Review Article

Laparoscopic adrenalectomy

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Abstract: In the last three decades, endoscopic adrenalectomy has become the gold standard for the surgical treatment of most adrenal diseases. Gagner *et al.*, first reported in 1992, the lateral trans-abdominal laparoscopic approach to adrenalectomy. Afterwards, several retrospective and comparative studies addressed the advantages of minimally invasive adrenalectomy specifically consistent in less postoperative pain, improved patients' satisfaction, shorter hospital stay and recovery time when compared to open adrenalectomy. The lateral transabdominal approach to the adrenals is currently one of the most widely used, since it allows an optimal comprehensive view of the adrenal region and surrounding structures, and provides and adequate working space. On the other hand, from a technical point of view, essential requirements for a successful laparoscopic adrenalectomy are an appropriate knowledge of retroperitoneal anatomy, a gentle tissue manipulation and a precise haemostasis technique in order to identify appropriately the structures of interest and avoid the troublesome 'oozing' that could complicate the surgical procedure.

Keywords: Laparoscopic adrenalectomy; endoscopic adrenalectomy; adrenal tumours; personalized medicine

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Introduction

Gagner *et al.* first described trans-abdominal laparoscopic adrenalectomy with the flank approach in the lateral decubitus position in 1992 (1). Subsequently, the technique has been further standardized (2,3) and quickly became the gold standard treatment for most surgical adrenal disorders (4,5).

The successful application of minimally invasive surgery to adrenals is mainly due to some key factors: the endoscopic approach allows an optimal exposure of the adrenal area; the magnification provided by the endoscope is particularly helpful during the dissection of an anatomically complex and dangerous region as retroperitoneum is; from an anatomically point of view the adrenal vascular supply is well defined; the adrenalectomy is an ablative procedure, thus particularly suitable for an endoscopic approach (6).

Several retrospective and comparative studies addressed the advantages of minimally invasive adrenalectomy specifically consistent in less postoperative pain, improved patients' satisfaction, shorter hospital stay and recovery time when compared to open adrenalectomy (5,7-12).

These results have been more recently, validated by several USA national surveys that confirmed that laparoscopic adrenalectomy has significantly lower perioperative morbidity and shorter length of hospital stay than open adrenalectomy (13-15).

The laparoscopic transabdominal lateral adrenalectomy (TLA) is currently the most widely used approach, since it allows an optimal comprehensive view of the adrenal lodge and surrounding structures, and provides adequate working space. An additional advantage of the transabdominal approach is the possibility to explore the abdominal cavity

allowing the treatment of eventually associated abdominal pathologies during the same procedure. Moreover, this approach allows a quick conversion to hand-assisted or open surgery in the case of difficult dissection or intraoperative haemorrhage.

However, previous abdominal surgery particularly when performed on the retroperitoneal area (kidney, pancreas, or spleen) can produce significant adhesions in the adrenal region and may render the trans-abdominal approach challenging particularly for surgeons with limited laparoscopic experience. Despite this, several series reported that up to 55% of patients had previous abdominal surgery but conversions to open surgery were very rarely attributed to adhesions (5,16,17).

The aim of this article is to review briefly the experience gained with TLA, and to evaluate its effectiveness for the surgical management of adrenal disease.

Operative techniques

One of the main advantages of the trans-abdominal lateral approach is to allow the gravity-facilitated exposure of the adrenals (2,3,6). Indeed, after the mobilization of the structures overlying the adrenals, the liver on the right, and the spleen and tail of the pancreas on the left, there is no need to manipulate further these structures during the following steps of the procedure.

From a technical point of view, essential requirements for a successful laparoscopic adrenalectomy are an appropriate knowledge of retroperitoneal anatomy, a gentle tissue manipulation and a precise haemostasis technique in order to adequately identify the structures of interest and avoid the troublesome oozing that could complicate the surgical procedure (2,3,6).

