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ORIGINAL ARTICLE

Laparoscopic adrenalectomy—10-year experience at a teaching hospital

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Abstract
Background Minimally invasive adrenalectomy has been adopted as the treatment of choice for benign adrenal tumors. This study aimed to investigate the outcome of laparoscopic adrenalectomies performed over a 10-year period at a teaching hospital.
Methods All laparoscopic adrenalectomies carried out between 1 April 2000 and 31 March 2010 were evaluated with respect to perioperative management, complications, conversion rate, learning curve, tumor size, and surgically relevant characteristics of different adrenal pathologies.
Results Over a period of 10 years, 215 laparoscopic lateral transabdominal adrenalectomies were carried out for Conn's syndrome (n=90), Cushing's syndrome (n=72), pheochromocytoma (n=30), metastatic disease (n=8), incidentalomas (n=10), and other rare adrenal pathologies (n=5). Morbidity, mortality, and conversion rate were 7.0, 0.9, and 4.2 %, respectively. Patients with Cushing's disease and bilateral adrenalectomy showed a higher complication rate. In retrospect, the indication for a laparoscopic approach was at least questionable in five cases. During these 10 years, four surgeons unfamiliar with the technique received intensive training to a defined plan.
Conclusions Laparoscopic adrenalectomy represents a safe operating technique associated with few complications and a low conversion rate. Patients with severe Cushing's disease are prone to complications and require intensive monitoring postoperatively. Laparoscopic adrenalectomy is associated with a learning curve, and particular emphasis should be given to surgical training.

Keywords Laparoscopic adrenalectomy · Complications · Pheochromocytoma · Conn syndrome · Cushing syndrome

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Introduction

Over the last 20 years, minimally invasive adrenal surgery has become the standard operation for removing the majority of benign adrenal masses. It is associated with fewer complications, less postoperative pain, a faster recovery, and a shorter hospital stay [1–3]. Several techniques have been described, the most popular being the lateral transabdominal approach and the posterior retroperitoneoscopic adrenalectomy [4–7]. Each of these techniques is highly successful in experienced hands, and it is recommended that surgeons choose the approach most familiar to them. However, adrenalectomies are not common operations and in general practice, it may be difficult to overcome the learning curve of approximately 30 cases [8–10]. This means that intensive training is necessary for residents who are involved in endocrine surgery, and/or adrenalectomies should be performed in centers with great expertise. An adequate training of young surgeons has been one of our major concerns over the years, and we will report on our experience.

Initially, minimally invasive adrenalectomy was restricted to small benign tumors. Meanwhile, experienced surgeons are able to safely remove adrenal masses up to a size of 10 to 12 cm [11–13]. This technical progress raises the question whether laparoscopic surgery is appropriate in the treatment of adrenal cortical carcinoma (ACC). The available literature on this subject is limited with advocates for a laparoscopic

approach as well as those who strongly recommend open surgery [14–18]. In any case, it is mandatory to carry out an oncologic resection that includes en bloc resection of involved neighboring tissue and a radical lymphadenectomy [16]. We still endorse open adrenalectomy for ACC but will report on our experience with large adrenal masses without evidence of malignancy that were approached laparoscopically. Furthermore, we will analyze complications and reasons for conversion and try to define patient groups who may need particular attention.

Patients and methods

We conducted a retrospective cohort study using a prospectively collected database including all patients who underwent adrenalectomy between 1 April 2000 and 31 March 2010. All indications for surgery were approved by oncological or endocrinological tumor boards. The operations were carried out at the Department of Surgery, Klinikum Innenstadt, Ludwig-Maximilians University, Munich.

For patients with pheochromocytoma, an alpha adrenergic blockade with phenoxibenzamine was started at least 14 days before surgery. The initial dose of 20 mg per day was slowly increased up to 60 mg per day until signs of orthostatic hypotension became evident.

A lateral transabdominal approach was used for all laparoscopic adrenalectomies. The patients were placed in a lateral decubitus position with the tumor side up and the table flexed between the 12th rib and the iliac crest. Three 12-mm Optiview trocars (Ethicon Endo Surgery, Johnson & Johnson) were used for left adrenalectomies and four 12-mm trocars for right adrenalectomies. The additional port on the right was necessary to insert a liver retractor. Thirty-degree or 45° optics were used routinely, and the dissection was carried out using Ultracision scissors (Ethicon Endo Surgery, Johnson & Johnson). Larger vessels were divided between clips. All patients received prophylactic antibiotics perioperatively.

