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Guest Editor: Radu Mihai

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Aims and Scope

Gland Surgery (Gland Surg; Print ISSN 2227-684X; Online ISSN 2227-8575) publishes articles that describe new findings in the field of translational research in gland surgery, provides current and practical information on diagnosis, prevention and clinical investigations of gland surgery. Specific areas of interest include, but not limited to, multimodality therapy, biomarkers, imaging, biology, pathology, and technical advances related to gland disease (breast, thyroid, digestive gland, *et al*.). Contributions pertinent to gland surgery are also included from related fields such as nutrition, public health, human genetics, basic sciences, education, sociology, and nursing. The aim of the Journal is to provide a forum for the dissemination of original research articles as well as review articles in all areas related to gland disease. It is an international, peer-reviewed journal with a focus on cutting-edge findings in this rapidly changing field, while providing practical up-to-date information on diagnosis, prevention, and treatment of gland disease. It has been indexed in PubMed/ PubMed Central now and all articles published in the journal are available in PMC.

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Preface

Surgical anatomy of the adrenal gland

Due to the low incidence of adrenal disease most clinicians will rarely encounter a patient whose clinical signs are reminiscent of the description of Doctor Harvey Cushing or whose biochemical abnormalities are indicative of the syndrome described by Doctor Jerome Conn. Though most trainees preparing for postgraduate examinations will cover the management of a patient with phaeochromocytoma, the reality is that a practicing GP or hospital doctor might only meet one such patient during their entire career. It is therefore not surprising that several papers from United States classified as ‘high-volume surgeons’ those doing only 4 or more adrenalectomies per year as the vast majority of surgeons do only one such case per year (1). A similar situation was reported from the UK (2). We owe to our patients to correct this untenable situation and ensure that younger surgeons with an interest in endocrine surgery are being offered the knowledge and the practical training required in order to make right decisions for the surgical treatment of patients with adrenal disease.

In this context, I am very grateful to all contributors who have been involved in this issue dedicated to adrenal surgery. This material should complement recent publications from the 2019 meeting of the European Society of Endocrine Surgeons (ESES) discussing the need to centralize adrenal surgery in units with sufficient workload (3).

The papers presented cover the technical aspects of laparoscopic (4), retroperitoneoscopic (5) and open adrenalectomy (6), the benefits of collaborating with surgeons from allied specialties such as cardiac surgeons involved in the management of tumours invading the vena cava (7) and an overview of current training in adrenal surgery (8). In addition, new possible developments are also presented: the use of new adjuncts such as fluorescence (9) and the ‘non-anatomical approaches to the adrenal gland (10).

The expectation is that in coming years laparoscopic adrenalectomy will be offered by many centres doing at least 6 cases per year while retroperitoneoscopic surgery will be adopted in centres with significantly higher workload so that enough patients suitable for this technique are operated every year. Most likely open adrenalectomy for malignant tumours will be centralized in centres with specific interest in this condition but all surgeons undertaking minimally invasive adrenalectomy might be obliged to convert to open adrenalectomy in case of intraoperative complications that can not be managed through a laparoscopic approach.

If these papers will stimulate the interest of young surgeons to become involved in adrenal surgery, they should engage in future educational events organized by ESES. The society has established the *Jean-Francois Henry Travelling Fellowship* (http://www.eses.cc/jfh-travelling-scholarship.html) with the aim of supporting trainees who want to visit a centre of excellence to learn a new technique and see in practice many of the technical issues discussed in these papers.

I was honored by the invitation to act as Guest-editor and I remain very grateful to all friends who accepted the invitation to collaborate in this issue.

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Review Article

Challenges of training in adrenal surgery

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Abstract: While adrenal tumors are common, adrenalectomy is rather uncommon. This is one reason for the many challenges regarding the training of adrenal surgery. Here we focus on issues that are most pertinent regarding training of the young surgeons performing adrenalectomy. Due to the very limited literature, what is presented is mainly based on personal experience and/or from the literature published for other surgical operations and subspecialties. The discussed challenges include indications for surgery, surgical approaches and extent, and intraoperative complications. With advances in adrenal surgery, we expect some old challenges to be resolved, and some new challenges to arise. These challenges will be faced in order to continue to help our younger trainee acquire the knowledge and skills to best care for our patients with adrenal diseases.

Keywords: Surgery; adrenal gland; training; challenge

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Introduction

Training of surgical residents and fellows faces many challenges (1). Traditionally, the training followed the master-apprentice model of learning (2) and in many instances it still does (3). For surgeons, the operating theater is of particular importance since it is mainly there where the apprentice learns technical skills. In this regard, it is important to note that the residency training survey of American College of Surgeons Committee in 2017 found that residents are less prepared in technical skills compared to 10 years ago and this applies to both entering and graduating residents (4). This finding can only partly be explained by the effect of duty-hour restrictions (5,6). Another explanation is that surgical residents spend less time in the operating theater these days (5). The result is that surgical residents in general are less prepared and therefore less autonomous when finishing the residency program (7). Of interest, it appears that the number of laparoscopic procedures performed per resident is increasing while the number of more complex operations is still quite low (8).

Despite these challenges, training of surgical residents and fellows is as important as treating patients; we need to ensure that future patients will be treated at least as well as today's patients. Surgical procedures of the adrenal gland are no exception.

Adrenal tumors are common, with prevalence rates derived from systematic analysis of computed tomography investigations higher than 4% (9). In contrast, adrenalectomy is rather uncommon. The fact that only a minority of adrenal glands have to be operated on is one challenge in itself training surgical residents and fellows adequately with regard to adrenal surgery.

In this manuscript, we will focus on the issues that are most pertinent regarding training of the young surgeons performing adrenalectomy. It is beyond the scope of this manuscript to provide comprehensive information on how to perform specific procedures or how to do the preoperative preparation and postoperative follow-up. We will instead try to address the complexity of challenges when it comes to training in adrenal surgery. Of note, there are very few studies on the training of adrenal surgery (10). One reason is that residents have little or no experience with adrenalectomy, both in the past (11) but even more recently (12,13). From an endocrine surgeons' point of view, this is unfortunate since it has been shown that resident participation does not significantly increase operation time in laparoscopic and open adrenalectomy (10,14). One study reported that endocrine surgery fellows graduated with a median of 13 laparoscopic and 2 open adrenal operations (15). However, the ranges were immense: 0–60 for laparoscopic and 0–35 for open adrenal operations.

Due to the very limited literature, what is presented here is mainly based on personal experience and/or from the literature published for other surgical operations and subspecialties. While very important, we will not address other issues including ethical questions associated with the process of teaching and learning surgical procedures (16), challenges training left-handed surgeons (17,18), professionalism (5,6,19), and academic aspects (20).

Adrenal tumors

Adrenal tumors are very common, but the underlying diseases can vary. Adrenal tumors can overproduce various hormones, such as aldosterone and cortisol from the cortex and epinephrine, norepinephrine and dopamine from the medulla. However, most primary adrenal tumors are adenomas that do not produce hormones (21).

Indications for surgery

One main challenge is to teach the indications for adrenalectomy. Despite the numerous indications for adrenalectomy, most adrenal tumors are small non-secreting adenomas and do not need to be operated on. While size is an important criterion, some conditions, such as asymptomatic myelolipoma or simple cyst may not need surgery even if very large. In contrast, some patients with normal size adrenal glands may benefit from resection, such as for Cushing's syndrome due to micronodular hyperplasia or to treat Cushing's disease after a failed pituitary operation. Obviously, understanding the indications for surgery requires deep knowledge of adrenal physiology and pathology.

In general, adrenalectomy is indicated, if

(I) The tumor overproduces hormones,
(II) Malignancy is suspected or proven,
(III) The tumor exceeds a certain size (often 4–6 cm in diameter is chosen as a threshold because of an increased risk for non-secreting adrenocortical cancer), or is causing symptoms due to its size.

It is beyond the scope of this manuscript to discuss details regarding the recommended investigations for adrenal tumors or for excess adrenal hormone production. Detail recommendations have been published by the European Society of Endocrinology (22).

Surgical approach

Open approach, usually transabdominal, is the traditional approach to the adrenal gland (23). It offers good access. However, because of the deep retroperitoneal location, high in the retroperitoneum deep inside the rib cage, several abdominal organs may have to be mobilized to access the adrenal gland. On the right side, the liver usually needs to be mobilized and sometimes this may include the hepatic flexure of the colon or the duodenum. On the left side, the splenic flexure of the colon, distal pancreas and spleen may have to be mobilized.

In open adrenalectomy, the initial steps can often easily be seen and followed by the trainee. However, as the surgeon dissects deeper into the retroperitoneum, visual access is more challenging and it becomes more difficult for the trainee to follow every surgical step.

Endoscopic procedures and surgical simulation

Compared to open approaches, endoscopic approaches have several advantages. Because of a direct, well-lit and magnified operating field, the trainee can see exactly what the teacher does. Endoscopic approach has become the preferred approach in the majority of adrenal surgery. In endoscopic adrenalectomy, the teacher faces similar challenges as in other endoscopic procedures. These include entry approaches, lack of depth perception with 2D image and instruments with limited mobility (except in robotic operations) (24). Although laparoscopic adrenalectomies are uncommon, cross-specialty program can be implemented by training with the more common types of other laparoscopic procedures (25). Robotic adrenalectomy is performed in some institutions, but the benefit is small and the cost is high (26,27). Use of robot for adrenalectomy would also require another set of skills and training.

Animal surgery and surgical simulators have been used to improve trainees' performances (2,28,29). The anatomy of animal adrenal glands, such as that of the pig, is not similar enough to the human anatomy, so animal surgery may only be useful to teach general laparoscopy but not sufficient to teach adrenalectomy. Simulation could improve performance of laparoscopic operations through practice (29). While performance of some tasks can be improved with simulation, these skills acquired through simulation may or may not be transferable to the operating theater (2). The decreased haptic feedback in endoscopic surgery contributes to this problem (30). Therefore, a predictive validity has not been established for training laparoscopic procedures using simulation (24).

Three-dimensional printed models based on computed tomography have been used to recreate the anatomy of the adrenal gland and tumor, for preoperative planning of approaches to adrenalectomy (31). However, high-fidelity simulators such as those available for laparoscopic cholecystectomy (32) do not yet exist for adrenal surgery.

Learning curve

It is acknowledged that individual surgeons will have a personal learning curve that for laparoscopic transperitoneal approach is deemed to be approximately 30 cases (depending on previous experience/expertise with laparoscopic surgery) and for retroperitoneoscopic approach can be between 20–40 cases (33). As the workload of most surgical units around the world remains very limited, there is probably no chance for a trainee to complete his/her own personal learning curve during training. The need and benefits for centralizing adrenal surgery cannot be overestimated. The 2019 meeting of European Society of Endocrine Surgeons (ESES) will aim to review the evidence for volume-outcome correlation and its impact on training and, hence, formulate guidance for a process of establishing and assessing 'centres of excellence' that might provide the care for such patients in the future.

Laparoscopic versus retroperitoneoscopic approaches

The two most common approaches for endoscopic adrenalectomy are transabdominal (laparoscopic) approach and retroperitoneal approach. "Laparoscopy" in generic terms include both transperitoneal and retroperitoneal approaches. In this paper, we use laparoscopy in the narrower meaning to only include the transperitoneal approach. Laparoscopic adrenalectomy was first reported in 1992 (34). Shortly thereafter, the first series on patients operated through a retroperitoneoscopic approach were published (35,36). There is an additional challenge with training for the retroperitoneoscopic approach, because most general surgery trainees are more familial with anatomical landmarks in the abdomen than those in the retroperitoneum. The adrenal gland may be difficult to identify in obese patients with increased retroperitoneal fat obscuring the kidney. The pressure of carbon dioxide insufflation is also different. For laparoscopy, the pressure is often set to 12–15 mmHg. For retroperitoneoscopic approach, the pressure is usually set at 18–25 mmHg to provide a sufficient operating space. Despite this, the retroperitoneoscopic approach has been reported to have a rapid learning curve (37).

Larger adrenal tumors without infiltration/invasion

Adrenal tumor size limits the choice of surgical approach. The current recommendation by the European Society of Endocrinology is that tumors up to 6 cm in size can be resected by endoscopic approaches (either laparoscopy or retroperitoneoscopy), if no local infiltration is suspected (22). Tumors larger than 6 cm may be technically challenging for the retroperitoneal approach (38). The transabdominal approach can be used for large tumors (up to 8–10 cm for the right and 10–12 cm for the left). The current guidelines recommend an individualized approach in these larger tumors (22). Robotic surgery may be useful for large tumors, because the flexibility of instruments with increased degree of freedom of movement makes dissection easier (27). However, the costs of using robot seem to outweigh its benefits. The additional learning curve required and the rarity of large tumors where robotic surgery may be advantageous also limit its usefulness (27).

Tumors with signs of infiltration/invasion

If there are signs of invasion to adjacent organs (e.g., vena cava, liver, pancreas, bowels, kidney), an open transabdominal approach is generally recommended (39). Depending on the experience of the "endocrine" surgeon, other specialists may need to be involved (e.g., vascular surgeons, upper-GI-hepatobiliary-surgeons, lower-GI-surgeons, urologists). These cases are particularly difficult to teach, because they are rare and the responsible surgeon usually wants to operate with an experienced colleague, rendering the trainee to be a second assistant.

Subtotal adrenalectomy

In patients with bilateral adrenal tumors that require bilateral surgery, subtotal adrenalectomy may be indicated to avoid steroid dependency with its side-effects and risks (40). This may be indicated in patients with bilateral pheochromocytomas, or in those with a unilateral pheochromocytoma and a high risk of developing a contralateral pheochromocytoma, e.g., in patients with multiple endocrine neoplasia type 2 or von Hippel-Lindau-syndrome (41). Indication for patients with bilateral adrenal metastases is less clear (42). Subtotal adrenalectomy is rarely useful in patients with aldosteronoma or Cushing's syndrome. If subtotal adrenalectomy is indicated, endoscopic approach is better than open approach because of the magnified operating view (43), making it also better for training.

Intraoperative complications and collaboration with the anesthesiologist

While communication with the anesthesiologist is very important in any surgery, surgery for some endocrine tumors require particularly close collaboration.

Pheochromocytomas produce catecholamines, and cause hypertension and tachycardia. Most surgeons pretreat these patients preoperatively with alpha-adrenergic receptor blocker, although whether this pretreatment is routinely needed is questioned (44). Some patients may require beta blockers to treat tachycardia. Despite the preoperative treatment, some patients may have extreme fluctuation of blood pressure and heart rate during adrenalectomy, that will require intervention by the anesthesiologist. The hemodynamic changes can be worsened by manipulation of the tumor and sometimes the surgeon may need to pause the operation. Sometime high insufflation pressure can cause increased blood pressure and heart rate, and the insufflation pressure may need to be lowered until the situation improves.

Hypercapnia can be caused by carbon dioxide insufflation. It is usually managed by hyperventilation of the patient by the anesthesiologist, but sometime carbon dioxide insufflation needs to be stopped by the surgeon.

Carbon dioxide embolism is a rare but serious complication occurring in both laparoscopic (45) and retroperitoneoscopic procedures (46). The treatment is similar to that for other procedures where carbon dioxide embolism occurs (47).

There are several causes of bleeding during adrenal surgery.

(I) Bleeding of smaller veins or arteries: this can usually be prevented by carefully cauterizing the vessels during dissection. Pheochromocytomas and malignant tumors may have larger pathologic vessels that will require vessel-sealing devices or clipping. Bleeding affects visibility, especially in retroperitoneoscopic approach because of the limited space. If the bleeding cannot be stopped immediately, direct pressure with gauze is recommended. Smaller vessels bleeding will readily stop. Larger, pathologic vessels, in particular veins, may slow but not stop and may require sealing devices or traditional techniques like ligation and/or suturing.

(II) Bleeding of larger veins or arteries: on the right side, the adrenal vein is short and drains directly in into the inferior vena cava. On the left side, the left adrenal vein joins the inferior phrenic vein then drains in into the left renal vein. Because the increased pressure during endoscopic procedures flattens the veins, holes in larger veins may not bleed immediately. Bleeding from large veins can be slowed by increasing the insufflation pressure, especially for the retroperitoneoscopic approach. This is also the reason to desufflate and wait for a while at the end of operation and check the operating field for blood to avoid missing an injured vein. The lower part of the adrenal glands is very close to the main renal artery. Mistakenly ligating the upper pole branch can cause ischemic renal vascular hypertension. Injury to the main renal artery requires immediate action. The bleeding is brisk and delay control can lead to ischemic kidney injury. Immediate conversion to open surgery may be required and immediate reanastomosis should be attempted.