Patient and trocars position

The TLA requires general anaesthesia, with muscle relaxation and controlled ventilation. The operating table should be capable of flexion with a kidney rest that can be elevated. The patient should be placed initially in a supine position for induction anaesthesia. An orogastric tube for gastric decompression (mainly helpful in left-sided adrenalectomy) and a Foley catheter are usually placed and generally removed at the end of the procedure. The current guidelines for antibiotic prophylaxis (18) and for prevention of venous thromboembolism (19) are applicable to most of adrenal pathologies, whereas some diseases (e.g., Cushing) are associated with a higher operative and perioperative risk (20).

Atraumatic graspers, scissor, hook, and clip applier are common to many laparoscopic procedures. More specific for adrenalectomy are small swabs, allowing atraumatic retraction of the gland. A right-angled grasper or vascular clamp should be ready on the operative table. An atraumatic grasper is useful for the mobilization of the adrenal gland in order to avoid bleeding during the manipulation of periadrenal fat. A needle holder must be available to perform laparoscopic suturing if required to repair vessel injury. Safe dissection requires a high-quality CCD camera. The operation is performed using a 0-30 degree 5–10-mm laparoscope.

The patient is turned in a full lateral left decubitus position for the right and in a full lateral right decubitus position for the left adrenalectomy respectively, with the 10th rib directly over the breakpoint in the table. A cushion is placed under the opposite flank with respect to the side of adrenalectomy. The table is flexed in order to maximize the exposure of the space between the costal margin and the iliac crest, avoiding an excessive tension of the abdominal wall, which may decrease its distensibility during CO_2 insufflations. The right/left arm is elevated and secured on an elevated arm board. The patient's legs are flexed to avoid stretching of the crural nerve. The area from the umbilicus to the spine and from the nipple down to the superior anterior iliac crest should be exposed. Adequate patient positioning is essential for technical success in laparoscopic adrenalectomy (2). The surgeons stand on the abdominal side of the patient, facing the monitor at the head of the patient.

Initial peritoneal access is achieved 2 cm inferior to the right/left costal margin in the midclavicular line, with either the blind (Verres Needle) access, with the open (Hasson) access or with the optical access trocar (1-3,5,6,21). The Verres technique implies CO_2 insufflation starting in the right/left subcostal area with a Verres needle up to 15 mmHg. The Verres needle is placed under the right/left costal margin at the anterior axillary line and lateral to the rectus muscle. It is mandatory to perform a saline test in order to exclude organs injuries. Otherwise, pneumoperitoneum is induced by an open approach at the site of the first trocar. Optical access trocars allow inserting the endoscope directly inside the clear tip trocar, enabling the surgeon to visualize all the abdominal layers during port placement. A pressure of 12–14 mmHg is generally used for CO_2 insufflation.

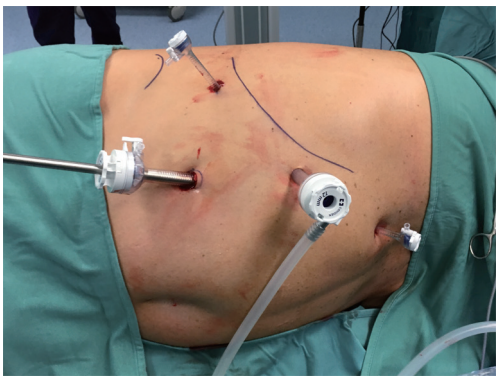

Figure 1 Trocars position for right laparoscopic transabdominal lateral adrenalectomy (TLA).

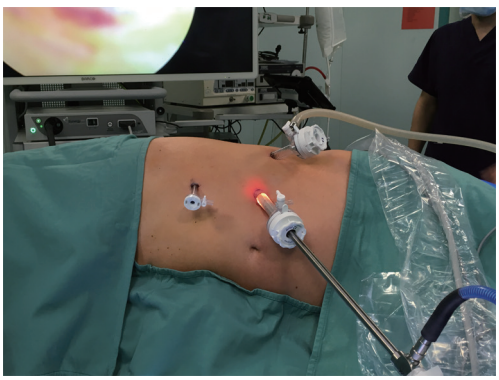

Figure 2 Trocars position for left laparoscopic transabdominal lateral adrenalectomy (TLA).

