29]. Although not addressed specifically with adrenalectomy, the cost of using the robot system is an issue that should be considered.

Single-port

As surgeons' skills and experience continue to improve and technical advances in instruments continue to develop, the era of single-port surgery is being explored in the field of minimally invasive surgery. Although the technique is still being developed in selected centres of excellence, it is appealing to many patients, because of its cosmetic advantage. It is technically challenging when done with the standard laparoscopy setting and instruments. The advances in the robotic technology system might further simplify the procedure. The adrenal gland is again a good candidate because it is relatively small. The specimen can be retrieved with ease using the single-port access. The initial experience is promising [30], but it is left to further technical developments and confirming advantages to the patient before the technique finds wider acceptance and practice.

Outcome

The application of LA has expanded to include almost all adrenal pathology, but most cases are performed for endocrine causes [23].

Phaeochromocytoma was one of the initial indications for LA [1]. The concern that pneumoperitoneum can result in increased haemodynamic fluctuations has not been confirmed. The safety and effectiveness of the procedure is well documented, with cure rates of up to 98% [3,23,35]. The upper size limit to consider LA has been increased from 6 cm to 10–11 cm, although the size

issue is left to the judgement of the operating surgeon and expertise of the team [36,37]. Malignant phaeochromocytoma as suggested by imaging should still be considered a contraindication to LA, due to the increased risk of tumour rupture, spillage and recurrence.

For Cushing's syndrome, LA has been used for unilateral and bilateral adenomas and hyperplasia, pituitary-dependent disease and ectopic adrenocorticotrophic hormone (ACTH) secretion [23]. Patients with Cushing's syndrome are known to be at an increased risk of perioperative morbidity and mortality after open surgery, due to poor tissue healing, obesity and increased thromboembolic events. This makes the laparoscopic approach more appealing, with its advantages of small incisions, less pain and faster ambulation and recovery. A high success rate in achieving endocrinological cure has been reported with unilateral disease, but rates with bilateral disease are lower [38,39].

In the case of primary hyperaldosteronism, LA has been reported to give excellent results in curing the hypokalaemia, but hypertension can persist in up to 25–30% of patients even with normalisation of aldosterone and renin levels [23], possibly due to the coexistence of essential hypertension [40].

LA for adrenal incidentaloma is indicated when the endocrine evaluation shows adrenal hyperfunction, and if the lesion is > 4–5 cm. If follow-up shows an increase in size or if symptoms develop, LA should be offered for any size.

Complications

LA is an advanced procedure that can cause complications during or after surgery, with morbidity or even death. Gumbs and Gagner [23] reviewed 2565 cases reported in large series and found that the complication rate was 2.9–15.5%. Bleeding was the most common intraoperative complication, followed by visceral injury. Postoperative complication rates are less than for open adrenalectomy, due to early ambulation and faster recovery. However, these postoperative complications should be considered, especially the thromboembolic, urinary, gastrointestinal, pulmonary and cardiovascular events [23,41,42], in addition to rare but high-grade complications [43]. The overall perioperative mortality rate when reported was 0.8–1.2% in large series [23].

LA for malignancy

ACC

Primary ACC is a rare and aggressive disease. The goal of its surgical excision is to achieve the highest cure rate by complete resection with no capsular rupture or tumour dissemination.

Several series reported the outcome of laparoscopy for ACC in a few patients [44–48]. The locoregional

recurrence rate was noted to be high and many patients died from their disease, although the results were no worse than those of open adrenalectomy [49,50]. These findings suggest that the advantages of laparoscopy should be weighed against the biological aggressiveness and the natural history of ACC.

Preoperative imaging suggesting malignancy with signs of local invasion, lymphadenopathy or venous tumour thrombus should be a contraindication to LA. Likewise if intraoperative findings suggest malignancy and the surgeon is not confident of performing an oncologically optimal procedure, conversion to open surgery should be considered.

Metastasis

Surgical excision of solitary adrenal metastasis might give some patients a survival advantage [51–53]. Several studies of LA for metastasis have been reported, with low morbidity and low recurrence rates [45,54,55]. The upper limit of lesion size to consider for LA is left to the surgeon's expertise and competency.

Bilateral adrenalectomy

Bilateral adrenalectomy is mainly indicated for ACTH-dependant adrenal hyperplasia with hyperfunction, either from a pituitary (Cushing's disease) or ectopic source. Less common indications, when partial adrenalectomy cannot be done, include familial pheochromocytoma (MEN2, von Hippel-Lindau, NH1), bilateral adrenal metastasis, or multiple adenomas. Several reports on bilateral LA have been published and confirm the safety and effectiveness of this technique, either simultaneously or sequentially [41,56–58].

Partial adrenalectomy

Partial adrenalectomy can be indicated for bilateral adrenal tumours, familial pheochromocytoma, solitary adrenal gland lesion and unilateral aldosterone-secreting adenomas. The lesion should be small, well-defined and located on the periphery of the affected gland. Several reports showed the efficacy and safety of partial LA, with a low recurrence rate and need for hormonal replacement [59–63]. The use of intraoperative US might help, especially with bilateral disease [64]. There are still some issues among surgeons on whether the main adrenal vein should be preserved and how much adrenal tissue needs to be preserved to maintain adequate endocrine function.

Conclusion

The surgical treatment of adrenal tumours has advanced tremendously with the introduction of laparoscopy, and LA is now the standard treatment for most adrenal le-

sions of acceptable size and no signs of surrounding structure invasion. While LA is safe and effective and gives patients all the advantages of minimally invasive surgery, appropriate judgement is needed when applying the technique to larger adrenal tumours.

Conflict of interest

The authors have no conflict of interest to declare.

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