(III) Bleeding of the adrenal capsule: the adrenal is surrounded by a thin and fragile capsule. Damage of the capsule will lead to bleeding. This applies even to the normal adrenal gland. Pheochromocytomas, can bleed profusely.

Cauterizing the bleeding capsule often worsens the situation. Instead, applying pressure with a gauze works better. Breaching the adrenal capsule should be avoided whenever cancer is a concern. Even spilling of otherwise benign pheochromocytoma can lead to pheochromocytomatosis. Routinely resecting the periadrenal tissue with the adrenal gland is the best oncological practice and it also avoids capsular injury and bleeding.

(IV) Bleeding of one of the adjacent organs: bleeding of any of the adjacent organs, especially liver, spleen and kidney, is cared for in the usual manner.

Open surgery

Even when most adrenal surgery is done endoscopically, open surgery is still needed sometimes, either electively because of concerns for invasive cancer or large tumor size, or conversion is required because of bleeding or other difficulty during endoscopic surgery. Teaching open surgery is more challenging because it may be performed in fewer than 10–15% of all adrenal surgery cases (15); this is similarly observed for other mainly endoscopically procedures (8). The judgment required to know when to timely convert endoscopic to open surgery can be complex and it improves with experience. The rarity of conversion (<5%) also makes it difficult to teach.

Conclusions

Adrenal Surgery is uncommon and has very heterogeneous indications and management issues, thus making training of adrenal surgery a challenge. In this paper, we write from the perspective of two experienced endocrine surgeons and trainers, but with dearth of studies and evidence to firmly support our views and advise. We acknowledge that the trainers and trainees may have different perceptions when assessing training programs and their challenges (48). With advances in adrenal surgery, we expect some old challenges to be resolved, and some new challenges to arise. As teachers of endocrine surgery, we will face these challenges and continue to help our younger trainee acquire the knowledge and skills to best care for our patients with adrenal diseases.

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Footnote

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

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Review Article

Robotic adrenalectomy

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Abstract: With the recent advances in equipment and surgical techniques, robot-assisted surgery has become accepted and efficient in the surgical field. It is an emerging technology that can safely be applied for a broad spectrum of surgical procedures. As a result of increased ergonomics, three-dimensional view of the operative area and improved moving capacity of the robotic arms with multi-articulation, robotic technology also has found place in adrenal surgery. Recently, robot-assisted adrenal surgery has been adopted widely in many high-volume tertiary centers. Although there are expected theoretical benefits to this approach, the literature is lacking regarding high level evidence. In this review, we will discuss implementation of robotic adrenalectomy as well as perioperative and postoperative measures that helped improved outcomes, offer a comparison of outcomes between conventional laparoscopic adrenalectomy and robotic adrenalectomy and summarize recent developments that may offer evidence for or against a paradigm shift in this specific field of endocrine surgery.

Keywords: Robotic surgery; adrenalectomy; minimally invasive adrenalectomy

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Introduction

With the increased use of robotics in the operating theatre, robotic adrenalectomy has been adopted by many high-volume tertiary centers as an alternative treatment to conventional laparoscopic adrenalectomy. In adrenal gland surgery, minimally invasive surgery has been proven being effective, compared to open adrenalectomy. It is accepted as the standard surgical method for the majority of adrenal masses. Robotic adrenalectomy is a safe, feasible and effective method, which is positioned as an option, since it is accepted as associated with a three-dimensional perception, a tremor-free surgery, improved moving capacity of the robotic arms with multi-articulation and precise camera control, increasing the ergonomics of this type of surgery (1). These advantages are useful, especially when meticulous dissection is warranted in a deep and narrow field. Overall, this robotic technology allows us to carry out complex tasks in a minimally invasive manner, with an expected faster learning curve than conventional laparoscopy. In adrenal surgery, the application of robotics has not gained that much popularity among surgeons. On the other hand, the "robotic endocrine surgeon" places robot-assisted adrenal surgery as a potential procedure largely supplanting conventional laparoscopic adrenalectomy. The aim of the present review is to give an overview of robotic adrenalectomy and summarize recent outcomes in this field.

Surgical technique

Preoperative preparation

Surgery is performed under general anesthesia. Preoperative preparation and positioning of the patient is the same as for

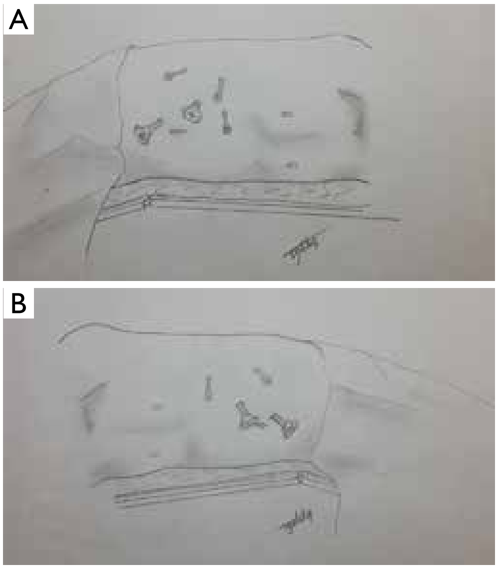

Figure 1 Positioning of the patient and trocars for right (A) and left (B) adrenalectomy.

laparoscopic adrenalectomy. The transperitoneal approach provides greater working space, facilitates orientation by providing readily identifiable anatomical landmarks and better visualization of surrounding anatomical structures. The patient is placed in the left or right lateral decubitus position according the tumor location (left decubitus for right side adrenal tumor and right decubitus for left side tumor) and positioned in a slight Trendelenburg position. Extreme care is taken with pressure points and correctly padding them with pillows and foams. Four trocars are used for left adrenalectomy and one additional port used for right adrenalectomy to aid in liver retraction.

Setup of patient

Currently, robotic surgery is performed with the DaVinci Si or Xi robotic surgical systems (Intuitive Surgical Sarl, Aubonne, Switzerland). These systems consist of three-arm robotic manipulator and remote-control surgical console. After positioning the patient, four or five trocars are used for the procedure. After entering the abdomen with open technique, following insufflation, one camera port (12 mm), two ports for the robotic arms (8 mm) and one port for manual assistance (12 mm) (and one additional port for right sided to aid in liver retraction) are placed. First the camera port (12 mm) is inserted above and lateral to the umbilicus, at the lateral border of the abdominal rectus muscle across from the 12th rib. After the first port insertion, the endoscope is inserted and the abdomen is carefully inspected to rule out any accidental injuries or in terms of other intra-abdominal masses.

After exploration, other ports are inserted under direct vision (*Figure 1A,B*). To avoid clashing between the robotic arms, the ports must be placed about 8–10 cm in distance from each other. The role of the assistant on the surgical table is to change the robotic instruments when necessary, to assist in dissection through the assistant's port, to attach the clip to the adrenal vein or to seal with the vessel sealing device and to perform the wash & aspiration process. A 30-degree endoscope is used for surgery.

Steps of surgery

Left-sided robotic adrenalectomy

Left-sided robotic transabdominal adrenalectomy is performed with the patient in the right lateral decubitus position. For the perfect gland exposure, a complete medial colonic mobilization may be needed. After dividing the lateral adhesions of the spleen and splenorenal ligaments, the spleen, colon, and the pancreas are mobilized medially until the adrenal gland is clearly visualized. During this mobilization, attention should be paid to the tail of the pancreas. Dissection continues into the periadrenal fat in order to identify the following landmarks: inferiorly the left renal vein, laterally the superior pole of the kidney, medially the tail of the pancreas and splenic vessels and posteriorly the psoas muscle. Then the adrenal vein is carefully dissected and clipped by using the robotic clip applier or standard laparoscopic clips placed by the bedside assistant. A vessel sealer also can be used. For hemostasis control, before the mass is removed from the abdomen, it is advised to wait 3–4 minutes after the intra-abdominal gas is evacuated and re-check the operation site. After the adrenalectomy is complete, the robot is undocked, and the gland is removed using a specimen retrieval bag and delivered through the auxiliary port site. After the operative site is irrigated and suctioned, trocars are removed.

Right-sided robotic adrenalectomy

Right-sided robotic transabdominal adrenalectomy is performed with the patient placed in the left lateral decubitus position. On this, different than the left side, five trocars are used (one additional port to aid in liver retraction). The triangular ligament is divided via a robotic monopolar hook and the liver retracted with a laparoscopic retractor superiorly by the assistant to provide wide exposure of the inferior vena cava. Gerota's fascia is incised at the level of the upper pole of the kidney. After the precise dissection of the vena cava and identify the major landmarks (laterally the superior pole of the right kidney, posteriorly the psoas muscle), the right adrenal vein is identified and divided after a clip or vessel sealer has been applied by the assistant. After completion of the dissection of the adrenal space with robotic hook, bipolar forceps and/or vessel sealer, hemostasis is controlled as in left adrenalectomy, and the gland is removed using a specimen retrieval bag.

Bilateral robotic adrenalectomy

Surgery of both adrenal glands as a single operation is possible, also for minimally invasive adrenalectomy. This can be carried out either retroperitoneally or peritoneally with the robotic surgical system. Repositioning is warranted in the peritoneal approached cases that will undergo a lateral decubitus positioning. For these cases, two ports (the assistant and most medial ports) can be used in common to avoid redundant trocar insertion. Details regarding trocar positioning and surgical technique for robot-assisted laparoscopic bilateral adrenalectomy have been described by us previously (2).

Postoperative care

After surgery, the patient is kept in the intensive care unit for a few hours. Antibiotics and prophylaxis for deep vein thrombosis are given according to hospital protocol to all patients. Pain control is performed using intravenous non-opioid and intramuscular opioid analgesics. The vital signs and fluid balances of the patients are closely monitored for the first 24 hours. Oral intake of the patients will be started on the first day of surgery with clear liquids and gradually advanced to a normal diet. All patients are mobilized at 8 hours postoperatively. The urethral catheter is generally removed on the first day and—if used—the drain is removed on the first or second day. Patients who do not develop additional complications are discharged on the 2nd or 3rd day after surgery.

Outcomes

The benefit of robotic adrenalectomy compared to conventional laparoscopic adrenalectomy is still a matter of debate. Although the literature seems to be fruitful especially for the last decade, it is lacking of high quality trials in terms of evidence-based medicine. *Table 1* represents perioperative outcomes after robotic transabdominal adrenalectomy in some case studies (3-13). In this section, an overview of comparative assessment of robotic adrenalectomy and conventional laparoscopic adrenalectomy in terms of efficiency and cost will be presented.

A controversy to be taken into consideration in minimal invasive adrenal gland surgery is whether the technique of posterior retroperitoneal approach or lateral transabdominal approach is a more appropriate method. Although the results of both techniques are similar, in 2013, the minimal surgical approach protocol of the American Society for Gastrointestinal and Endoscopic Surgery (SAGES) has provided recommendations regarding the surgical technique for adrenal gland pathologies for specific clinical conditions (14). These recommendations are:

- ❖ Retroperitoneal approach may result in shorter operative time and less complications in the presence of previous abdominal surgery;
- ❖ In patients undergoing bilateral adrenalectomy, the posterior retroperitoneal approach may be a more appropriate option because of the advantages of not having to re-position the patient during the operation;
- ❖ The lateral transabdominal approach in morbid obese patients (body mass index >35 kg/m^2) and for large tumors (>6 cm) is more advantageous in terms of applicability compared to other surgical methods.

Although these recommendations help the surgeons in the surgical procedure, it is important to note that the most appropriate surgical technique is the surgeon's most experienced technique. Regarding robotic surgery, Kahramangil & Berber showed that both robotic approaches, retroperitoneal and transabdominal are equally safe and efficacious, based on their experience in 200 robotic adrenalectomies (15).

In the literature, there are many studies comparing robotic and conventional laparoscopic adrenalectomy. There have been numbers of systematic reviews and meta-analysis (16-19). Before focusing on the outcomes of these meta-analyses we should mention a few words regarding the learning curve for robotic adrenalectomy. Brunaud *et al.* defined the learning curve for transabdominal robotic adrenalectomy as 20 cases and found that the previous clinical experience and duration of first assistance are effective factors (4).

Table 1 Case series data for robotic adrenalectomy

Case series	Patient (n)	Mean tumor size (cm)	Mean operative time (min)	Blood loss (mL)	Conversion	Complication [n]	Hospital stay (days)	Mortality, n
Winter (3) [2006]	30	2.4	185	NR	0	Ileus [1]; atelectasis [1]	2	0
Brunaud (4) [2008]	100	2.9	171	NR	4 COA; 1 CLA	Bleeding [3]; cyst rupture [1]; urinary infection [1]; wound infection [1]; facial edema [1]; pneumonia [1]	6.4	0
Giulianotti (5) [2011]	42	5.5	118	27	0	Adrenal capsular tear [1]	4	1
Nordenström (6) [2011]	100	5.3	113	NR	2 COA; 1 CLA	Bleeding [4]; arrhythmia [2]; adrenal insufficiency [2]; subcutaneous emphysema [1]	NR	0
Agcaoglu (7) [2012]	24	6.5	159	NR	1 COA	None	1.4	0
Aksoy (8) [2012]	42	4.0	186	50	0	Urinary infection [1]; pneumothorax [1]	1.3	0
D'Annibale (9) [2012]	30	5.1	200	<50	1 COA	Capsular disruption [1]; marked arterial instability [1]; abdominal wall hematoma [1]; pneumonia [1]; myocardial infarction [1]	5.2	0
Brandao (10) [2014]	30	3	120	50	0	Hyponatremia [1]; postoperative bleed requiring blood transfusion [1]; wound infection [1]; atrial fibrillation [1]	2	0
Lee (11) [2016]	33	NR	234	392	5 CLA; 2 COA	Ileus [1]; adrenal insufficiency [2]	2.8	0
Morelli (12) [2016]	41	NR	177	NR	NR	Pneumonia [1]; arrhythmia [1]	3.3	0
Greilsamer (13) [2018]	303	3.6	89	NR	1 CLA; 8 COA	Incisional hernia [8]; parietal abscess [5]; renal infarction [1]; hematoma [2]; paresthesia [1]; chronic pain [4]; urinary infection [2]; pulmonary infection [3]; postoperative hypotension [1]; facial oedema [1]	5.5	0
Makay (unpublished data)	76	4.2	127	83	1 CLA; 2 COA	Arrhythmia [1]; atelectasis [1]; urinary infection [2]; incisional hernia [4]; chronic pain [2]	2.4	0

NR, not reported; COA, converted to open adrenalectomy; CLA, converted to laparoscopic adrenalectomy.

Complications

Complications associated with robotic adrenalectomy are hemorrhage, hematoma, wound infection, urinary tract infection, adjacent organ injuries, ileus, complications due to the laparoscopic procedure and atelectasis. The complication rate between the robotic and laparoscopic groups was similar in many studies. Besides, postoperative morbidity and mortality have been shown to be comparable to conventional laparoscopy (1). A recent comprehensive meta-analysis, pooling 1,162 (747 robotic and 415 conventional laparoscopic) cases out of 27 studies, revealed that there was no significant difference between the robotic and the laparoscopic groups for intraoperative complications [odds ratio (OR): 1.20; 95% CI, 0.33–4.38], postoperative complications (OR: 0.69; 95% CI, 0.36–1.31), mortality (OR: 0.42; 95% CI, 0.07–2.72), conversion to laparotomy (OR: 0.51; 95% CI, 0.21–1.23) and conversion to laparotomy or laparoscopy (OR: 0.73; 95% CI, 0.32–1.69) (16). Data regarding complications was also supported by another detailed recent systematic review (19). In a paper carried out by Greilsamer *et al.*, based on an experience of more than 300 robotic cases, independent risk factors for perioperative complications after robotic-assisted unilateral adrenalectomy were described as conversion to laparotomy and patient age. Tumor size >5 cm was the only predictive factor for conversion to laparotomy in that series (13).

Operative time

The publications that have longer operative time are publications in which the robotic technology is being used for the first time and the first experiences of the teams performing the work are reflected. A systematic review published in 2014 by Chai *et al.* compared robotic and laparoscopic adrenalectomy. There were six studies in accordance with the compilation criteria, and in the first two studies that matched the early stages of the use of robotic surgery, the operation time was longer in the robotic group, but in the other four studies, there was no significant difference between the groups in terms of operative time (20). In the more recent meta-analysis of Economopoulos *et al.*, there was a significantly longer operating time for patients treated with robotic adrenalectomy (16). Another recent meta-analysis, including 1,710 open and minimally invasive adrenalectomies, revealed that operative time was significantly shorter for open adrenalectomy than for the robotic approach and there were no differences were found between laparoscopic and robotic approaches (19).