Right adrenalectomy

A 10–12 mm trocar for the endoscope is placed in the subcostal area in the anterior axillary line. A diagnostic laparoscopy is then performed. The ascending colon, the liver, the right kidney, the diaphragm, and the duodenum are inspected. If there are signs suggestive of adrenal malignancies (e.g., local invasion, though this is rarely apparent at this stage in the procedure) conversion is mandatory.

Under direct vision, the second 10–12 mm trocar is placed in the subcostal area medially to the first one. This receives graspers for exposure of the operative field, hook, scissors, retractors, instruments with peanut swabs and energy devices to achieve adequate haemostasis. The third trocar (5 mm) is inserted between the anterior axillary line and the epigastrium, receiving a smooth retractor in order to retract the liver during the whole procedure. The fourth trocar (5 mm) is inserted at the subcostal angle (*Figure 1*).

Figure 3 Real time laparoscopic lateral transabdominal right adrenalectomy (22).
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Left adrenalectomy

Left TLA may be performed with three trocars in most of cases, although a forth additional port can be optional (*Figure 2*). A 10 mm trocar is positioned in the subcostal space at the anterior axillary line for the endoscope. Diagnostic laparoscopy is then performed. The ligament of the colonic splenic flexure and the descending colon are inspected. The spleen, the lateral segments of the left liver, the diaphragm, and the greater curvature of the stomach are inspected. If there are signs suggestive of adrenal malignancies (e.g., local invasion) conversion is mandatory. If the inspection is satisfactory, two other 5–10 mm trocars are placed under direct vision about 7 cm on each side of the first trocar below the costal margin. As in the right side, they will take graspers for exposure of the operative field, hook, scissors, retractors, instruments with peanut swabs and energy devices to achieve adequate haemostasis. The forth trocar, when necessary, is positioned below the first one, at distance of 4 to 5 cm.

Right TLA: surgical steps (Figure 3)

Exposure

The key factor for an adequate exposure is an effective dissection of the liver right triangular ligament and of the hepatoparietal ligament wide enough in order to achieve a complete mobilization of the liver, that can be retracted upwards and medially (*Figure 4*). After the effective liver mobilization, the adrenal gland and the inferior vena cava are adequately exposed (*Figure 5*).

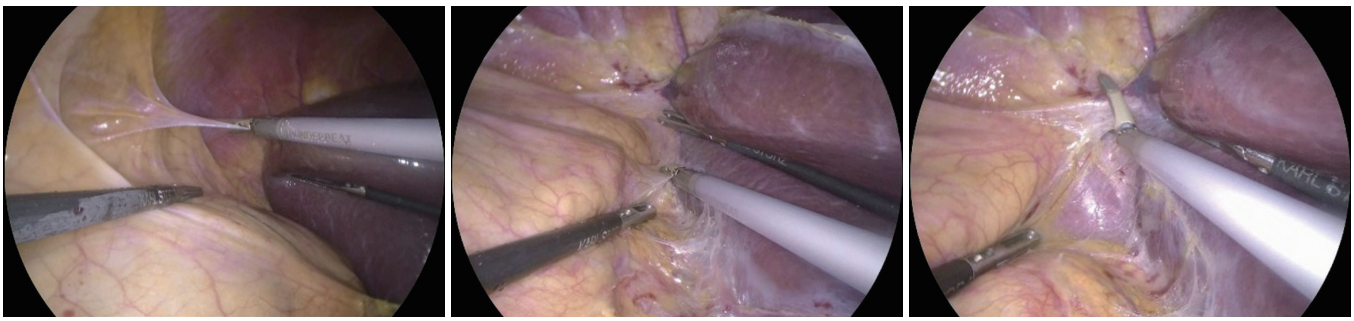

Figure 4 Dissection of the right triangular and hepatopatietal ligaments allow obtaining an effective mobilization of the liver.