The data collected included demographics, indication for operation, comorbidities, body mass index (BMI), intraoperative parameters, tumor size, conversion to open adrenalectomy, complications, and histology. Complications were categorized by using the Clavien–Dindo classification [19].

All data were collected by trained medical personnel and saved in an electronic spreadsheet (Microsoft Excel). The Kolmogorov–Smirnov test revealed no normal distribution. Next to standard descriptive statistics, we conducted a Kruskal–Wallis H test and a Mann–Whitney U test. The level of significance was set to $p<0.05$. Statistical analysis was performed using SPSS (SPSS version 22.0, IBM, Chicago, IL, USA).

Results

Between 1 April 2000 and 31 March 2010, 215 laparoscopic lateral transabdominal adrenalectomies on 197 patients were carried out for Conn's syndrome (n=90), Cushing's syndrome (n=72), pheochromocytoma (n=30), metastatic disease (n=8), incidentalomas (n=10), and other rare adrenal pathologies (n=5). One hundred four patients were females (52.8 %), and 93 were males (47.2 %). The median age was 51 years (range 21 to 77 years). One hundred ten (55.8 %) operations were carried out on the left side, 69 (35.0 %) on the right side, and 18 bilaterally (9.7 %). The median body mass index (BMI) was 26.3 kg/m^2 (range 16.7 to 48.1). Morbidity, mortality, and conversion rate were 7.0, 0.9, and 4.2 %, respectively. The demographic details of all completed unilateral adrenalectomies are listed in Table 1.

Conn's syndrome–Cushing's syndrome–pheochromocytoma

The data of the three groups representing the main indications for adrenalectomy are presented in Table 2. Significant differences regarding the hospital stay were observed between patients with Conn's syndrome and pheochromocytoma. Patients of the latter group were postoperatively regularly transferred to the Medical Department to monitor the blood pressure. Further, significant gender differences were observed between patients with Cushing's syndrome and the two other groups.

Bilateral adrenalectomy for ACTH-dependent Cushing's disease

Eighteen patients were scheduled for a bilateral adrenalectomy (14 females/4 males). Their median age was 49 years (23 to 74 years), and the median body mass index was 28.2 kg/m^2

Table 1 Demographic data of all unilateral laparoscopic adrenalectomies

	Unilateral laparoscopic adrenalectomies, n=171
Mean age, median (range)	51 years (21–77)
Male/female	86/85
BMI, median (range)	26.3 kg/m^2 (16.7–42.5)
Side (left/right)	109/62
Operating time, median (range)	75 min (35–300)
Estimated blood loss, median (range)	100 ml (10–700)
Tumor size, median (range)	5.5 cm (0.5–12.5)
Complications, n (%)	13 (7.3)
Major complications n (%)	5 (2.8)
Mortality	0

The data of eight unilateral conversions (4.2 %) are not included

Table 2 Comparison between Conn's syndrome, Cushing's syndrome, and pheochromocytoma

	Conn's syndrome, n=90	Cushing's syndrome, n=36	Pheochromocytoma, n=30
Age, median (range)	51.0 years (27–77)	46.8 years (23–75)	50.5 years (21–76)
Male/female	59/31	2/34	18/12
BMI, median (range)	26.1 kg/m^2 (19.5–39.6)	28.1 kg/m^2 (18.3–42.5)	26.6 kg/m^2 (16.7–34.9)
Side (left/right)	58/32	26/10	14/16
Operating time, median (range)	70 min (35–180)	75 min (50–180)	80 min (53–300)
Blood loss, median (range)	100 ml (0–700)	150 ml (0–2600)	75 ml (0–700)
Tumor size, median (range)	5.5 cm (0.8–12.5)	5.5 cm (0.5–10.0)	5.1 cm (2–9.7)
Major complications	2 (2.2 %)	3 (10.0 %)	0
Conversions	0	4 (13.3 %)	2 (7.14 %)
Mortality	0	0	0
Hospital stay, median (range)	5 days (1–17)	6 days (2–15)	8 days (4–21)

Only unilateral adrenalectomies were considered. Significant differences regarding the hospital stay were observed between patients with Conn's syndrome and pheochromocytoma. Further, significant gender differences were observed between patients with Cushing's syndrome and the two other groups

(21.0 to 48.1). The median operating time was 140.5 min (range55 to 650 min) including a median of 23 min (14 to 40 min) to turn the patient from one side to the other. There were two major and lethal complications. A 23-year-old obese female patient died 15 h after the initial operation from disseminated intravascular coagulopathy after injury of the splenic vein, massive bleeding, mass transfusion, and repeated laparotomies. A 42-year-old male patient sustained a severe pulmonary embolism on the second postoperative day and subsequently developed a Candida pneumonia. He died on the 20th postoperative day.