Blood loss & hospital stay

According to an early systematic review, two studies reported lower blood loss for robotic adrenalectomy. In one of these, it was emphasized that robotic had less pain on the first postoperative day. While the length of hospitalization was similar in both groups, one study reported a shorter hospital stay in the robotic group (20).

In the meta-analysis and systematic reviews comparing the robotic adrenalectomy with laparoscopic adrenalectomy published in 2017, Agrusa *et al.* reviewed 13 papers that met the criteria and compared 798 patients, 379 of whom underwent robotic surgery and 419 of them underwent laparoscopic surgery. There was no significant difference in age, gender, laterality and tumor size between the two groups, whereas the robotic group had significantly less blood loss and shorter hospital stay (21). This was also the case in the review of Economopoulos *et al.* for hospital stay, but not for blood loss. In their analysis they report no significant difference between groups in terms of blood loss. It is important to mention that they pooled 1,162 cases (16). The meta-analysis of Heger *et al.* reports the superiority of robotic adrenalectomy, regarding blood loss and hospital stay, after pooling 1,710 cases out of 26 trials (19).

Cost analysis

In a very recent study conducted by Feng *et al.*, costs of 58 patients undergoing robotic adrenalectomy and 64 patients undergoing laparoscopic adrenalectomy were calculated. According to this study, cost calculations were made on the anesthesia fee, procedure time and consumable fees. Calculated relative costs were $3,527 for the robotic procedure, while it was $3,430 for the conventional laparoscopic procedure (P=0.59). The average duration of anesthesia was 172.4 and 178.3 min (P=0.40) for the robotic and laparoscopic approach respectively, and the average operative time was 124.4 min for robotic surgery and 129.1 min for laparoscopic surgery (P=0.50). The procedure time for the retroperitoneal approach was significantly shorter than the transabdominal approach for both robotic (101.2 *vs.* 126.6 min, P=0.001) and laparoscopic group (104.4 *vs.* 135.4 min, P=0.001). Average consumable prices were reported as $1,106 for robotic adrenalectomy and $1,009 for laparoscopic adrenalectomy (P=0.62). This study shows that anesthesia and procedure times for robotic adrenalectomy are similar to those of laparoscopic adrenalectomy and that the cost of robotic surgery can be comparable to that of conventional laparoscopic surgery by limiting the number of robotic instruments and energy devices by an experienced surgical team (22). Bodner *et al.* reported adrenalectomy to be 1.5 times more expensive compared to laparoscopic adrenalectomy (23), while another study reported no difference in cost outcomes (3).

From a cost perspective, shortening the length of hospital stay, improving ergonomics for the surgeon and the good perioperative outcomes in some difficult cases such as presence of large masses, obesity, and history of abdominal surgery may reduce the additional costs associated with the robotic system.

Summary

Robot-assisted adrenalectomy is a safe and effective treatment for the management of most adrenal masses. This is what comes out of the more than 200 published reports in the current literature. Compared to conventional laparoscopic surgery, cumulative level III evidence indicates similar rates of intraoperative and postoperative complications, similar operative times, less blood loss and decreased duration of stay. Definitive outcomes studies, including randomized controlled trials have yet to establish its benefits and costs relative to the conventional laparoscopic approach.

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Footnote

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

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Review Article

Adrenal natural orifice transluminal endoscopic surgery (NOTES): a step too far?

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Abstract: Surgical approach to adrenal gland has evolved from open to minimally invasive surgery. With the advent of technology, multiple techniques and approaches are available in a surgeon's armamentarium today to deal with adrenal nodules that require surgical intervention. Each approach has its own advantages and disadvantages. The era of minimal invasive surgery has fuelled our quest for better cosmesis, faster recovery, early return to work and reduced hospital stay. While minimal invasive method is the preferred approach for most benign adrenal masses less than 6 cm, its application for large adrenal lesions as well as adrenocortical carcinoma is still debatable. Single incision minimal invasive procedures further try to reduce the incisions and wound morbidity. With the aim to completely remove visible scars and possibly reduced morbidity, the concept of natural orifice transluminal endoscopic surgery (NOTES) has been proposed by some surgeons as well as interventional gastroenterologist. In NOTES, the peritoneal cavity is accessed through a hollow viscus to perform therapeutic as well as diagnostic procedures. While the theoretical advantages of scar less surgery and its advantages sound encouraging, the precise indications and its potential advantages for adrenal pathologies is yet to be defined. It should in no way, compromise our goal of safe patient surgery and outcomes.

Keywords: Natural orifice surgery; natural orifice transluminal endoscopic surgery (NOTES); transvaginal surgery; endoluminal surgery; adrenalectomy

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Introduction

Surgery on adrenal gland is challenging, irrespective of the pathology. In addition to the surgical proximity to vital organs and major vessels, the physiological interaction of the adrenal hormones is also at play. Both in hormonally active glands as well as in insufficiency, perioperative optimisation and post-operative support is paramount. Adrenal gland surgery is done for a wide variety of reasons, from adrenal tumours to functional adenomas, lesions with suspicion of cortical carcinomas to metastatic deposits. Based upon pathology and laterality the surgery can range from total to partial adrenalectomy.

Ever since Gagner performed the first laparoscopic adrenalectomy in 1991 (1) laparoscopic adrenalectomy is considered gold standard for small and medium sized benign adrenal tumours (1,2). Though we find isolated cases describing resections of large adrenal mass, ranging up to 15 cm (1,3), application of laparoscopic adrenalectomy for lesion >6 cm is still debatable and lacks consensus (4-7). Today, more surgeons prefer to use the retroperitoneal approach for adrenal lesions, as it offers all the benefits of minimal invasive surgery, with the added advantage of avoiding violation of peritoneum (8-10). The benefits of laparoscopic surgery are many: safe, feasible, better cosmesis, reduced pain, shorter hospital stay, early recovery after surgery and reduced wound morbidity, particularly in obese (7,10).

Over the years, surgeons and researchers quest for even smaller incisions has led to the advent of novel techniques like laparo-endoscopic single site surgery (LESS) (11) and natural orifice transluminal endoscopic surgery (NOTES) (12). While the principle of access to abdomen in LESS remains the same as for any laparoscopy, NOTES is an emerging technique wherein the peritoneal cavity is accessed through a hollow viscus or natural orifice, e.g., vaginal vault, stomach, etc., to perform a variety of diagnostic and interventional procedures, allowing a totally scarless surgery. NOTES offer us new possibilities and challenges in term of the technique, endoscopic expertise and scope for technological innovation. But for any new technique to be successful, the fundamental principles of patient safety and post-operative outcomes cannot be comprised. The cost benefit analysis also needs to be weighed, as compared to conventional minimal invasive techniques.

Evolution of NOTES

The goal of any minimally invasive procedure is to minimising access related trauma by reducing the size and number of abdominal incisions (13,14). NOTES as a concept was put forward in 1990's by a team of researchers who called it "flexible transluminal endoscopy" (15). The term NOTES was coined in year 2005 by the American Society of Gastrointestinal Endoscopy and the Society of American Gastrointestinal and Endoscopic Surgeons working group (16). The idea of elimination of any visible surgical scar seemed so promising that more and more researchers started experimenting with this concept, both in animal studies as well as isolated cases in humans. Natural orifices like vagina, anus, mouth and urethra were utilised to gain access (17).

In animal models a variety of surgical procedures were performed, including transgastric adrenalectomy (18). The potential benefits suggested when compared to convention open and minimal invasive procedures were reduced pain, wound related complications, port site hernia, reduced hospital stay, improved cosmesis and patient satisfaction (19). The greatest advantage suggested for NOTES was retrieval of the specimen, avoiding the need for large incisions.

Kalloo *et al.* in 2003, utilised NOTES to perform liver biopsies (20). Marescaux *et al.* in 2007 reported the first transvaginal cholecystectomy (21). Ever since, the acceptability of NOTES has spread, with more surgeons translating it into clinical practice. In the following years, the spread of NOTES was limited due to limitations of technology, inappropriate instrumentation and standardization of techniques. However, for the few years multiple abdominal and retroperitoneal surgeries have been performed using NOTES, and these include cholecystectomy, appendicectomy, adnexal and tubal surgery, hernia repair, splenectomy and nephrectomy (16).

NOTES for adrenalectomy

In 2002, Gettman *et al.* completed and reported in animal model the use of NOTES for nephrectomy using transvaginal access (22). Following this, multiple researchers have demonstrated the application of NOTES in surgeries in the retroperitoneum, namely total and partial nephrectomy, cystectomies and prostatectomies, utilising transgastric, transrectal, transvesical and transvaginal access (23-25). Endoscopic instruments, combined with laparoscopic assistance and robotic assisted surgery were used in these studies involving animals or cadavers (23,26,27).

Fritscher-Ravens *et al.* in their studies on porcine model reported transgastric adrenalectomy using pure NOTES and NOTES in combination with endoscopic ultrasound (EUS) (28). They performed pure NOTES in four pigs and combined NOTES with EUS in six pigs. They failed to safely perform and complete adrenalectomy in the NOTES only group, due to excessive bleeding during access and lack of safety. But in the remaining cases under EUS guidance adrenalectomy was performed safely, with a mean operative time of 78 min.

Similarly, Perretta *et al.* in 2009, performed retroperitoneal right and left adrenalectomy in female pigs through the transvaginal access with a mean operative time of 70 minutes (29). No intra-operative complications were reported. They also reproduced the transvaginal access in cadaver model and demonstrated proper identification of all the retroperitoneal anatomy and landmarks. They suggested that this technique may benefit particularly in obese patients and patients with multiple abdominal surgeries. They also suggested that by avoiding the peritoneal breach, the cardio-pulmonary complications associated with carbo-peritoneum could be avoided. The same team further reported their experience with animal and cadaveric experiments on retroperitoneal surgeries using pure NOTES in 2009 (30).

In 2013, Eyraud *et al.* demonstrated feasibility of robotic assisted transrectal hybrid NOTES nephrectomy and adrenalectomy in a male cadaver (31). They placed an 8-mm transrectal robotic trocar, followed by periumbilical trocars. They were able to successfully complete the procedure in 145 min, including the rectal closure. Based on the available evidence it is too early to reach a conclusion regarding wider application and acceptability of NOTES in adrenal surgery outside the purview of research and experimental studies.

One of the first clinical experience in transvaginal NOTES assisted adrenalectomy was reported by Zou *et al.* on 11 patients (32). They used conventional laparoscopic instruments through umbilical access and a 30-degree laparoscope through posterior vaginal fornix. The same posterior vaginal fornix incision was used to extract the resected specimen. They reported splenic injury in one patient with Cushing disease for whom they needed to perform splenectomy and hence conversion to open. The median operative time was 102 min (80–310 min) with a median estimated blood loss of 80 mL. The median size of adrenal mass was 4.7 cm (2.2 to 6.6 cm). As all patient were females, they performed Female Sexual Function Index, pre- and postoperatively and found no difference in the median scores. Except the patient who needed conversion to open, all the other patients were satisfied with the cosmetic outcome. They concluded that transvaginal NOTES assisted laparoscopic adrenalectomy is safe and feasible for adrenal tumours in female patients.

In the absence of large series, comparative studies, standardization of techniques and instrumentation, it is advisable to tread with caution when offering patients NOTES adrenalectomy. However, theoretically there are potential benefits of reduced post-operative pain, wound related complications mainly surgical site infections and port site hernias. The immunomodulatory effects of NOTES by a reduction in TNF-alpha levels in the postoperative period in NOTES subgroup as compared to laparoscopy and laparotomy groups were demonstrated in a swine model by McGee *et al.* (33). Similarly, benefits in obese patients have been shown for transvaginal cholecystectomy (34).

Pitfalls in NOTES adrenalectomy

There is a lot to be learned about NOTES, a novel operative technique for abdominal surgery. Most of the published literature about application of NOTES for adrenal as well as other retroperitoneal pathologies is based on animal studies and isolated case reports. It remains to be seen whether the animal models can be successfully replicated in larger human studies. Hence, it is difficult to prove the benefits of NOTES when compared to conventional laparoscopic surgery (35).

Standardization of the procedure is still awaited, ideal access route yet to be defined. Most of the published animal, cadaveric and isolated case reports published have utilised transvaginal access, which is considered the safest access route. But this approach cannot be used in males, who will invariably account for half of the cases. Most animal studies which show the intra-peritoneal access techniques in NOTES to be safe, were conducted in virgin abdomens (20,36). This technique may be difficult in patients with previous surgeries.

In 2006, the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) published a white paper advised a zero tolerance for NOTES associated complications (37). A difficult problem is the safe closure of the luminal access site and NOSCAR considers this to be the main obstacle. They have pitched for achieving 100% success in closure of luminal access, for which researchers must develop better anastomotic or suturing devices. Palanivelu *et al.* reported a complication rate of 16% in their series of NOTES transvaginal cholecystectomy (38).

Access related surgical site infections, inadvertent injuries, bleeding, post-operative leaks have been reported, and we are yet to address these issues conclusively. Instrument sterilisation is not clearly defined. Learning curve with regards to achieving expertise in endoscopy, orientation with flexible scope in a retroflexed view leading to an off-axis movement of instruments are potential issues (39). Other issues particularly in transgastric or trans-rectal access techniques is inadvertent bowel distention caused due to air leaking into the bowel (39).

The steep learning curve in NOTES and difficulties in its incorporation into surgical residency programs is another issue raised (40,41). Current residency programs are already falling short to incorporate a variety of open, conventional laparoscopy, LESS procedures, robotic surgery and this may be burdened with addition of another technique. Once NOTES reach the stage of human trials, maintaining a balance between quality of care, patient safety during service delivery and residency training issues need to be considered.

To conclude, over the last decade NOTES is gaining popularity, especially the concept of scarless abdomen seems promising to most surgeons. Whilst its use has increased over the years, mainly in animal studies and small sample human studies, the technique is not without its problems.

Some of the unaddressed issues include academic protocols, medico-legal issues, patient safety and bureaucratic and administrative challenges. Experimental studies have been conducted in NOTES adrenalectomy but require larger studies, with focus on clinical outcomes, cost effectiveness and benefits. A this point in time; adrenal NOTES is probably a step too far.

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Footnote

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Review Article

Fluorescence techniques in adrenal surgery

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Abstract: This chapter describes the use of fluorescence via indocyanine green (ICG) in minimally invasive adrenal surgery (laparoscopic and robotic). ICG is a non-toxic dye that can aid identification of vascular structures and parenchymal tissue planes in real time. The primary utility of ICG fluorescence in adrenal surgery is to help delineate the margins of resection, to guide a more precise operation. In particular, for patients with bilateral adrenal disease or a heredity associated with high risk of recurrence (e.g., VHL, MEN2a) this may facilitate subtotal adrenal resection (e.g., cortical sparing adrenalectomy), obviating the incidence of iatrogenic adrenal insufficiency and its numerous sequelae including lifelong hormone supplementation, osteoporosis and risk of Addisonian crisis.

Keywords: Adrenal surgery; fluorescence angiography; indocyanine green (ICG); near infrared imaging (NIR imaging); laparoscopy

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History

Fluorescence is a natural phenomenon known to humans for thousands of years. It was initially used in ophthalmology for retinal angiography (1) but as its utility was further understood, clinical application expanded to include various surgical procedures such as cholecystectomy (2,3), gastrointestinal anastomoses, renal auto-transplantation (4) and nodal dissections (5-10). More recently indocyanine green (ICG) has become available for minimally invasive surgery, with the development of more advanced laparoscopic and robotic platforms that can display ICG-enhanced images on the same screen (11). The utility of ICG is to provide additional visual information regarding tissue perfusion, critical vascular structures and planes of dissection (6,7,11-15).

ICG was first developed by Kodak Laboratories (Rochester, NY, USA) in 1955, for photography using near infrared (NIR) imaging technology. It was approved for medical use by the US FDA in 1959 (6,16) and the technology gradually crept into laparoscopic surgery offering real-time fluorescence angiography and assessment of vascular status of solid and hollow viscera (7,17,18).

The feasibility of ICG fluorescence for adrenal surgery was first described by Dip *et al.* in 2015 following a case series in pigs (19). They reported that adrenal fluorescence was distinct from the surrounding retroperitoneal tissue in all five animals and persisted for a mean of 4 hours.