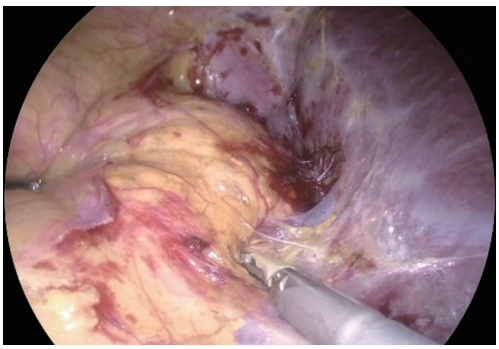

Figure 5 Exposition of the adrenal gland and of the inferior vena cava.

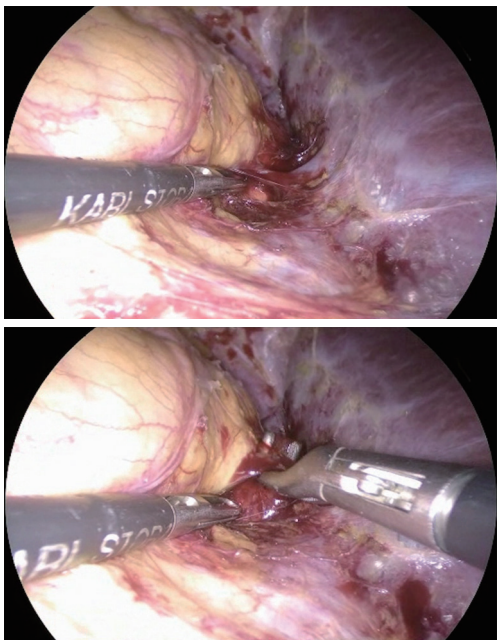

Figure 6 Dissection of the plane between the adrenal gland and the inferior vena cava and identification of the right main adrenal vein.

Dissection of the main vein

Once, the medial edge of the adrenal gland is identified, the plane between the vena cava and the gland is opened (*Figure 6*), allowing the lateral retraction of the adrenal and thus exposing the area where the main adrenal vein runs. The main landmark for the identification of the right adrenal vein is the inferior vena cava. The dissection of the lateral edge of the vena cava should carry out starting from the right renal vein and heading superiorly. Once the main adrenal vein is identified and dissected by the means of a right angled (*Figure 6*), it is doubly clipped and divided, completing the most difficult step of the dissection (*Figure* 7). The dissection of the adrenal vein as first step of the adrenalectomy, can be more demanding in case of large size adrenal lesion. Indeed, in this case can be suitable starting the dissection from the lateral and superior aspect of the lesion and then moving inferiorly along the vena cava. In about 20% of cases, an accessory adrenal vein is encountered 2–3 cm above the main adrenal vein and when present should be dissected, clipped, and divided.

End of the dissection/extraction

The adrenalectomy then proceeds with the dissection of the inferior aspect of the adrenal *en bloc* with the periadrenal fat. Than the adrenal is lifted up and the dissection is continued at the posterior and lateral aspect of the gland and finally superiorly. The last step of dissection is the identification and the division of the three main adrenal arteries and

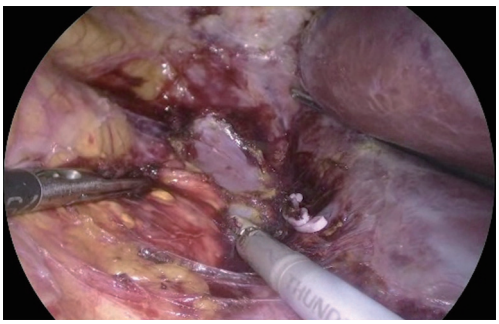

Figure 7 Dissection of the right main adrenal vein.