Incidentalomas–metastases–other adrenal pathologies

The series includes ten incidentalomas. The median tumor size was 7 cm (3–11 cm). Indication for surgery was progressive enlargement of the adrenal gland above a size of 5 cm in eight patients, a concomitant adrenal cyst in one patient, and the request of one patient to resect a 3-cm large tumor. The largest incidentaloma with a size of 11 cm was histologically a myelolipoma. Other adrenal pathologies included one hemangioma, two lymphangiomatous cysts, and one lymphoma. There were no complications but one conversion to open surgery upon suspected malignancy.

We resected eight metastases. Three originated from bronchial carcinomas: two from renal cell carcinomas, and one from a malignant melanoma, a Merkel cell carcinoma, and a carcinoma of unknown primary (CUP), respectively. There were no complications but one conversion to open surgery due to severe bleeding.

In summary, 12 malignant tumors were approached laparoscopically: eight metastases, three malignant pheochromocytomas, and one incidentaloma diagnosed as an adrenal cell carcinoma in final histology. One malignant pheochromocytoma was operated laparoscopically; in the other two cases and in the case of the incidentaloma, we converted to open surgery upon suspected malignancy. Preoperatively, all patients were discussed in the endocrine tumor board with the unanimous opinion that there were no obvious signs for malignancy.

Complications–conversions

Postoperative complications were categorized according to the Clavien–Dindo classification [19]. Table 3 provides a comprehensive overview. Patients with Conn's syndrome developed five postoperative complications, two of which required surgical revision. During one right adrenalectomy, it became necessary to suture the diaphragm after opening the pleural cavity. Complications following unilateral adrenalectomy for Cushing's syndrome were one trocar hernia a few days after the operation, one bleeding from a port site, one hematoma of the abdominal wall, and one wound infection. Two conversions became necessary due to severe intraoperative bleeding. Regarding bilateral adrenalectomy for Cushing's disease, there were two lethal complications. These cases have already been discussed. Severe bleeding from the vena cava in a patient with a metastasis led to conversion.

It became necessary to convert to open surgery in nine cases (4.2 %). The reasons for conversion are listed in Table 4. Bleeding was the most frequent cause. Difficulties to dissect in the right plane together with the intraoperative impression of malignancy accounted for three conversions. Two patients presented with severe intraabdominal adhesions due to previous laparotomies.

Table 3 Intraoperative and postoperative complications

	Complications	Clavien–Dindo classification
Conn's syndrome	Opening of the pleural cavity	
	Retroperitoneal hematoma	Grade IIIb
	Bleeding from a port site	Grade IIIa
	Pneumonia	Grade II
	Extensive hypertension	Grade II
	Hematoma abdominal wall	Grade I
Cushing's syndrome	Severe intraoperative bleeding	
	Severe intraoperative bleeding	
	Trocar hernia	Grade IIIb
	Bleeding from a port site	Grade IIIa
	Hematoma abdominal wall	Grade I
	Wound infection	Grade I
Cushing's disease (bilateral adrenalectomy)	Pulmonary embolism, pneumonia	Grade V
	Disseminated coagulopathy	Grade V
Metastases	Severe intraoperative bleeding	

Postoperative complications are categorized according to the Clavien–Dindo classification

Learning curve–surgical training

The first laparoscopic adrenalectomy was carried out in 1998, and when starting this series, two surgeons were familiar with the operation. Between 2000 and 2010, four senior residents were trained in the particular technique according to a defined plan. Due to the proximity of the vena cava, we regarded right adrenalectomies to be more dangerous, and therefore, left adrenalectomies were trained first maintaining the following principles: mobilizing the splenic flexure of the colon, dividing the splenic ligaments up to the gastric fundus, dissecting the plane between pancreas and kidney, finding and dividing the adrenal vein, and finally mobilizing the adrenal gland. After five or six successful left adrenalectomies, right adrenalectomies were trained, again following strict principles: sufficient mobilization of the right lobe of the liver, dissecting the plane between vena cava and adrenal gland, dividing the major blood vessels at the upper pole, identifying the renal vein, and finally completely mobilizing the adrenal gland. For at least 30 operations, the residents were supervised by an experienced surgeon. Figure 1 summarizes the number of laparoscopic adrenalectomies including conversions for each year together with the operating time and the number of complications and conversions.