The first clinical application of ICG in humans was made by Manny *et al.* in 2013 (20). In their case series of three patients undergoing robotic partial adrenalectomies, all of the adrenal tumours (phaeochromocytoma, lipoadenoma and follicular lymphoid hyperplasia) were hyperfluorescent. Subsequently, DeLong *et al.* reported the use of ICG in a series of five patients undergoing laparoscopic adrenal surgery and showed superior identification of adrenal vasculature and demarcation of the tumour from the retroperitoneum in all cases (11).

What is it?

ICG is an amphiphilic (water soluble), tricarbocyanine

Figure 1 Photograph from robotic platform demonstrating a plane of dissection between the left renal vein (yellow arrow) and left adrenal tumour (red star) following ICG administration (original image).

organic dye (MW 751.4 Da) that exhibits fluorescence when excited by NIR light (wavelength ~800 nm).

Its use in biomedical applications is attributed to the variable concentration of ICG within different tissue types, which is related to their blood supply. Endocrine organs have an abundant blood supply and therefore are ideally suited to the use of ICG (5). In particular the adrenal glands have multiple feeding arteries and collecting veins. The mean organ blood flow of the adrenal gland is 1.87 mL/g/min, which is the third highest among the intra-abdominal organs after the spleen and renal cortex (21).

How does it work?

The mechanism of action of ICG fluorescence is incompletely understood. Upon intravenous administration, ICG becomes strongly bound to plasma proteins (especially lipoproteins) and is confined to the intravascular space (22). Its configuration is not altered by binding, resulting in a relative lack of toxicity. ICG enters the hepatic sinusoids, is uptaken by hepatocytes and ultimately excreted into bile via protein glutathione S-transferase (GST) (6).

When excited by NIR light, tissues are illuminated with light 750–800 nm corresponding to the excitation wavelength of ICG (22,23). Signal intensity is proportional to the relative blood flow to that organ (20). Furthermore, receptor mediated uptake of ICG by different tissues, depends on the differential expression of bilitranslocase, a carrier protein for ICG expressed in normal renal parenchyma (proximal and convoluted tubercles but not glomeruli) (24).

Observation of ICG fluorescence in real time provides different information based on the flow of the dye throughout the tissues. Similar to a phased CT contrast study, the arterial anatomy is first to be delineated. This is followed by the parenchyma and lastly the adrenal vein. Enhancement of the vascular anatomy is especially important when it is altered, as is the case with adrenal tumours (*Figure 1*).

Uses

Since Gagner *et al.* reported the first laparoscopic adrenalectomy in 1992, minimally invasive surgery has become the gold standard approach to remove both benign functional and non-functional tumours (25). Compared with conventional open surgery, minimal access surgery is associated with improved optics, decreased pain and wound complications and improved recovery time and cosmesis (26). On the other hand, it has eliminated tactile feedback traditionally used to determine the margin of resection.

The use of ICG in adrenal surgery is advantageous for two primary reasons. First, it provides contrast distinction between very vascular, hyperfluorescent adrenocortical tissue and less vascular, hypofluorescent retroperitoneal tissue, which helps with dissection (*Figure 2*). Secondly, it can guide cortical sparing adrenalectomy by demonstrating the borders between normal adrenal tissue and tumour when operating for phaeochromocytomas (medullary lesions). ICG also provides information in real time to the surgical team. It is quick to perform only adding minutes to the procedure. The real time feedback of ICG fluorescence helps to compensate for the lack of tactile feedback in minimally invasive surgery (27).

By contrast laparoscopic ultrasound which is a widely adopted intra-operative adjunct, requires interruption of dissection for scanning and might not be possible if there is not a good contact plane between the piezoelectric probe surface and the tissue.

In 2018 Kahramangil *et al.* characterized patterns of fluorescence exhibited by different adrenal pathological conditions in order to define the best clinical indications for the use of ICG (28). They reported that the adrenal, liver and retroperitoneal tissues all fluoresced after administration of ICG. Fluorescence of retroperitoneal tissue was transient. The liver and adrenal fluorescence persisted throughout the duration of the procedure and in particular, healthy adrenal cortical tissue was always hyperfluorescent (*Figure 3*). From 100 patients, 74% were hyperfluorescent and 26%

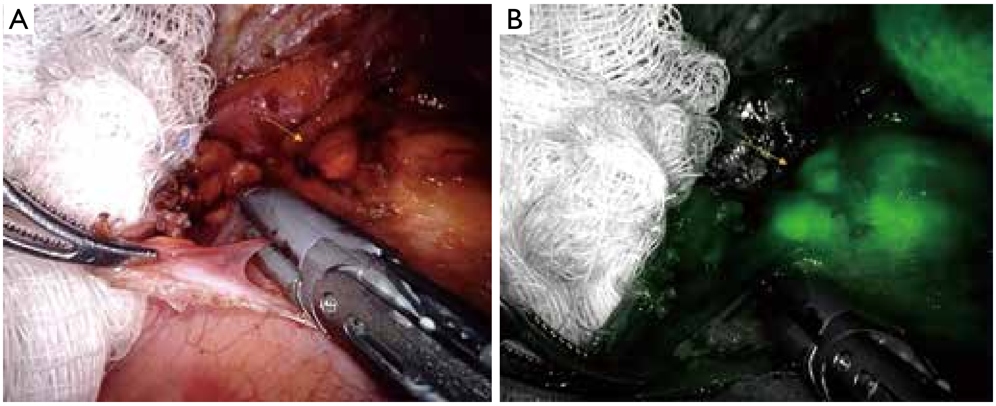

Figure 2 Photograph demonstrating the utility of ICG in delineating adrenal cortical tumours (yellow arrow) from the surrounding retroperitoneum, before ICG administration (A) and after ICG administration (B) (original image). ICG, indocyanine green.

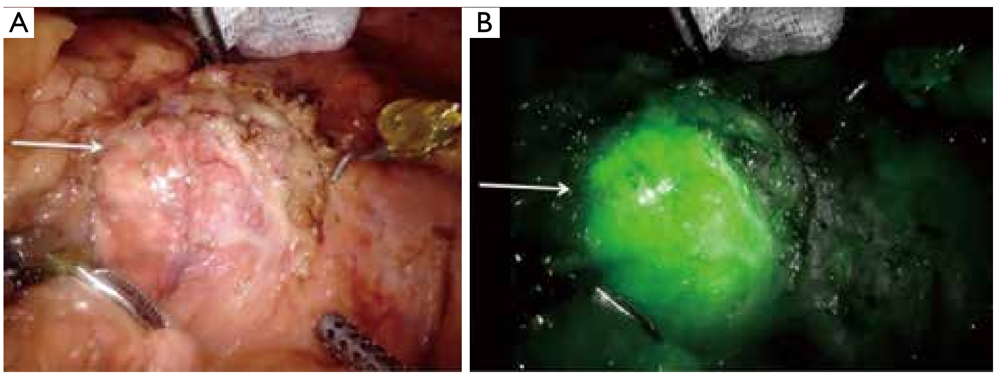

Figure 3 Photograph demonstrating hyper-fluorescence of adrenal cortical tumours (white arrow) before (A) and after ICG administration (B) (original image). ICG, indocyanine green.

were not. Exhibition of fluorescence was dependent on the histological origin (medullary *vs.* cortical). On multivariate analysis, adrenal cortical tissue origin was the only predictor of hyperfluorescence following ICG administration: 95%, 33% and 50% for tumours of adrenocortical, medullary and other tissue origins respectively. Of note, adrenal cortical cancer (ACC) manifested higher intensity of fluorescence than differentiated tumours. The weaker fluorescence from phaeochromocytomas compared with other adrenal tumours has been related to the lack of expression of bilitranslocase (20).

It should be anticipated that the utility of ICG in the resection of right sided tumours and or tumours of medullary origin will be inferior (27). The exception to this is cortical sparing resection of phaeochromocytomas where there is sufficient tissue distinction between the hyperfluorescent healthy adrenal cortex and the hypofluorescent medullary tumour.

Dosing/administration

Owing to its pharmacokinetics, the specifics of intraoperative ICG administration change with the organ system it is being used in. For adrenal surgery, our group prepares a solution by mixing 25 mg of ICG (Akron Inc., Lake Forrest, IL, USA) in 10 mL of distilled water, making a preparation with final concentration of 2.5 mg/mL (*Figure 4*). Doses less than 5 mg do not provide sufficient contrast discrimination between tissue types, whereas doses greater than 5 mg are associated with too much fluorescence and all the tissues are overexposed (29).

A single dose of this concentration (5 mg or 2 mL) is administered by the anesthetist, via a peripheral intravenous line. The timing is critical and nominated by the primary

Figure 4 Photograph of ICG vial and sterile (distilled) water required for constitution prior to intravenous administration (original image). ICG, indocyanine green.

Figure 5 Photograph prior to ICG administration of left adrenal gland (original image). ICG, indocyanine green.

surgeon. ICG is most effective if it is administered after exposure of the retroperitoneum but before dissection of the adrenal gland. Typically, fluorescence of the adrenal gland and retroperitoneal tissues occurs with 30–60 s of ICG administration. Optimal contrast distinction between tissues is achieved at 5 minutes, when the retroperitoneal fat releases the ICG but the adrenocortical tissue still retains the molecule. Adrenal fluorescence can persist for up to 20 min (29,30).

Repeat doses of ICG can be administered to maintain contrast distinction if required.

The median lethal dose for ICG is relatively high (LD50 of 50–80 mg/kg) (6). In our experience most patients require an average of three doses (15 mg), irrespective of BMI and tumour size over the course of their adrenal resection (5,29).

Figure 6 Photograph after ICG administration of left adrenal gland and hyper-fluorescent liver parenchyma in the background) (original image). ICG, indocyanine green.

ICG fluorescence systems are available for laparoscopic and conventional open surgery. There are multiple commercially available products. The ideal product fuses the laparoscopic or robotic images with the fluoresced images, avoiding the need to switch back and forth between platforms.

Limitations

Following administration, ICG circulates to the liver and is rapidly uptaken by hepatocytes. Hepatic fluorescence is bright and remains present for several hours, often the duration of the procedure. This can interfere with tissue plane discrimination for tumours on the right-hand side, as the hyperfluorescent liver obscures visualization of adjacent tissue (*Figures 5,6*). This is most problematic if the surgical approach is posterior because there is limited room for retraction of the liver in the smaller retroperitoneal space. A practical strategy to minimize this effect, is to zoom in on the adrenal gland to reduce the fraction of liver visualized in the NIR image. However, in general for right sided adrenal tumours, the lateral/anterior approach is preferable when using ICG.

Current ICG fluorescence systems provide qualitative data only. These need to be interpreted by the operating team and there may not be consensus. Ideally ICG and NIR imaging are used via a platform that integrates with the remote access set up as this enables the visual information to be visualized in real time.

Adverse reactions and contraindications

Contraindications against the use of ICG in adrenal surgery include iodine allergy, previous anaphylaxis to dye injections, renal disease, liver disease and pregnancy (31). There have been no reported mortalities attributed to ICG.

Adverse reactions to ICG have primarily been reported to be allergic and vasovagal in nature. The rate of severe adverse reactions is 0.05% (7). In extremely rare instances (3 out of 240,000 cases in the largest reported case series), ICG has been associated with bronchospasm and cardiac arrest (32) but these were associated with administration of much higher doses (0.5 mg/kg) than is typically required (6).

Conclusions

ICG and NIR imaging are safe and useful adjuncts to remote access adrenal surgery. The intensity of fluorescence is related to differential perfusion of tissue types and expression of bilitranslocase. The pattern of fluorescence is dependent on histological origin of the tumour.

Utilization of fluorescence in adrenal surgery is particularly useful for patients requiring a subtotal resection to minimize the sequelae of adrenal insufficiency and in refractory cases where it is critical to resect all adrenal tissue. Future systems will hopefully enable quantitative interpretation.

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Footnote

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

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Review Article

Open adrenalectomy

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Abstract: In an era when minimally invasive adrenalectomy is the gold standard treatment for majority of patients presenting with adrenal tumours, open adrenalectomy has become an operation that should be centralised in regional referral centers. Its main indication is represented by patients with large (>8 cm) phaeochromocytomas and patients with cortical adrenal tumours suspected of malignancy either because of their size (>4–6 cm) or because of radiological appearance of local invasion. Based on local expertise some of these patients might benefit from multidisciplinary input from liver or transplant surgeons. This chapter will discuss the anatomical landmarks and will comment on different steps in the procedure for right- or left-sided procedure. It is outside the scope of this chapter to settle the ongoing debate about patient selection for laparoscopic or open adrenalectomy when the diagnosis of adrenocortical cancer is suspected preoperatively.

Keywords: Adrenalectomy; surgical technique

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Historical notes

Before the introduction of laparoscopic adrenalectomy in early 1990s, open adrenalectomy was the only surgical option. Surgery of the adrenal glands emerged as part of abdominal surgery at the end of the 19th century. In 1889, Knowsley-Thornton reported the removal of a large adrenal tumour and in 1926, Roux in Lausanne, Switzerland, and Charles Mayo in Rochester, Minnesota, successfully removed a phaeochromocytoma (1).

The anterior approach was initially advocated by Cahill, one of the pioneers of adrenal surgery (2). The posterior approach was originally described by Young (3) and offered the technical advantage of being extraperitoneal, extrapleural, and subdiaphragmatic and the clinical advantage of being associated with low postoperative morbidity. In current day surgical practice the posterior approach has become obsolete, as all patients who in the past were deemed to benefit from this procedure are currently being offered laparoscopic or retroperitoneoscopic adrenalectomy.

This chapter will focus on the technical aspects of open adrenalectomy. More detailed discussion of the assessment and management of patients with adrenocortical cancer (ACC) have been summarised in the recent guidelines written by the European Society of Endocrinology (4) and the perioperative care has been discussed in guidelines written by the European Society of Endocrine Surgeons (ESES) and the European Network for Study of Adrenal Tumours (ENSAT) (5). Issues related to training in adrenal surgery and the need to centralise such operations in centers with a defined annual workload will be addressed I the upcoming meeting of the European Society of Endocrine Surgeons and will be published later this year.

Indication for open adrenalectomy

Even though minimally invasive techniques for adrenalectomy have been adopted in many surgical centres, there is a need to be, remain or become confident with open adrenalectomy. Patients with large adrenocortical tumours (>6–8 cm) and those with CT suspicion of locally invasive tumours expected to have an adrenocortical cancer should have an open operation. In addition, laparoscopic adrenalectomy should be converted to open operation in case there is macroscopic appearance suspicious of malignancy (invasion in surrounding structures, presence of regional lymphadenopathy) or if the surgeon is concerned that the tumour could not be removed without avoiding tumour fragmentation/spillage. Conversion to open operation might also prove necessary if intraoperative incidents (e.g., uncontrolled bleeding) cannot be managed laparoscopically.

Adrenal tumours with extension into major venous structures should all be approached through an open operation.

Large phaeochromocytomas of up to 8–10 cm might still be approached laparoscopically by surgeons with appropriate experience but the larger the diameter of such tumours the more likely is that open adrenalectomy will be necessary.

Bilateral adrenalectomy is not an indication for open approach as laparoscopic or retroperitoneoscopic surgery is feasible in these patients [discussed in (6)].

Previous abdominal surgery is not a strict contraindication for laparoscopic surgery. Though some of these patients might benefit from retroperitoneoscopic approach (i.e., avoiding the possible need to deal with adhesions after previous surgery), laparoscopic approach is feasible in the vast majority of them.

Who should perform open adrenalectomy?

The current provision of adrenal surgery is inadequate. Analysis of Hospital Episodes Statistics showed that in the United Kingdom over 200 surgeons are performing adrenal surgery of whom only 34 surgeons performed more than 6 cases per year and 189 surgeons had a median number 1 adrenalectomy/year (7). Knowing that the 2017 report national audit kept by the *British Association of Endocrine and Thyroid Surgeons* recorded 331 open adrenalectomies and 1,555 laparoscopic adrenalectomies one can extrapolate that 1 in every 5 adrenalectomies are open and that the vast majority of surgeons involved in this type of surgery would perform one single such cases every few years. This situation is untenable as it compromises the care of the subgroup of patients with most aggressive adrenal tumours. The need for change is imperative and drives the ongoing efforts to centralise adrenal surgery in the UK. The situation is likely to be similar in most other countries. It is expected that the 2019 meeting of the European Society of Endocrine Surgeons focused on volume-outcome correlations will formulate guidance for establishing centres of excellence in adrenal surgery and this would help patients and referring clinicians make more informed choices.