Figure 8 Real time laparoscopic lateral transabdominal left adrenalectomy (23).
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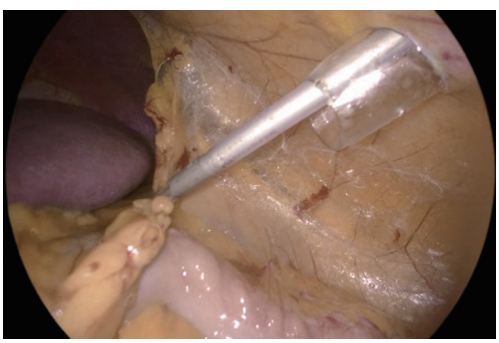

Figure 9 Dissection of the left colonic flexure.

accessory veins. The adrenal within the retrieval bag is removed through a 10–12 mm trocar. Trocar sites can be slightly enlarged if needed. The placement of a drain in the adrenal lodge is optional but generally advisable. Careful port site closure is recommended in order to prevent incisional hernias.

Pitfalls

Besides the general pitfalls related to the laparoscopic approach (bowel and vascular injuries, gas embolism, operative difficulties linked to adhesions, obesity, etc.), in the right adrenalectomy there are some specific side-related problems as: liver injury; duodenum injury; vena cava injury; division of a polar renal artery; rupture of the adrenal capsule; injury of the diaphragm.

Left TLA: surgical steps (Figure 8)

Several factors as the lack of major anatomic landmark (e.g., the inferior vena cava in the right side), the relative small size of the left adrenal gland, the main vein within the retroperitoneal fat and the close proximity of the pancreas tail, may render the left adrenalectomy a challenging procedure.

The prerequisite in order to achieve an adequate exposure of the left adrenal gland is a complete mobilization of the splenopancreatic bloc. Indeed, an effective dissection of the spleen along with the tail of the pancreas allow to take advantage of the gravity-facilitated exposure of the left adrenal, since the spleen will fall away from the operative field.

Exposure

The first step of adrenalectomy is the dissection of the left colonic flexure (*Figure 9*).

Afterwards, the next step of the procedures is the mobilization of the spleen, accomplished by dissecting the splenoparietal ligament (*Figure 10*). The lateral decubitus position allows for an easy exposure of the splenoparietal ligament. The dissection of the splenoparietal ligament is starting at posterior and inferior edge of the spleen, taking care to left a margin of about 2 cm of peritoneum for an effective retraction of the spleen allowing the exposition of its posterior aspect. The splenoparietal ligament dissection is continued until the diaphragm, far enough to visualize the fundus of the stomach (*Figure 10*) and the left crus of the diaphragm.

The full dissection of the splenoparietal ligament allows a complete mobilization of the spleen.

Then, the dissection proceeds with the dissection of the splenorenal ligament, starting from the posterior aspect of the spleen and continuing with the tail of the pancreas. The medial and anterior retraction of the splenorenal ligament allows its dissection in a superficial plane, avoiding the deep dissection in the perirenal fat. At this point, the

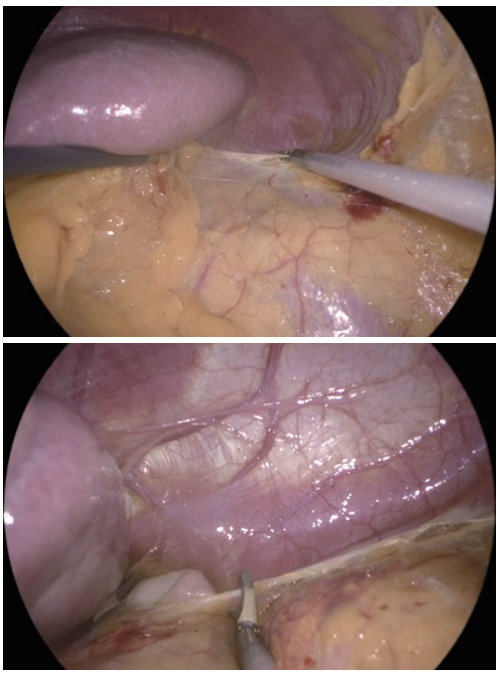

Figure 10 Dissection of the splenoparietal ligament: the dissection is performed far enough to visualize the greater curvature of the stomach.