Discussion

This study is an audit of our experience with laparoscopic adrenalectomy over a period of 10 years. Like in other large series, it could have been shown clearly that the new technique is safe and meanwhile rightly represents the standard operation to treat benign adrenal tumors [1–3]. Today, the lateral transabdominal and the posterior retroperitoneoscopic approaches are the most popular operations with hardly any difference regarding the overall outcome [4–7]. Fifteen years ago, we began using the lateral transabdominal approach and never saw a reason to change the technique. Regarding the overall small number of adrenal operations, it seems to make sense to stick by one procedure. However, we agree that the retroperitoneoscopic approach may be easier for bilateral adrenalectomies.

Comparing the three main indications for laparoscopic adrenalectomy, i.e., Conn's syndrome, Cushing's syndrome, and pheochromocytoma, we did not observe major differences regarding the outcome. Conversion rates, morbidity, and

Table 4 Reasons for conversion to open adrenalectomy

	Diagnosis	Reason	Side	Commentary
1	Cushing's syndrome	Adhesions	Left	Previous left pancreatic resection
2	ACTH-dependent Cushing's disease	Bleeding	Left	Injury of the splenic vein
3	Cushing's syndrome	Adhesions	Right	Previous multiple laparotomies
4	Cushing's syndrome	Bleeding	Right	Injury to the vena cava
5	Pheochromocytoma	Suspected malignancy	Right	Malignant pheochromocytoma in final histology
6	Incidentaloma	Suspected malignancy	Right	Seven-centimeter cystic tumor, intraoperatively suspicion of malignancy, conversion for lymphadenectomy
7	Cushing's syndrome	Bleeding	Right	Obesity, bleeding from a hepatic vessel
8	Pheochromocytoma	Suspected malignancy	Right	Intraoperatively suspicion of malignancy, laparoscopic adrenalectomy not possible, malignant pheochromocytoma in final histology
9	Metastasis	Bleeding	Right	Bleeding from the vena cava, blood loss 2600 ml

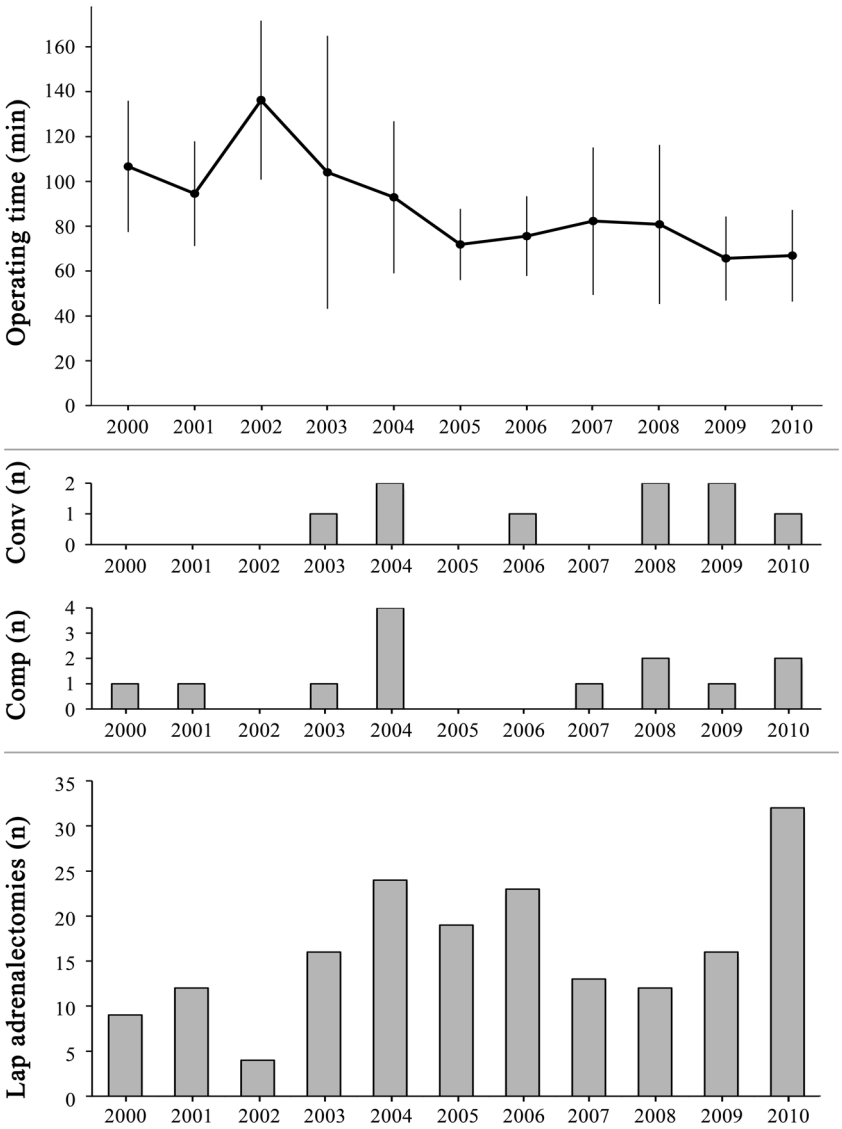

Fig. 1 Illustration of operating time, number of complications, and conversions for unilateral laparoscopic adrenalectomies