During the process of writing the joint guidelines from ESES and ENSAT for the surgical care of patients with adrenocortical cancer the author collected information from surgeons involved in the working group (listed in Acknowledgements). Data on 123 patients operated in 13 centres over 5 years was analysed and formed the basis of many of the comments made in this paper.

Informed consent

The preoperative imaging facilitates staging of the disease and influences the extent of the planned operation. For patients with small-volume/localised disease, excision of tumour and perinephric fat and local lymph nodes is deemed beneficial and can be achieved with minimal morbidity hence the consent will focus mainly on generic risks associated with extensive abdominal surgery (ileus, chyle leak, deep vein thrombosis, respiratory difficulties). Patients with locally advanced disease should be informed about the possibility of ipsilateral nephrectomy, splenectomy and/or distal pancreatectomy and the consent process should include information about the risks associated with each of these additional procedures (e.g., decrease of renal function, pancreatic leak, post-splenectomy sepsis).

In our analysis, the use of multivisceral resection was not strictly dependent on the size of the primary tumours (*Figure 1*). Out of 101 patients who had open adrenalectomy for ACC, adrenalectomy-only was performed in 49 patients while the other had also nephrectomy (n=37), splenectomy (n=12), pancreatectomy (n=9) or liver resection (n=12).

Whether or not the need for such multivisceral resections is apparent preoperatively, the informed consent has to include all these possible procedures as each can trigger a specific set of complications. This issue has become increasingly significant after the change in the principle guiding the consent process from the Bolam test ('*what will be done by the majority of clinicians in a similar situation*') to the Montgomery rule ('*everything that can have a serious impact on the life of the patient*, *irrespective of how small is the risk*'). In this context it has become increasingly important to allow patients to choose from the range of options, including avoidance of surgery. Therefore the decision to offer surgery to patients with metastatic disease or when a complete (R0) resection is unlikely to be achieved should be discussed in a multidisciplinary meeting, with input from clinicians with previous experience with the management of such cases. The threshold for referral to a tertiary centre

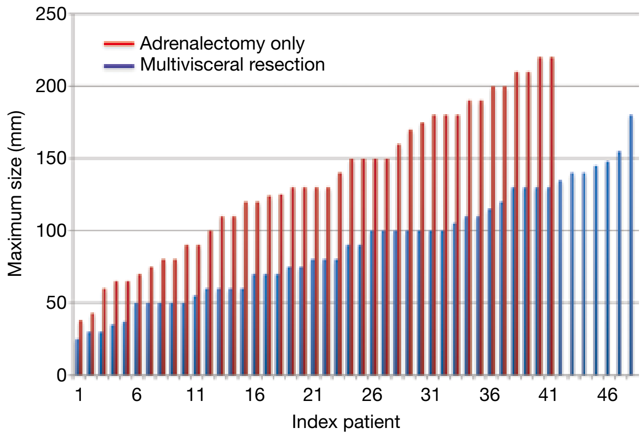

Figure 1 Size of tumour in patients with adrenocortical cancer undergoing adrenalectomy only or multi-visceral resections.

should be very low unless the local surgical/medical/oncological teams have accumulated already significant experience with the management of ACC.

For patients with phaeochromocytomas, the consent process should include details of the preoperative adrenergic blockade. Based on local practice, a preoperative meeting with the anaesthetist involved in the operation is very important for establishing the appropriate dose of medication. Though this is routine practice in our unit, other centers are moving away from using adrenergic blockade in all patients and some might not include the anaesthetist in the preoperative preparation of patients.

Perioperative management

Deep vein thrombosis prophylaxis is provided by intraoperative use of flowtron pumps followed by postoperative TEDs (anti-embolism stockings) and subcutaneous low molecular weight heparin (Clexane/Daltaparin/Fragmin, according to local protocol).

Antibiotic prophylaxis is routinely used in patients with Cushing syndrome but can be omitted in patients with non-secreting cortical tumours or phaeochromocytomas. If splenectomy is anticipated as part of the procedure patients should be considered for preoperative vaccination. Alternatively post-splenectomy prophylaxis with Penicillin V is started immediately postoperative period and vaccination can be completed 3–4 weeks later.

Intravenous steroids should be given intraoperatively (100 mg Hydrocortisone on induction) in patients with Cushing syndrome.

Adrenergic blockade for patients with phaeochromocytomas is used in vast majority of patients and is decided based on local experience/availabilities.

Position on table

In our practice patient is supine, with a wedge placed on the side operated on. More pronounced lateral decubitus can be considered based on personal references.

Choice of incision

It is the author's preference to use a bilateral subcostal incision ('roof top') with a possible midline vertical extension. Some reported the use of a thoracoabdominal incision to allow better access to the upper pole of large tumours or in cases when there is radiological evidence of diaphragmatic invasion.

Surgical technique for right open adrenalectomy for ACC

- After initial general inspection of the abdominal cavity, the operation starts by mobilising the colonic hepatic flexure by dividing the lateral part of the gastrocolic ligament and the peritoneal reflection over the ascending colon. In order to achieve full access to inferior vena cava (IVC) the duodenum is Kocherised.
- *Mobilising the liver*. In order to facilitate the dissection of the tumour at a later stage in the operation, the 'mobility' of the liver has to be increased by dividing the falciform ligament and the lateral triangular ligament. In our practice, at this stage of the operation the Thompson retractor is secured in position so that the ribs can be lifted and better access be secured.
- *Mobilising the right kidney*. For small adrenal tumours that can be easily dissected off the upper pole of the right kidney the Gerota fascia is opened towards the upper pole of the kidney and the perinephric fat mobilised upwards so that it becomes part of the future surgical specimen. For larger adrenal tumours that overlap renal vessels should be removed en bloc with the right kidney. In such cases, the dissection of retroperitoneal space starts at the lower pole of the kidney from lateral to medial. The right ureter is identified, tied and divided. The right gonadal vessels should be identified and protected up to their drainage point into the IVC. The renal vessels are tied and

divided. A sling should be passed around the IVC and the left renal vein if it is expected to need to clamp the IVC later in the procedure.

- *Mobilising the liver*. If there is evidence of IVC invasion on preoperative CT scan or if the tumour is densely adherent to IVC and the right adrenal vein cannot be safely demonstrated, one needs to secure control of IVC at subdiaphragmatic level. The liver is fully mobilised off the diaphragm until de suprahepatic veins are demonstrated and the left triangular ligament is divided so that access to suprahepatic IVC is secured. Careful dissection close to the crus of the diaphragm allows the IVC to be prepared for later clamping, if needed. In such cases it is routine practice to get control of distal IVC just distal to the insertion of the right renal vein and to sling the left renal vein.
- *Dissection off the IVC*. From the infrarenal IVC exposed earlier the dissection progresses proximally aiming to create a "groove" between the tumour and the IVC. Care should be shown close to small veins draining the caudate lobe of the liver into the IVC—ligation and division of these veins allows further upwards mobilisation of the liver.
- *Dissection off the right lobe of the liver*. One needs to assess if there is a dissection plane that would allow mobilisation of the tumour without breaching its capsule. If there is direct invasion into the liver, one has to ask support from a liver surgeon who could assist in performing a limited right hepatectomy in continuity with the tumour. This emphasis the need for careful preoperative multidisciplinary input and the need to centralise such cases in centres where appropriate multidisciplinary expertise exists.

Perioperative findings of such a case are presented in *Figure 2*.

Surgical technique for left open adrenalectomy for ACC

- *Mobilising the left colon*. The splenic flexure is mobilised by dividing the gastrocolic ligament and the peritoneal reflection along the descending colon so that the left colon mobilised distally and towards the midline until the fourth part of duodenum becomes visible (Treitz angle).
- *Management of the spleen*. If the splenic artery is seen on preoperative CT scans to be surrounded or displaced by the tumour, it is safer (and easier) to perform a simultaneous splenectomy. This also allows easier access to subcostal space as in patients with very large adrenal tumours it might be impossible to dissect the upper pole of the tumour off the diaphragm if the spleen has not been removed earlier in the operation.

  Identifying the splenic artery at the upper border of the pancreas early during the dissection allows control of the main arterial splenic inflow and might minimise blood loss later during en bloc resection. The gastrosplenic arteries are divided individually with attention to preserving the anastomotic vessels along the great curvature of the stomach within the gastrosplenic ligament. Direct invasion of the adrenal tumour into the stomach has not been encountered in any of the ACC cases reported by the ESES working group.
- *Mobilising the left kidney*. The retroperitoneal space is dissected from lateral to medial, starting at the lower pole of the kidney. The left ureter is identified, tied and divided. The gonadal vessels should be identified, tied and divided distal from their drainage point into left renal vein. Soft tissue along the IVC is mobilised en bloc as it is likely to contain the regional lymph nodes.
- *Management of the pancreas*. In the presence of a large left adrenal tumour, the tail of the pancreas is "stretched" over the tumour and a distal pancreatectomy might provide a safer oncological procedure. This can be avoided in many cases as the ACC rarely (if ever) invades directly into the pancreas. When deemed beneficial to perform distal pancreatectomy, a tunnel is created under the body of the pancreas to the left of inferior mesenteric vein and the body of the pancreas is transected using a linear stapler. The resection line is usually sutured. A Robinson drain is left next to the pancreatic bed as a pancreatic leak is a common postoperative complication.

Perioperative findings of such a case are presented in *Figure 3*.

Role of lymphadenectomy

Lymph node dissection (LND) is yet to become a formal component of radical adrenalectomy. Because the lymphatic drainage of the adrenal gland includes the renal hilum lymph nodes, and the para-aortic and paracaval lymph nodes, it is expected that many of these lymph nodes are included if *en bloc* resection of the ACC is performed to include the kidney, perinephric fat and Gerota's fascia.

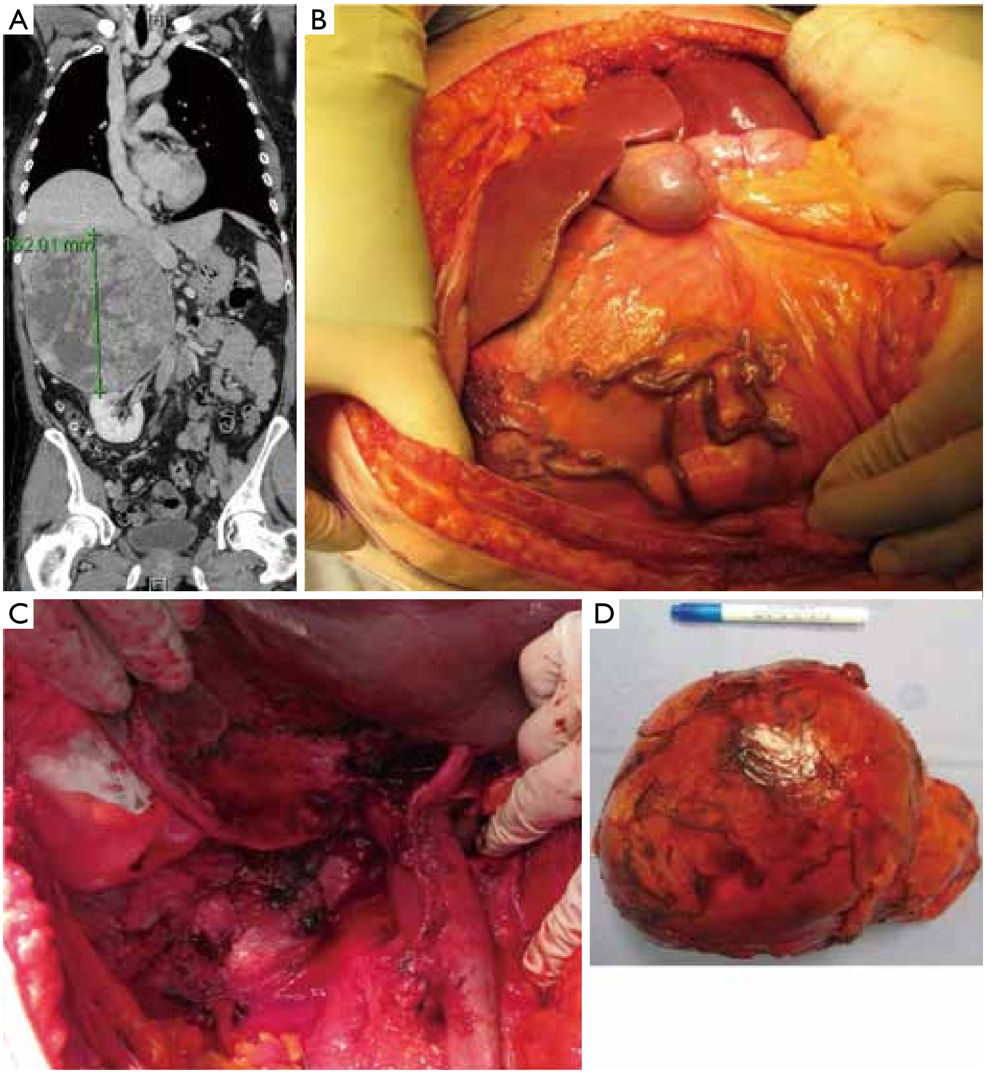

Figure 2 Right-sided adrenalectomy for adrenocortical cancer. Patient presented with clinical signs of excess androgen secretion and was found to have a 16-cm right-sided adrenal tumour (A). At laparotomy the mass was easily apparent under the lower border of the liver (B). After removal of the mass in continuity with right kidney, the IVC is clearly seen without any soft tissue in front of the posterior abdominal wall muscles (C). Specimen was resected intact (D). IVC, inferior vena cava.

The wide range of reported lymph node involvement in ACC (from 5% to 75%) suggests that formal regional lymphadenectomy is neither formally performed by surgeons nor accurately assessed or reported by pathologists. According to large American and French series, approximately one-third of patients with ACC had formal lymphadenectomy as part of the tumour resection, reflecting the heterogeneity of operative management. Similarly, the ESES-ENSAT working group declared that in their practice lymph nodes were 'not seen/not dissected' (n=21) or were 'likely excised en bloc' (n=5), excised *en bloc* (n=5) or dissected on purpose (n=11) (*Figure 4*). It is the authors' experience that macroscopic identification of such lymph nodes is very challenging and the en-bloc resection of the soft tissue surrounding the large vessels is commonly associated with postoperative chyle leak. In our experience we attempted to use indocyanine green to identify periadrenal lymph nodes (similar to the protocol introduced in colonic resection) but failed to visualise convincing uptake of the dye in local lymph nodes (personal data, unpublished).

The guidelines published recently by the European

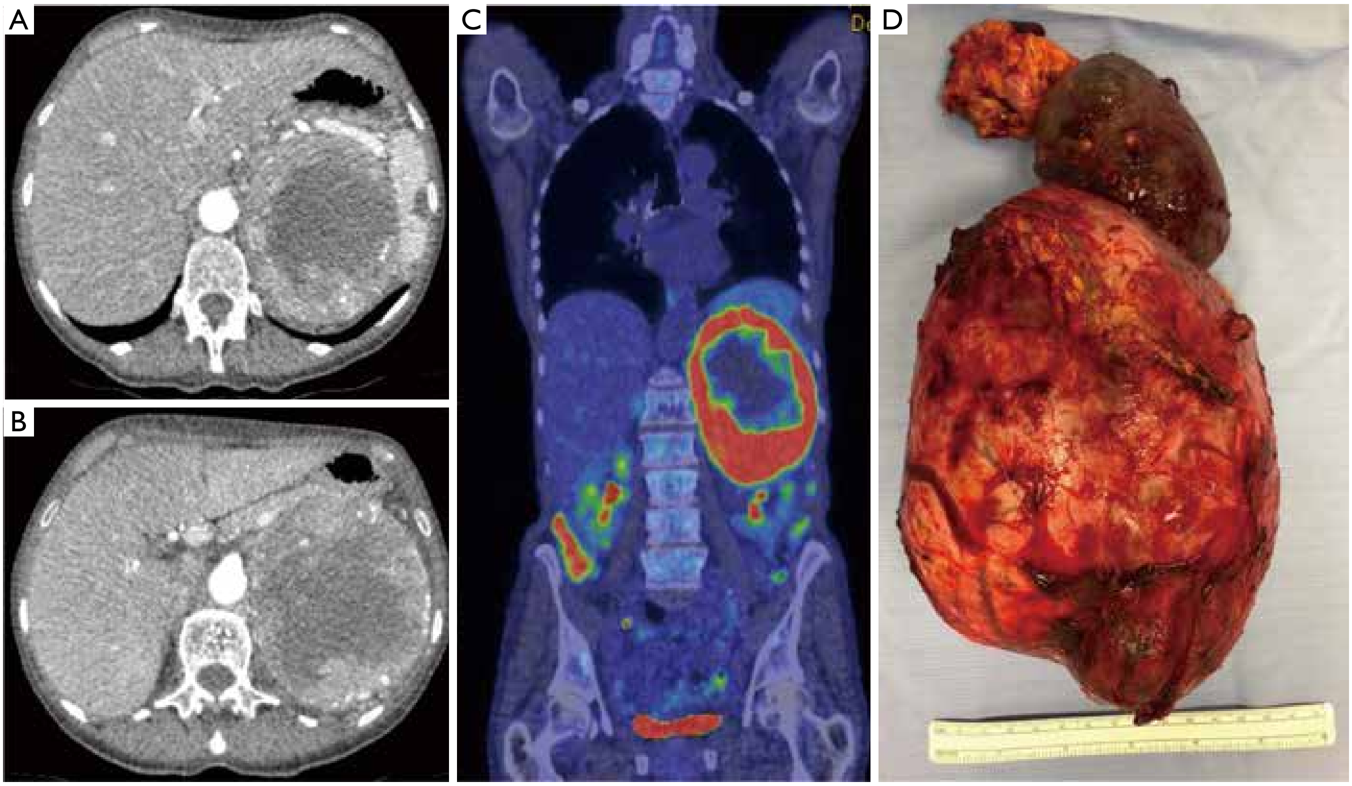

Figure 3 Left-sided adrenalectomy for adrenocortical cancer. Patient with non-functional ACC identified during cross sectional imaging for respiratory complaints. CT scan shows splenic artery stretched over the top the tumour (A) and tail of the pancreas in extensive contact with the tumour (B). PET scan showed no local lymphadenopathy (C). Tumour was resected intact together with the spleen and tail of pancreas (D). ACC, adrenocortical cancer.