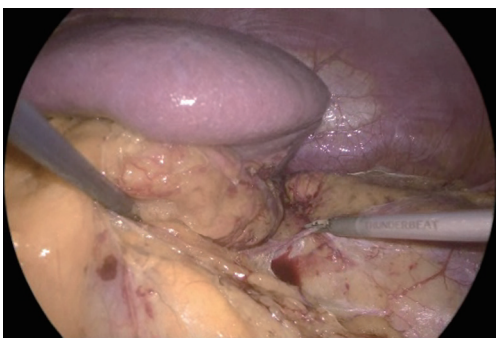

Figure 11 The splenopancreatic bloc is displaced medially.

splenopancreatic bloc is displaced medially, out of the operative field, with gravity playing a major role (*Figure 11*), and the kidney upper pole and the adrenal area are exposed.

Dissection of the main vein

The dissection of the left adrenal should start on the medial aspect of the gland proceedings from upper to lower adrenal pole, keeping close to the posterior muscular plane. This manoeuvre allows the lateral rotation of the adrenal and exposes the space where the left adrenal vein runs.

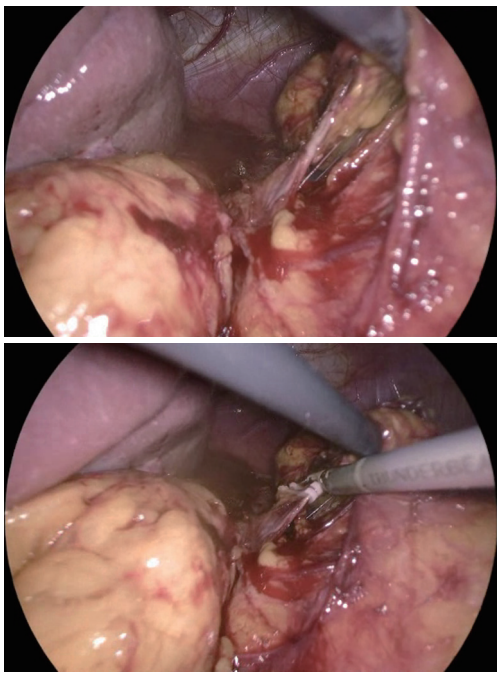

Figure 12 Identification and dissection of the left main adrenal vein.

The dissection of the lateral aspect of the gland should be avoided, since the adrenal would fall medially preventing the access to the medial and inferior edge of the gland. During the dissection of the medial aspect of the adrenal gland the diaphragmatic vein is often encountered: it represents an important landmark for the identification of the main left adrenal vein. Once the main adrenal vein is identified, it is isolated, often using a right-angled dissector, and doubly clipped and divided (*Figure 12*).

End of the dissection/extraction

After the dissection of the main adrenal vein, the adrenal *en bloc* with the periadrenal fat is lifted up, and the dissection continues at the posterior and lateral aspect of the gland. The adrenal upper pole is dissected lastly, allowing the 'hanging technique'. Dissection can be performed using a hook, coagulating scissors or energy devices. The adrenal within the retrieval bag is removed through a 10–12 mm trocar (the trocar site can be enlarged if needed). The placement of a drain in the adrenal lodge is optional but generally advisable. Careful port site closure is recommended in order to prevent incisional hernias.

Pitfalls

Specific side-related problems that can be observed for a

left adrenalectomy are splenic injury and pancreatic injury. In the left sided lesion, moreover, confusion can occur between the main adrenal vein and the renal vein especially in the case of large adrenal tumours that can displaced horizontally the generally oblique left adrenal vein. As in the right, also in the left adrenalectomy inadvertent division of an unrecognized polar renal artery, rupture of the capsule of the gland and diaphragmatic injury can occur.

Indications to TLA

Endoscopic adrenalectomy is the gold standard treatment for small to medium-sized (≤6 cm) benign adrenal tumours, both functioning and non-functioning (5,6,24).

However, the increasing experience with the endoscopic adrenalectomy produced the broadening of the indications to this approach, proposing it also for large and potentially malignant adrenal tumours (25,26).