mortality were low and comparable to other studies [20, 21]. With few exceptions, the blood loss was minimal and the median operating time of 75 min was significantly shorter than the average time of 105 min we needed for open posterior adrenalectomies in the pre-laparoscopic era [22].

However, we encountered several pitfalls. Two of 18 patients who underwent bilateral laparoscopic adrenalectomy for persistent ACTH-dependent Cushing's syndrome died within the first 30 postoperative days. In a 27-year-old obese woman, the accidental injury of the splenic vein, although treated immediately and with great intensity, induced a fatal disseminated intravascular coagulopathy. Another patient with severe COPD sustained a massive pulmonary embolism and later died of pulmonary complications. This group of patients often suffers from severe comorbidities caused by the chronic effects of hypercortisolism. Obesity, large amounts of retroperitoneal fat, difficult localization of the adrenal gland, tissue that easily tends to bleed, and the prolonged operating time due to the bilateral approach make these operations especially challenging. Postoperatively, there is an increased risk for complications such as impaired wound healing, infection, bleeding, or thrombosis [23–25]. As a consequence, we decided to monitor these patients on an intensive care unit at least until the first postoperative day. Further, these patients are admitted to the Medical Department a few days prior to the operation with the intention to optimize their condition.

Regarding adrenal cortical carcinomas and malignant pheochromocytomas, we still prefer a conservative approach. A margin-free complete resection of the tumor and a meticulous lymphadenectomy provide the only means to achieve long-term cure, and in our opinion, this is best achieved by doing a laparotomy. The available literature is limited and inconclusive with advocates for the open as well as the laparoscopic approach [14–18]. In our experience, tumor size itself is not the major problem but dissecting in the right plane in the presence of adhesions and potential tumor invasion. In

the present series, we converted three times for these reasons, and in all cases, the final histology confirmed a malignant pheochromocytoma.

Residency training has been a major focus. By implementing a strict training program, dividing the operations into small well-defined steps, and supervising the first 30 adrenalectomies, we were able to adequately train four residents. In our experience, the identification of the adrenal vein on the left side, a sufficient mobilization of the right lobe of the liver, and the dissection of the upper pole of the right adrenal gland have been the most difficult parts to learn. Right adrelanectomy seemed to be the more difficult operation with a higher risk of causing major bleeding or injuring the adrenal capsule. Operations for Conn's syndrome were the most straightforward ones. Pheochromozytomas can be particularly challenging as it may be difficult to dissect close to the renal vein on the left side and to mobilize and divide a large adrenal vein. The number of approximately 30 adrenalectomies follows the recommendations of other authors who estimated their learning curve [5, 9, 26, 27]. This number reflects our experience with 10–15 operations on each side being adequate for a comprehensive training. The society of Gastrointestinal and Endoscopic Surgeons (SAGES) addressed the issue in their 2013 guidelines, citing data that suggest a learning curve of 20–40 cases [28].

A previous study from Turrentine et al. showed that lower-volume Veterans Association hospitals had higher morbidity and mortality rates after adrenalectomy than university medical centers [29]. A recent Italian multi-institutional survey regarding the treatment of adrenocortical carcinoma revealed that the expertise of dedicated centers had a positive effect on the outcome, resulting in a lower recurrence rate and a longer recurrence-free interval. The authors related the improved patient outcome not only to a better surgical expertise regarding adrenal surgery but also to a more adequate multidisciplinary approach [30]. The present SAGES guidelines address this topic and recommend that adrenalectomies should be carried out by surgeons experienced in adrenal surgery and that until proficiency in laparoscopic adrenalectomy is attained, and referral to a center with expertise in minimally invasive adrenal surgery should be considered [28].

Adrenalectomies are uncommon operations in most hospitals, and irrespective of the operation itself, all patients need a comprehensive endocrinological assessment. A close cooperation between endocrinologists, surgeons, radiologists, and nuclear-medical specialists is of utmost importance in order to ensure a successful treatment and to avoid unnecessary operations. For these reasons, it would seem advisable to treat adrenal pathologies in specialized centers [28–30].

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Conflicts of interest None.

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