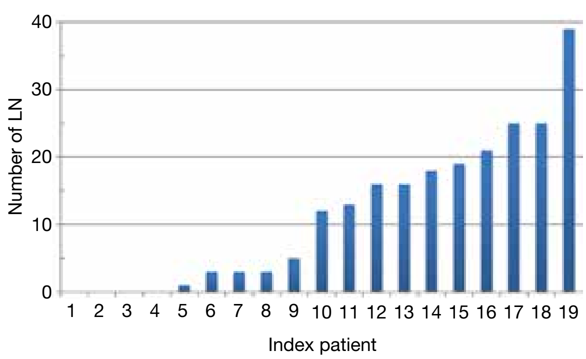

Figure 4 Lymph node yield in patients with adrenocortical cancer. In a group of unselected patients with ACC, the number of lymph nodes described on pathology reports varied widely even though for all cases the surgeon aimed a radical local excision of adrenal tumour and surrounding soft tissue. ACC, adrenocortical cancer.

Society of Endocrinology state: '*The panel suggests that routine locoregional lymphadenectomy should be performed with adrenalectomy for highly suspected or proven ACC. It should include (as a minimum) the periadrenal and renal hilum nodes. All suspicious or enlarged lymph nodes identified on preoperative imaging should be removed*' (4).

A prospective multicentre cohort study would be invaluable to address the issue of feasibility of lymphadenectomy for ACC and to quantify its benefits (staging) and associated added morbidity.

En bloc multivisceral resections

A retrospective study compared the oncological results of patients with stage II ACC treated by radical adrenalectomy

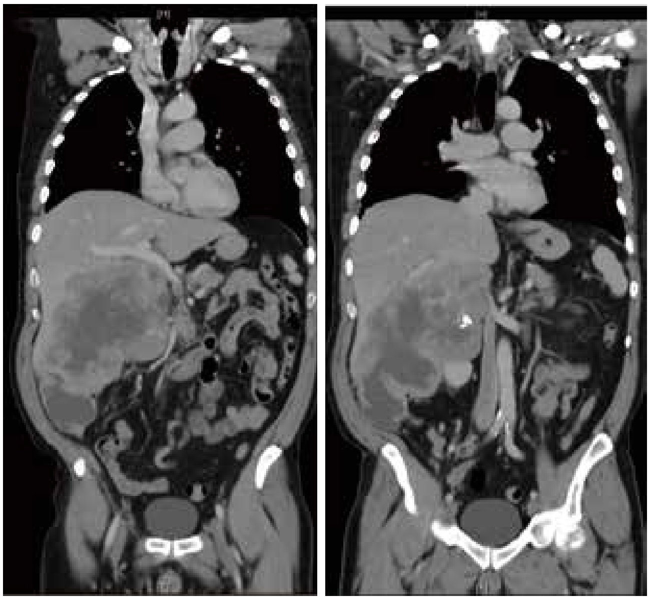

Figure 5 Unresectable adrenocortical cancer.

alone (n=16) or by nephron-adrenalectomy (n=25). The results did not support the hypothesis that nephrectomy improves the oncological outcome (8). In a multicenter European study on surgery for ACC, pathological invasion of the kidney was observed in only 30% of the patients with combined nephrectomy. Combined nephrectomy, however, offers a lower risk of tumour capsular rupture and can facilitate complete lymphadenectomy of the renal hilum. The ESE guidelines state: '*The panel recommends that adjacent organs should be resected en bloc if they are suspected to be invaded. This includes the spleen, distal pancreas, stomach, kidney, right liver, colon, diaphragm, and the wall of the IVC or left renal vein. No data to compare outcomes but it is deemed to be 'good surgical practice'*. The panel suggests that in the absence of direct renal invasion routine resection of the ipsilateral kidney should be avoided' (4).

Surgery for ACC with venous tumour thrombus

Extension of ACC to the adrenal, renal vein or IVC occurs in approximately 25%. Venous involvement consists mostly of intravenous tumour thrombus, but can be associated with direct vascular invasion. Thrombectomy may require IVC cross-clamping above or below the hepatic vein confluence or cardiopulmonary bypass, depending on the upper level extent of the thrombus. The resection should include complete thrombectomy, a flush manoeuvre and, occasionally, vascular cuff or prosthetic IVC replacement. A 3-year overall survival rate of 25–29 per cent in a large series encourages the performance of a venous resection in the presence of IVC or renal vein invasion (9). The ESE guidelines state: '*The panel recommends that individualised treatment decision have to be made for such patients based on multidisciplinary input from endocrine surgeons, liver surgeons, cardiac/vascular surgeons. Such patients should not be declared as 'unresectable' until review in a regional centre where adequate expertise exists*' (4).

The role of multidisciplinary input cannot be overestimated in this context. When extensive vascular involvement or tumour extent around portal vessels is encountered a decision to not operate is mandatory (*Figure 5*).

Postoperative care

DVT prophylaxis continues during the admission, in parallel with early mobilisation. Oral intake can be resumed within 24 hours postoperatively.

Steroid replacement: for patients with Cushing syndrome intravenous steroids (100 mg hydrocortisone iv tds or qds) are maintained until diet is restarted and then converted to oral steroids (hydrocortisone, 20–20–10 mg/day, aiming to decrease by 5 mg/day every 3–5 days). Involvement of the endocrinology team is important for monitoring of long-term steroid replacement.

Summary comments

In an era when minimally invasive adrenalectomy is the gold standard treatment for majority of patients presenting with adrenal tumours, open adrenalectomy has become an operation that should be centralised in regional referral centers. The need for preoperative and postoperative multidisciplinary input and the technical challenges of the operation should convince most surgeons to refer such cases to recognised centres with previous experience in the management of these patients.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Review Article

Retroperitoneal adrenalectomy—learning curve, practical tips and tricks, what limits its wider uptake

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Abstract: The minimally invasive retroperitoneal approach to the adrenal surgery has been described in the early 90s following the first description of laparoscopic adrenalectomy. Although the advantages of the technique compared to laparoscopic surgery have been demonstrated in many studies, it remained for a long period confined to few centers. The operation has been standardized over the years into a safe and reproducible procedure that finally gained worldwide acceptance in the last 10 years. The present paper summarizes the surgical steps of the procedure focusing on the recent technical developments. Retroperitoneoscopic adrenalectomy should be part of the surgical armamentarium of any center dedicated to endocrine surgery.

Keywords: Adrenalectomy; retroperitoneoscopic adrenalectomy; minimally invasive adrenalectomy; laparoscopic adrenalectomy

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Introduction

Following the introduction of minimally invasive surgery in the early 1980s, it took about ten years to see this innovative approach to be applied in the endocrine surgery, as the first description of laparoscopic adrenalectomy was published in 1992 by Higashihara in Japan (1) and by Gagner in Canada (2). During the same year a minimally invasive retroperitoneal approach was described by Gaur for urologic procedures including uretero-lithotomy, renoscopy, renal biopsy, para-aortic lymph node biopsy and ligation of the internal spermatic vein (3). In 1993 Brunt *et al.* developed a technique for endoscopic adrenalectomy in a domestic swine model using insufflation of the retroperitoneal space with CO_2 and retroperitoneoscopy (4). The results of this study suggested that the posterior route could have been potentially suitable to the treatment of adrenal lesions. In 1994 retroperitoneal adrenalectomy in humans has been described in Japan, New Zeeland and Sweden (5-7).

The obvious advantages of the minimally invasive approach, either laparoscopic or retroperitoneoscopic, in terms of postoperative pain, reduced morbidity and shorter hospital stay have made this operation the procedure of choice for small adrenal tumours (8,9).

As in the era of open surgery, there is still an on-going discussion whether the anterior or posterior approach represents the best route to the adrenal gland. Laparoscopic transperitoneal adrenalectomy has been demonstrated to be a safe and standardized procedure with a short learning curve and low morbidity rate. Nevertheless, many studies indicate that posterior retroperitoneoscopic adrenalectomy is superior to laparoscopic one regarding operation time, pain score, blood loss, complications rate and return to normal activity (10). A recent meta-analysis suggests that retroperitoneoscopic adrenalectomy has equivalent outcome to laparoscopic surgery but may be associated with a shorter hospital stay (11). According to the position of the patient (lateral decubitus versus prone position) two different technique of retroperitoneal adrenalectomy have been described in the second half of the '90s (12). The results

Figure 1 Position of the patient.

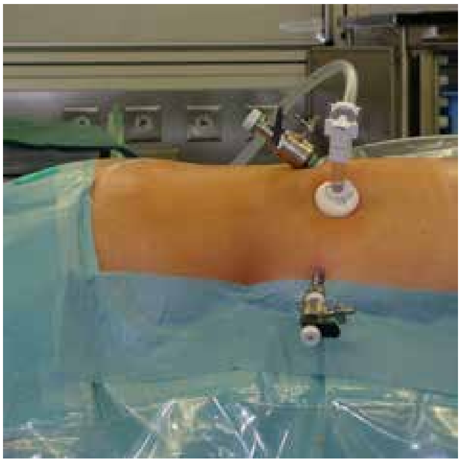

Figure 2 Trocar position: a blunt trocar with an inflatable balloon and an adjustable sleeve is introduced into the initial incision, a 5 mm trocar for the working instruments is used at the tip of the 11th rip and a 10 mm trocar is placed medially between spine and first incision.

of retroperitoneoscopic adrenalectomy in lateral decubitus were reported to be very promising in a large series published by Bonjer and co-workers (13). Nevertheless, the operation failed to obtain wide acceptance. On contrary, the retroperitoneoscopic adrenalectomy in prone position has been developed by Walz into a standardised technique (14), which has gained a recognised place worldwide over the last 15 years.

The technique of retroperitoneoscopic adrenalectomy

The procedure is performed with the patient in prone position lying on a rectangular support empty in the middle that allows the abdominal wall to hang ventrally through with a 90° angle between the body and the legs (*Figure 1*). A single shot antibiotic is given before induction of the anaesthesia. A 1.5 cm skin incision is performed at the level of the 12th rib and the retroperitoneal space is reached by blunt and sharp dissection with scissors. A finger is than inserted into the space and the tip of the eleventh rip is localized. A 5 mm trocar is inserted under finger control just below the tip of the 11th rip. At the beginning of the experience the third trocar was placed, at the same level of the first one, under finger guidance without visual control at half distance between the spine and the first incision (14). Actually the technique has been modified and CO_2 insufflation at a pressure of 20 mmHg is started before the insertion of the third trocar. A blunt trocar with an inflatable balloon and an adjustable sleeve (Medtronic, Minneapolis, USA) is therefore introduced into the initial incision site and blocked. The working space is created by blunt dissection with the camera looking at the left diaphragmatic crus and consequently the 10 mm trocar is inserted under the view of the endoscope. This permits the visual identification of the subcostal nerve and avoids therefore its lesion. The position of the trocars is showed in *Figure 2*. The originally described method of balloon dilatation was stopped already at an early stage. Retroperitoneoscopy is performed by a 10 mm 30° endoscope, although in selected cases a 5 mm scope can be used. The 5 mm 30° endoscope is also adopted for the single access operation (SARA) described in 2009 (15). The Ligasure Maryland with curved tip (Medtronic, Minneapolis, USA) is actually the preferred instrument for dissection and vessels sealing. The first step of the procedure is the visualization and mobilization of the upper pole of the kidney (*Figures 3,4*). According to the different position of the adrenal gland between right and left side, extensive mobilization of the kidney is generally required on the left side while the adrenal is mostly in a suprarenal position on the right side. The dissection of the adrenal gland should start at the lower pole and achieved from lateral to medial. By this approach the vena cava is visualized on the right side and the adrenal vein on the left side (*Figures 5,6*). On the right side the retrocaval arteries are divided and the dissection is continued cranially to identify the adrenal vein (*Figure 7*). The manipulation of the gland is always performed carefully using blunt palpation probes to prevent injury to the capsule. The main adrenal vein is isolated and divided after coagulation without application of clips. The dissection is than

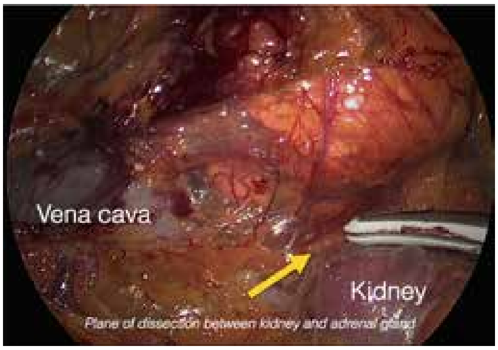

Figure 3 Right side: the dissection of the lower pol of the adrenal gland is started from lateral to medial, the vena cava is already visualized and partially dissected.

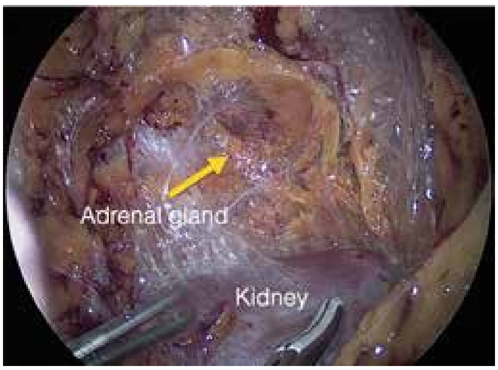

Figure 4 The kidney on the left side is widely mobilized to reach the lower pol of the adrenal gland generally located behind the kidney.

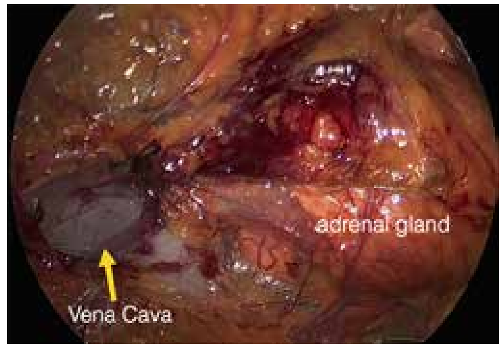

Figure 5 The vena cava is visualized medially to the lower pole of the adrenal gland.

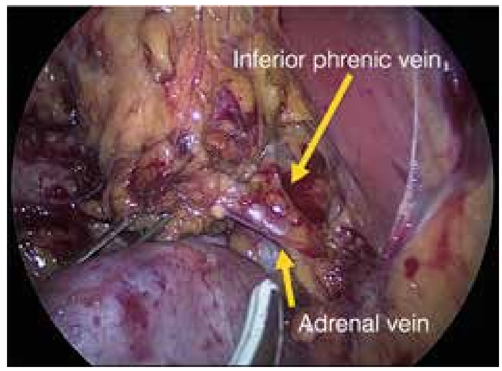

Figure 6 The left adrenal vein and inferior diaphragmatic vein are isolated.