Despite tumour size is usually considered a parameter predicting the malignancy of the adrenal lesion, it remains relatively insensitive and nonspecific (25). Indeed, the role of tumour size as a limiting factor for the choice of the surgical approach for adrenalectomy, seems unimportant for some surgeons (25-28). Conversely, other surgeons consider the tumours size as a key factor for the laparoscopic approach to adrenalectomy, assessing the adrenal lesion size threshold for endoscopic adrenalectomy between 6 and 10 cm (27,29-32). From a theoretical point of view, about 75% of adrenal tumours >6 cm will be benign at the final pathological report (28). Thus, if a tumour size >6 cm is recognized as a contraindication to laparoscopic adrenalectomy, the advantages of minimally invasive approach will be denied to patients having a most likely benign disease (27,33).

Moreover, the early experience on laparoscopic adrenalectomy reported that in experienced hands the endoscopic removal of large adrenal lesions (up to 10 cm in maximum diameter), in absence of suspicious radiological findings, was feasible and safe (5,25,34).

However, in the case of invasive adrenocortical carcinoma (ACC), open adrenalectomy remains the procedure of choice (27,35-42).

The large diffusion of minimally invasive adrenalectomy led to an increased referral to surgery in the case of adrenal incidentaloma (43), with a consequent increased risk of unexpected pathological diagnosis of ACC after endoscopic adrenalectomy (44). Indeed, the reported frequency of ACC in patients operated for adrenal incidentaloma reaches 10% in some series (45).

However, in absence of radiological suspicious findings (invasion of surrounding structures, lymph node or distant metastases, intravenous thrombus), it may difficult to predict malignancy pre-and even intra-operatively (45).

A complete surgical resection is the mainstay treatment of localized ACC [European Network for Study of Adrenal Tumors (ENSAT) stage I–III] (46), since a R0 resection is the only means to achieve long-term disease control in ACC patients (40,47). Some reports reported an increased risk of R1-R2 resection or tumour spill (44), peritoneal carcinomatosis (48,49) and earlier recurrence (44) in patients undergoing endoscopic adrenalectomy for localized ACC. Therefore, based on these findings, an international consensus conference on ACC strongly discouraged endoscopic adrenalectomy for the treatment of known or suspicious ACC (50).

On the contrary, recently published comparative studies based on single center (51) or multi-institutional series (52) demonstrated that the oncologic outcomes of localized ACC following endoscopic adrenalectomy and open adrenalectomy could be similar. Therefore, the role of endoscopic adrenalectomy in the treatment of localized ACC is one of the most controversial and debated topics in adrenal surgery.

Due to the low incidence of ACC, there are no randomized trials comparing endoscopic and open adrenalectomy (42). Indeed, the discussion on this subject should be on the basis of the retrospective study of single center series and multi-institutional surveys.

During the last years, several papers further supported the debate. Several series from the USA persist to discourage endoscopic adrenalectomy in patients with known or suspected ACC (53-56), while some reports from Europe showed that endoscopic adrenalectomy does not jeopardize the oncologic outcome of selected cases of ACC (57-59).

Therefore, nowadays, there are not definitive conclusion regarding the oncologic outcome of endoscopic adrenalectomy *vs.* open adrenalectomy in patients with ACC.

However, it could be argued that in referral centers the oncologic outcome of ACC treated with endoscopic approach is not inferior to that achieved whit open adrenalectomy, when strict selection criteria and the principles of oncologic surgery are observed. On the other hand, if performed by non-experienced surgeons, endoscopic adrenalectomy for ACC can involve a higher risk of R1/R2 resection and tumour bed and/or intraperitoneal recurrence, mostly if strict selection criteria

and the rule of conversion to open approach in case of challenging dissection are not followed.

However, if an endoscopic approach is considered for an adrenal tumour at increased risk of malignancy (a mass with radiological intratumoral signs of suspicion and without clear locoregional involvement), the transabdominal lateral adrenalectomy might be preferred approach because it might allow intraoperative evaluation of the presence of distant metastasis and larger *en bloc* resection of the tumour (42).

Operative and post-operative outcomes of TLA

The majority of studies have demonstrated that laparoscopic adrenalectomy by transabdominal lateral approach is a safe technique with low perioperative complications and rare postoperative mortality (16,60-73).

The average complication rate reported for TLA is difficult to evaluate because of the lack of standardized definition through the different studies. However, the average rate of complications seems to be less than 9%, with a range between 2.9% and 15.5% (5,16,61,63-65,69-73).

Several risk factors for complications and conversion, as surgeon and hospital volume (60-66), tumour- and patients-related characteristics (16,67-73), have been evaluated in single-center (16,64,70,71,73) and national studies (60-63,65-68,72).

The impact of surgeon and hospital volumes on postoperative outcomes for adrenalectomy appears relevant in different experiences (60-66). Park *et al.* (61) in a population-based retrospective analysis including 3,144 adrenalectomies, observed a significantly higher rate of complications (18.3% *vs.* 11.3%) and a significantly longer hospital stay (5.5 *vs.* 3.9 days) in procedures performed by low-volume surgeons.

In a national study by Palazzo *et al.* (65) the authors found a mean hospital stay and a rate of 30-day readmissions significantly higher in the low- versus high-volume adrenal surgeons. Bergamini *et al.* (63) found that age, patients BMI, tumour size and diagnosis of phaeochromocytoma are risk factors for complications but observed a significantly lower rate of these complications in referral with the respect of non-referral centers.

In contrast, Gallagher *et al.* (66) did not found any association between surgeon volume and complication rates or length of hospital stay. However, the definition of high- versus low-volume surgeon is highly variable across the different study, probably due to the lack of a method to set a volume threshold. A recent USA national-level analysis conducted on a large series of patients who underwent adrenalectomy, showed that higher surgeon volume was associated with better patients' outcomes and lower costs, suggesting an annual threshold of adrenalectomy ≥6 (60).

Among the patient's characteristic affecting the TLA operative outcome, the most relevant risk factors for complications and conversion were obesity (16,73,74), history of previous abdominal surgery (16,71,75), the tumour side (69), patients' comorbidities (73) and the diagnosis of pheochromocytoma (73).

Obesity with a body mass index ≥30 has been previously reported as risk factor of complication in laparoscopic adrenalectomy (74). However, more recently, it has been demonstrated that obesity is not associated with complications or prolonged length of hospital stay, but it significantly affects the operative time (16,73).

The history of abdominal surgery, especially previous upper mesocolic or retroperitoneal surgery, has been reported to increase the risk of intra- and post-operative complications as well as the risk of conversion (71,75). However, recently published study, did not find higher conversion and complications rate for TLA in patients who underwent previous abdominal surgery (16).

In a recent study, conversion to open surgery and left-sided adrenalectomy were founded to be independent risk factors for complications (69). The authors ascribed the finding of higher overall complications in left-sided tumours to the partial mobilization of the left pancreas and spleen required in left TLA (69).

The diagnosis of pheochromocytoma (69) and the patients' comorbidities (73) have been also reported as risk factors for post-operative complications.

Postoperative complications were reported to be higher in patients with tumour size ≥45 mm (71) and ≥6 cm respectively (73). However, no differences in terms of conversion and complication rate were found in a comparative analysis of TLA performed with different cut-off of adrenal lesion size (<6 *vs.* 6–8 *vs.* >8 cm) (76).

Overall, conversion of TLA to an open procedure occurs in approximately 2% of cases, with a wide range between 0% and 13% (5,16,61,63-65,69-73). The most frequent reported causes of conversion are vascular or organ injury and technical difficulties (5,16,61,63-65,69-73).

The mortality rate of TLA, even if a standard definition is lacking across the different study, is low and appeared to be between 0% to 0.8% (5,16,61,63-65,69-73). The most

frequent reported causes of mortality included massive bleeding, pancreatitis, pulmonary embolism, sepsis.

Conclusions

Minimally invasive adrenalectomy has become the standard approach for adrenalectomy in the proper clinical settings. The TLA has been shown to be safe and effective for most adrenal pathologies. Overall, the excellent results reported in the literature reflect the experience accumulated with TLA that remains an approach as relevant today as it was 25 years ago.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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