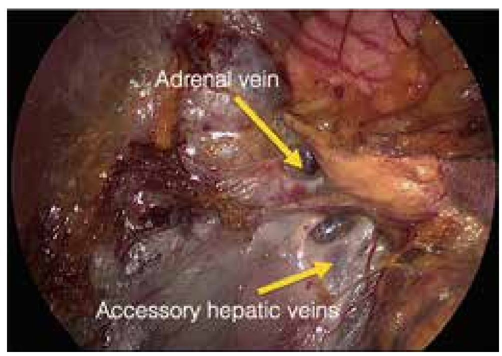

Figure 7 The adrenal gland is retracted laterally and the right adrenal vein is isolated; in this case two accessory hepatic veins are visible below the main adrenal vein.

completed cranially and ventrally taking care not to damage the Toldt's membrane and the peritoneal layer. The adrenal gland is extracted through the middle incision with a retrieval bag system (Endocatch, Medtronic, Minneapolis, USA). Depending on tumor size and on the underlying pathology morcellation of the tumor can be required. After optional drain insertion, skin and fascia are closed with reabsorbable sutures.

Bilateral tumors can be removed without repositioning of the patient necessary resulting in a significant reduction of the operating time if two teams can operate simultaneously.

During subtotal adrenalectomy the adrenal gland is dissected according to the position of the tumor preserving the adrenal arteries feeding the normal tissue. Preservation of the main vein is not necessary (16). To identify the margin of the neoplasia, it may be necessary to dissect or resect parts of the surrounding fatty tissue, which is normally resected "*en-bloc*" with the gland in case of total adrenalectomy. Retroperitoneoscopic ultrasonography by a 10 mm flexible 10 MHz probe can be applied individually for identification of the neoplasms. Division of the adrenal tissue is performed by bipolar coagulation. The insertion of drainage is generally not required.

Learning curve, practical tip and tricks

The complications rate of adrenalectomy ranges from 0% to 15% for unilateral operation and rises up to 23% for bilateral surgery. No significant differences are found between laparoscopic and retroperitoneoscopic operations. Nevertheless, splenic injuries and intra-abdominal abscesses are reported only after laparoscopic procedures, while relaxation and/or hypoesthesia of the abdominal wall are typical for posterior retroperitoneoscopic surgery (17). Switching from the anterior to the posterior view could be related with several troubles connected to the different anatomical view, the small working space and the limited degree of freedom of the laparoscopic instruments inserted below the ribs. Laparoscopic adrenalectomy has the advantage of a familiar anatomical view coupled to a wide working space.

The learning curve for laparoscopic adrenalectomy is reported to be of approximately 30 cases, if performed by an experienced laparoscopic surgeon (18). Barczynski and co-workers demonstrated that the introduction of the retroperitoneoscopic adrenalectomy was not related to an increased complications rate or longer operating time when supervised by an experienced team (19). The mean operative time could be reduced from 117 minutes reported during the learning period in Essen to 83 minutes for the initial phase in Krakow. The authors described one conversion and one early reoperation due to bleeding compared to seven conversions in the initial experience by Walz in Essen.

These results have been confirmed in a recent multicentre study undertaken at four endocrine centers. The analysis of the learning curve cumulative sum was used to evaluate the learning curve for the posterior adrenalectomy (20). The median overall duration of operation was 89 (range, 29–265) min. The surgical teams reached competency after 24, 29, 40 and 42 procedures, as demonstrated by crossing the established threshold. Male sex and high BMI were proven to correlate significantly with the duration of surgery.

Increasing experience and several improvements that have modified the originally described operation allowed us to reduce the median operating time to 45 minutes over 2,310 procedures performed between July 1994 and September 2018 and to reduce the complications rate to less than 1%.

Following some practical tips are summarized:

(I) The position of the patient with a 90° angle between the spine and the legs was adopted from the beginning of the experience and it is of crucial importance to obtain the optimal distance between the rib and the hip bone.

(II) A correct position of the trocar is necessary to avoid conflict between the instruments during surgery. According to the anatomy of the patient, if the 11^{th} rip is long the trocar could be inserted cranially to the rip to allow a better degree of freedom for the instruments. The insertion of the medial trocar should be performed with a flat angle under optical view to avoid lesion of the subcostal nerve and accidentally insertion of the trocar into the chest.

(III) CO_2 insufflation pressure can be increased up to 30 mmHg and modulated according to the anatomy of the patient and the diameter of the tumor to increase the space as required without side effects for the patient. Increase of the pressure can be also used in case of bleeding to obtain temporary haemostasis due to the compression of the small vessels.

(IV) The dissection should be always started at the upper pole of the kidney. A wide mobilisation is necessary on the left side prior to approach the adrenal gland. The lower pole of the adrenal gland is generally automatically visualized and dissected leaving the adrenal attached to the lateral and upper adhesions. Division of the retrocaval arteries on the right side can facilitate the exposition of the vena cava and of the retrocaval portion of the lower pole of the right adrenal gland. The dissection should than be conducted from 3 to 9 hours clockwise on the right side and from 9 to 3 hours counterclockwise on the left side.

(V) During the learning period it can be reasonably recommended not to approach tumors larger than 6 cm, as the tumor diameter is the most important prognostic factor for malignancy. Radiologic features suggestive of malignancy are generally not specific enough to discourage a minimally invasive approach for tumors <6 cm.

(VI) A BMI (body mass index) of more than 35 represents a relative contraindication during the learning phase. The dense retroperitoneal fat, especially in male patients, is generally attached very strongly to the capsule of the kidney and can make the dissection very difficult.

The ability to visit an institution with expertise in the technique can be helpful to successful adoption of the procedure in the own institution (20,21).

Acknowledgments

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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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.

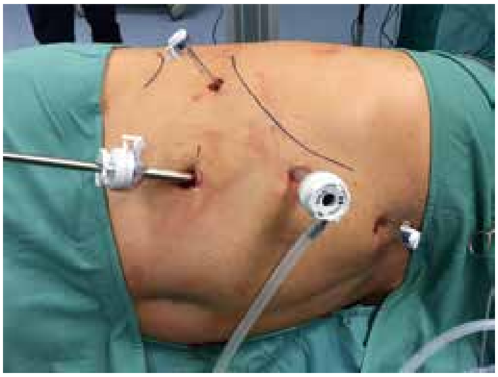

Figure 1 Trocars position for right laparoscopic transabdominal lateral adrenalectomy (TLA).

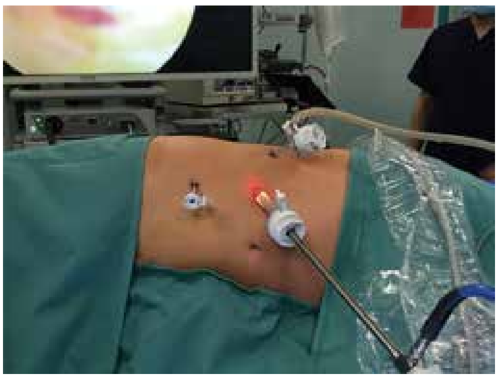

Figure 2 Trocars position for left laparoscopic transabdominal lateral adrenalectomy (TLA).

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).
Available online: http://www.asvide.com

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*).

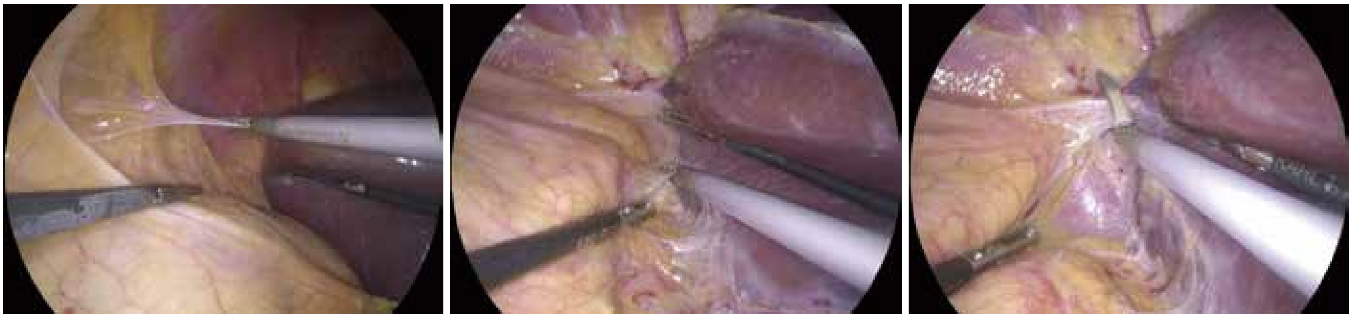

Figure 4 Dissection of the right triangular and hepatopatietal ligaments allow obtaining an effective mobilization of the liver.

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

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.

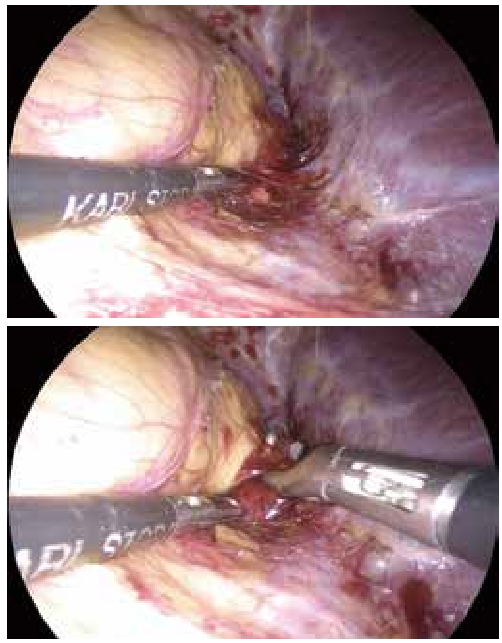

Figure 6 Dissection of the plane between the adrenal gland and the inferior vena cava and identification of the right main adrenal vein.

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

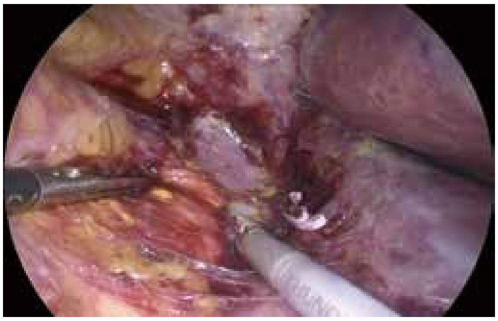

Figure 7 Dissection of the right main adrenal vein.

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

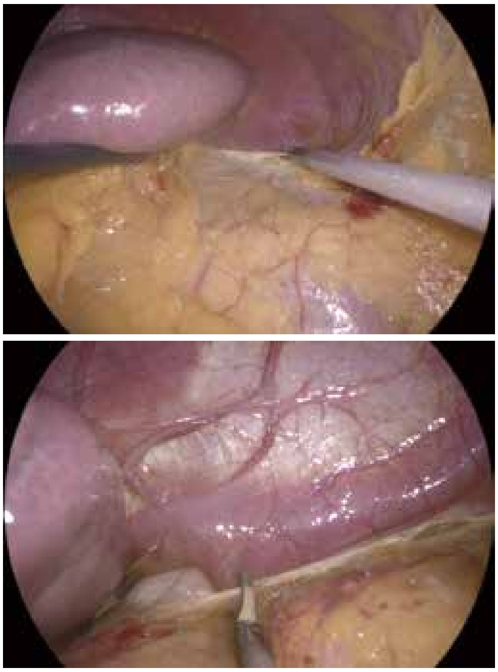

Figure 10 Dissection of the splenoparietal ligament: the dissection is performed far enough to visualize the greater curvature of the stomach.

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. The dissection of the lateral aspect of the gland should be

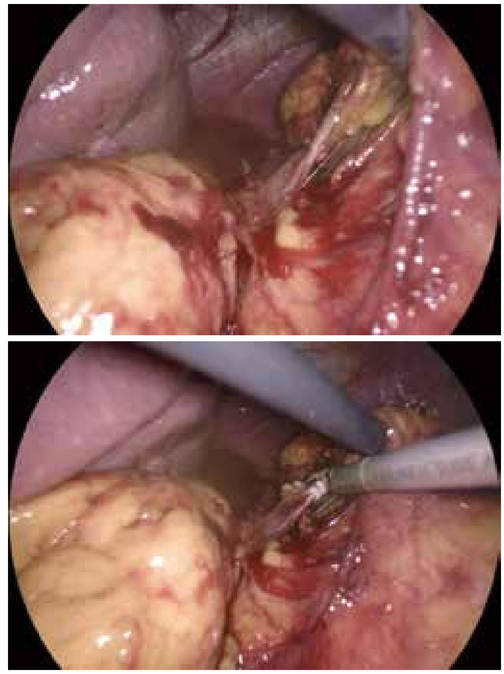

Figure 12 Identification and dissection of the left main adrenal vein.

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 complication 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.

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Footnote

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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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Review Article

Surgical management of adrenal tumours extending into the right atrium

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Abstract: This paper discusses the surgical approach for the treatment of adrenal tumours extending into the right atrium (RA), using a cardio-pulmonary bypass (CPB) associated with deep hypothermic circulatory arrest (DHCA). Pre-operative planning and surgical steps are described in details. The association of CPB with hypothermic circulatory arrest (HCA) provides a bloodless operating field, direct intra-vascular vision, reduces the risk of embolization and allows extensive inferior vena cava (IVC) or RA repair in cases of infiltration of the vascular wall. Establishing a dedicated multidisciplinary team with experience in managing these challenging cases is fundamental to offer treatment to patients with advanced disease, who would otherwise risk being turned down for surgery. A close collaboration between general and cardiac surgeons and a deep understanding of the surgical procedure steps are fundamental to safely performing these procedures. We advocate centralising adrenal surgery in a small number of units with adequate multidisciplinary support.

Keywords: Adrenal gland tumour; adrenocortical carcinomas; right atrial mass; inferior vena cava thrombus (IVC thrombus); deep hypothermic circulatory arrest (DHCA)

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Introduction

Adrenal gland tumours are relatively common, affecting 3% to 10% of the population (1). Small benign non-functional adrenocortical adenomas account for the majority of these tumours. Adrenocortical carcinomas, however, are rare, with an incidence of 1 to 2 per million cases per year. One out of three patients with adrenocortical carcinoma presents with involvement of the venous system and inferior vena cava (IVC) thrombus (2). Tumours of the right adrenal gland are more likely to involve the IVC, due to the right adrenal vein directly draining into it (3).

The aim of this report is to present our surgical experience of using cardio-pulmonary bypass (CPB) associated with deep hypothermic circulatory arrest (DHCA) for the treatment of adrenal tumours extending into the right atrium (RA).

Classification of tumours/thrombus for adrenal tumour

A classification in four levels has been described according to the location of the upper limit of the tumour/thrombus (*Table 1*). The technique used for intra-operatory venous control depends on the location and extension of the tumour/thrombus in the venous circulation (2,4,5).

Table 1 Intra-operatory approach (venous control) for adrenocortical mass with tumour/thrombus extending into the IVC/RA

Extension of the adrenocortical mass	Surgical approach
Tumour/thrombus below the hepatic vein, level I	Cross clamping of IVC
Infra-diaphragmatic tumour/thrombus (retro or supra-hepatic), level II–IIIa	HVE
Supra-diaphragmatic tumour/thrombus (IVC/RA), level IIIb–IV	Cardiopulmonary bypass ± hypothermic circulatory arrest

IVC, inferior vena cava; RA, right atrium; HVE, hepatic vascular exclusion.

Surgical techniques for venous control

Three different techniques can be used according to the level of extension of the tumour/thrombus in the venous circulation (6).

(I) Cross clamping of the IVC is sufficient if the upper limit of the tumour/thrombus is below the hepatic veins (level I).

(II) Hepatic vascular exclusion (HVE) is the technique of choice for tumour/thrombus extending into the hepatic veins or into the retro- or supra-hepatic IVC, but below the diaphragm (level II and IIIa). HVE is generally well tolerated, provided there is adequate fluid expansion before clamping.

(III) Treatment of tumours/thrombus extending into the cavoatrial junction or the RA (level IIIb and IV) requires the use of concomitant CPB. The advantage of this approach is that it provides haemodynamic stability during cross clamping of the IVC, reduces the risk of cardiac arrest and facilitates surgical dissection. Our technique of choice is the association of CPB with hypothermic circulatory arrest (HCA). This approach provides a bloodless operating field and direct intra-vascular vision, reduces the risk of embolization and allows extensive IVC or RA repair in cases of infiltration of the vascular wall.

A summary of the different surgical approaches is reported in *Figure 1*.

Surgical planning and CPB + HCA technique

Patients who present with an adrenal mass extending into the supra-diaphragmatic IVC are routinely discussed with the cardiac surgical team in a multidisciplinary team (MDT) setting. Pre-operative assessment includes CT scan and trans-thoracic echocardiography to assess the extension of the tumour and plan the surgical strategy (*Figure 2*).

The procedure is performed in the cardiac theatre, under the care of a wide team composed by a general/endocrine surgeon, a cardiac surgeon, a cardiac anaesthetist, a trans-oesophageal echocardiography (TOE) operator, a perfusionist and a cardiac scrub nurse. Taking into account that these are long procedures, we usually scheduled them as all-day cases.

TOE assessment plays an important role in planning the surgical technique, guiding the venous cannulation and ensuring that the mass is totally removed.

The surgical procedure starts with a laparotomy and the general surgeon mobilising the adrenal gland, the kidney and gaining control of the infra-diaphragmatic IVC. Once the dissection in the abdomen is completed, the cardiac surgeon proceeds with a median sternotomy, opening of the pericardium and systemic heparinization. It is important to maximise the amount of abdominal dissection performed before heparin administration to minimize the bleeding. Two Tycron 3.0 pursing sutures are placed at the level of the ascending aorta; a 24F aortic cannula is inserted and connected to the arterial line. A single Tycron 3.0 pursing is placed on the RA. A large atrial incision is performed to facilitate the introduction of a Ross basket (*Figure 3*) and establish the venous drainage. The rational of using a Ross basket instead of an ordinary venous cannula is to minimize the risk of dislodgement of the atrial mass. The venous cannulation is performed under TOE guidance to minimize the risk of embolization of the atrial mass. A small cannula is inserted into the ascending aorta, proximally to the arterial cannulation site for the cardioplegia administration.

A schematic view of CPB is described in *Figure 3* and a summary of the main steps of the procedure in *Table 2*. CPB is established and the patient is cooled to 18 degrees. This process takes 20–30 minutes, depending on the body surface area of the patient. As response to hypothermia the heart fibrillates and a vent is placed into the right superior pulmonary vein to avoid left ventricular distension. Once the cooling is completed a cross clamp is applied to the ascending aorta and a cardioplegic solution is

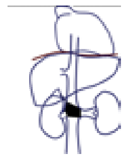
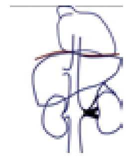
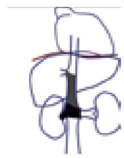
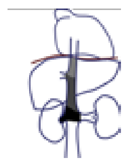
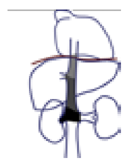
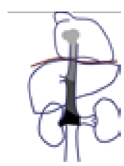
Level I	**Infra-hepatic** Thrombus in the adrenal vein or infra-hepatic IVC (the left adrenal vein drains into the left renal vein, the right adrenal vein is shorter and drains directly into the IVC)	 I  Ia  Ib
Level II	**Hepatic** Thrombus extends into the hepatic portion of the IVC and reaches ostia of the major hepatic veins	 II
Level IIIa	**Retro-hepatic IVC** Thrombus extends into the retro-hepatic IVC and above the major hepatic veins, but below diaphragm	 IIIa
Level IIIb	**Supra-diaphragmatic** Thrombus extends into the supra-diaphragmatic and intra-pericardial IVC, but not in the RA	 IIIb
Level IV	**Intra-pericardial** Thrombus extends into the RA	 IV

Figure 1 Classification of tumour/thrombus in adrenal tumour [Ekici and Ciancio, adapted from (2)]. IVC, inferior vena cava; RA, right atrium.

Figure 2 Intra-operative trans-oesophageal echocardiogram. Thrombus in the IVC extending into the RA. IVC, inferior vena cava; RA, right atrium.

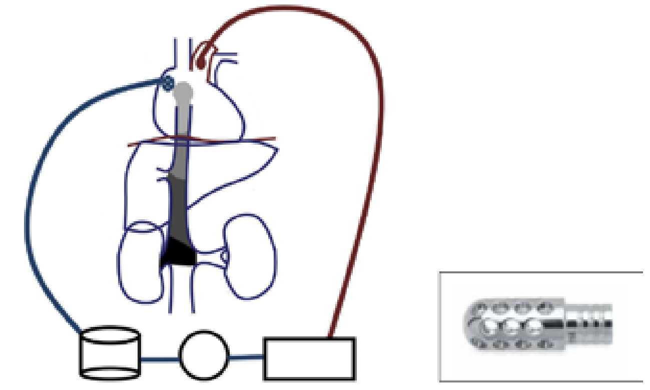


Figure 3 Schematic representation of cardio pulmonary bypass circuit and Ross basket for right atrium cannulation.

administrated into the aortic root. A clamp can be applied across the pulmonary artery to reduce the risk of pulmonary embolisation.

The circulation is arrested, the venous blood is drained into the pump reservoir and the CPB is stopped. The DHCA provides 20–30 minutes of safe bloodless field for both surgeons to expose the IVC and the RA, remove the thrombus and reconstruct the structures.

During DHCA the cerebral perfusion is interrupted, the low temperature protects the brain, but the risk of ischemic injury increases exponentially after 35–40 minutes (7,8).

During the DHCA both surgeons operate simultaneously. A right atriotomy and IVC cavotomy are performed to expose both abdominal and intrapericardial mass. The cardiac surgeon then carefully mobilised the mass, free from the wall of the IVC and RA.

The tumour/thrombus is pulled down into the IVC and pushed down from the atrium by both surgeons. The IVC and RA are carefully inspected to ensure that no thrombus is left behind. The IVC and the RA are directly sutured with 4.0 Prolene. For infiltrating tumours a bovine or autologous pericardial patch can be used to reconstruct or augment the IVC or the RA wall. In one case we used a homograft to replace an entire segment of the IVC, which was severely infiltrated by the tumour.

Once the structures are reconstructed, the circulation and the CPB are restarted and a rigorous de-airing drill is performed. The blood is re-warmed to 37 degrees. During this period the patient is coagulopathic due to the low temperature, the inflammatory response to CPB and the systemic heparinization.

Once a physiological temperature has been reached

Table 2 Summary of the main steps of the combined procedure

Laparotomy and mobilization of adrenal gland/kidney
Preparation of renal artery/vein
IVC exposed at the level of the hepatic veins
Median sternotomy and CPB
Systemic heparinization (ACT 400–450)
Ascending aortic cannulation
Right atrial cannulation (Ross basket)
CPB +/– pulmonary artery clamping
DHCA
Cooling to 18 degree
Patient's blood drained in the pump reservoir and CPB stopped
20–30 min safe time of DHCA
Nephrectomy and removal of IVC thrombus/mass
RA and IVC opened
Removal of IVC thrombus/mass under RA direct vision
Removal of abdominal mass
Closure/reconstruction of RA and IVC
Direct closure RA/IVC
Pericardial patch for infiltration of RA/IVC wall
IVC homograft reconstruction for severe infiltration
Restart circulation, off CPB
Restart of CPB and systemic circulation
Re-warm to 37 degree
Wean CPB
Haemostasis and closure
Protamine administration
Haemostasis
Routine chest and abdomen closure

IVC, inferior vena cava; ACT, activated clotting time; CPB, cardio-pulmonary bypass; DHCA, deep hypothermic circulatory arrest; RA, right atrium.

and maintained for few minutes, the patient is weaned and disconnected from CBP. TOE is used to assess the heart function, the right atrial cavity, tricuspid function and ensure that there is no significant gradient/obstruction across the IVC in the cases requiring a surgical reconstruction. Protamine reversal is administrated. A

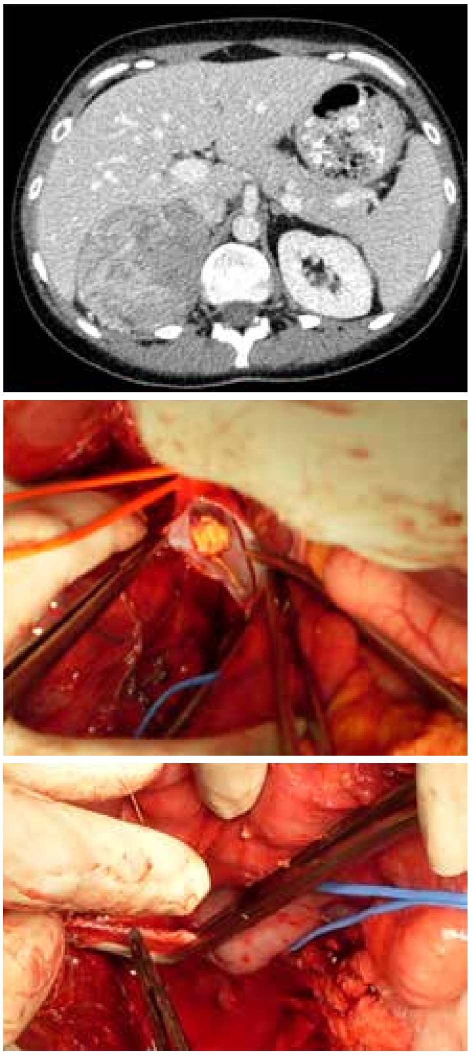


Figure 4 Radiological and intraoperative findings in a patient with level I tumour thrombus. Patient presenting with rapid progression of Cushing syndrome. During dissection of the tumour it became apparent that the right adrenal vein was invaded by tumour thrombus. After cross clamping of the IVC, a venotomy was performed, small volume tumour thrombus demonstrated in the lumen of the vein was fully removed and the IVC was sutured with 3.0 Prolene. IVC, inferior vena cava.

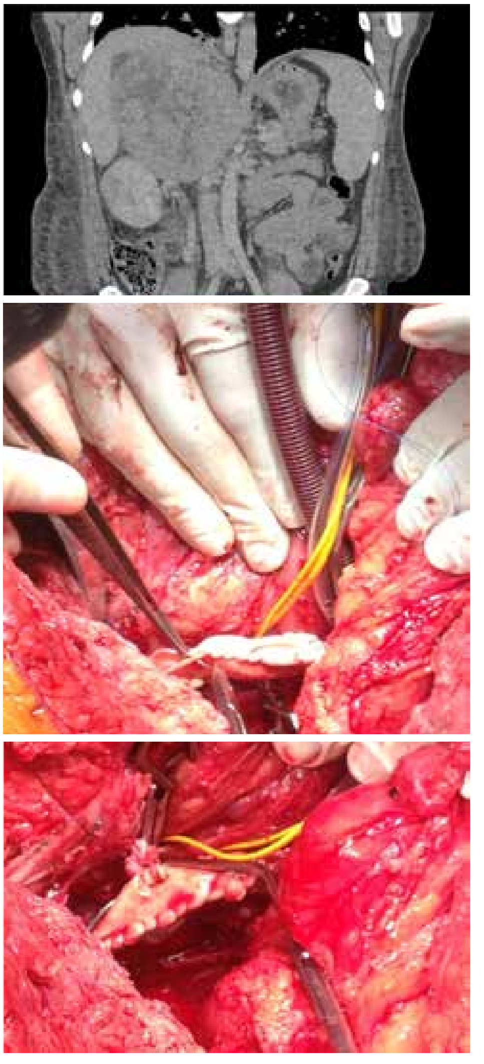


Figure 5 Radiological and intraoperative findings in a patient with level IIIa tumour thrombus. Patient with incidental finding of large nonsecreting ACC. Cardiopulmonary bypass allowed extraction of large volume tumour thrombus, repair of the IVC with a bovine pericardial patch and reanastomosis of left renal vein into the reconstructed IVC. Patient remains disease free 4 years after the operation. ACC, adrenocortical cancer; IVC, inferior vena cava.

systematic haemostasis is performed before proceeding with the closure of the chest and the abdomen. Clotting factors and platelets transfusion may be required to optimise coagulation status and haemostasis.

The Oxford experience

Due to the low incidence of ACC, the personal surgical experience for locally advanced tumours remains limited (9). In our unit the annual workload over the last decade has been in excess of 70 cases/year. Out of this large cohort of patients, nine patients with infra-hepatic IVC tumours extension were operated without establishing CPB (*Figure 4*). Cardiopulmonary bypass was used in seven patients with tumour/thrombus extending in the supra-diaphragmatic IVC (*Figure 5*) and DHCA in only two patients.

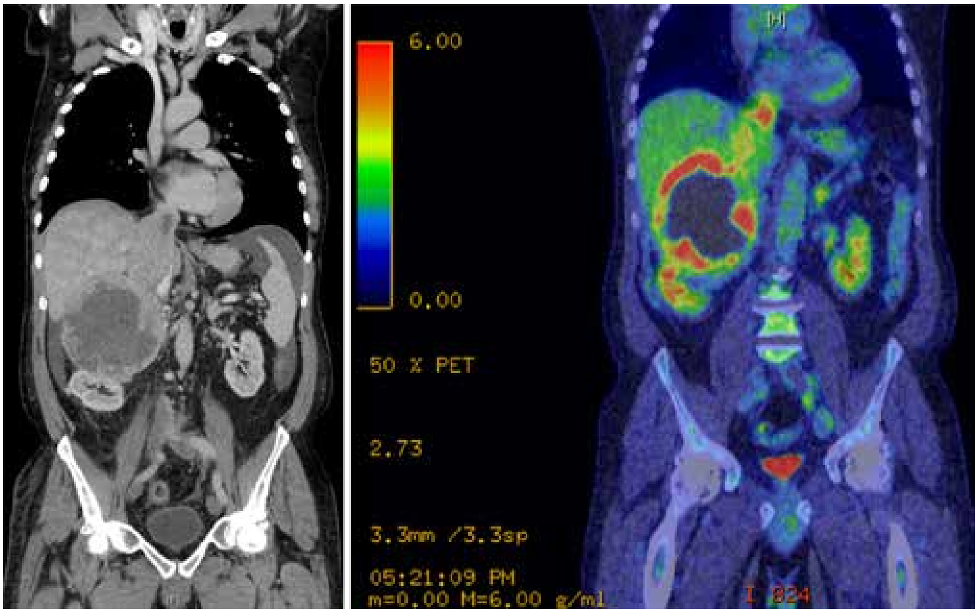


Figure 6 Radiological findings of patients with level IV tumour thrombus. Phaeochromocytoma invading the IVC demonstrated on CT scan and confirmed on PET scan. IVC, inferior vena cava.

Out of the 7 patients treated in Oxford with tumour/thrombus extending in the supra-diaphragmatic IV requiring cardiopulmonary bypass some patients experienced unexpected long disease-free survival. A patient operated in 2007 remains disease free (32 years, Cushing syndrome, left adrenal tumour with thrombus into the atrium) and patient described in *Figure 4* is disease-free over 4 years after the operation. There was a single in-hospital death (day 11 postop due to hypoxic brain injury and multiorgan failure).

The most recent case needing HCA was a 61-year-old man with a 12-cm malignant right phaeochromocytoma extending into the RA (*Figure 6*). After a 4-week adrenergic blockade he underwent right radical adrenalectomy. The HCA time was 14 minutes. His post-operative recovery was uneventful and he was discharged home on post-operative day 10. Histology showed an adrenal phaeochromocytoma with PASS score of 15/20. At 4 weeks after the operation, biochemistry was normal (metanephrine 0.25 µmol/24 h, normetanephrine 2.31 µmol/24 h). An metaiodobenzylguanidine (MIBG) performed at 6 weeks after the operation showed moderate MIBG uptake in a new 1 cm node medial to the IVC, three discrete MIBG-avid metastases identified in the liver and marked MIBG uptake in lytic lesion within C6 vertebral body, which was FDG negative. He received two doses of therapeutic I^{131} MIBG to control bone and lung metastases. The patient is alive with controlled metastatic disease over 4 years after his initial presentation.

These figures demonstrate encouraging outcomes in patients otherwise deemed inoperable and highlight the importance of centralising adrenal surgery in a small number of units with adequate multidisciplinary support.

Conclusions

We described the surgical technique of using CPB associated with DHCA for the treatment of adrenal tumours extending into the RA. Establishing a dedicated multidisciplinary team with experience in managing these challenging cases is fundamental to offer treatment to patients with advanced disease, who would otherwise risk being turned down for surgery. A close collaboration between general and cardiac surgeons and a deep understanding of the surgical procedure steps are fundamental to safely performing these procedures.

Acknowledgments

None.

Footnote

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

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