Delineating the role of laparoscopy in the treatment of large suprarenal masses

Original Article

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ABSTRACT

Background: Laparoscopic adrenalectomy (LA) for large adrenal tumors is controversial due to the risk of malignancy and difficult dissection. This study aims to evaluate the safety, efficacy, and feasibility of transperitoneal LA in patients with large adrenal tumors measuring 6 cm or more in diameter.

Patients and Methods: Forty patients with adrenal tumors were divided into two groups according to the size (group I≥6 cm and group II < 6 cm in diameter). In both groups demographic variables, tumor side and size, pathological diagnosis, operative time, conversion to open approach, estimated blood loss, intra and postoperative complications were compared.

Results: No significant difference was found between the two groups regarding demographic data including age, sex and BMI. Estimated blood loss in group i ranged from 100.0 to 400.0 ml with mean value 180.0±95.15 and in group II ranged from 100.0 to 300.0 ml with mean value 147.50±71.59. conversion to open approach was recorded in one (5%) patient in group I in a right sided 13 cm diameter tumor and no conversion was recorded in group II the operative time was significantly longer in group I with a mean duration of 2.04±0.5 h while in group II was 1.67±0.31 h (*P=0.020*). there was no significant difference between the two groups in the intra and postoperative complications and length of hospital stay.

Conclusion: LA for adrenal tumors greater than or equal to 6 cm in diameter is feasible and can be safely performed. More studies including a larger number of patients is needed to confirm our data.

Key Words: Laparoscopic adrenalectomy, large tumors, transperitoneal.

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INTRODUCTION

It was in 1992 when Gagner initially detailed the use of the flank route in the lateral decubitus position for trans-abdominal laparoscopic adrenalectomy (LA). The procedure was then further refined and swiftly established as the gold standard for treating the majority of surgical adrenal diseases[1].

The most commonly utilized procedure is laparoscopic trans abdominal lateral adrenalectomy, which affords an excellent full view of the adrenal gland and surrounding structures while also providing appropriate operating space. Another advantage of the trans abdominal method is the ability to investigate the abdominal cavity, allowing treatment of potentially linked abdominal pathologies during the same procedure. Furthermore, this method enables a rapid switch to hand-assisted or open surgery in the event of difficult dissection or intraoperative uncontrolled hemorrhage[2].

The best available care for benign adrenal tumors that are small to medium-sized (≤6 cm), whether they are functioning or not, is endoscopic adrenalectomy[3]. However, increasing expertise with the endoscopic adrenalectomy has resulted in the extension of the indications for this procedure, proposing it also for large and potentially malignant adrenal tumors[4].

Although tumor size is commonly used to predict the malignancy of an adrenal lesion, it is still relatively nonspecific and insensitive. Indeed, the use of tumor size as a limiting factor in the choice of the surgical method for adrenalectomy appears inconsequential to some surgeons[5].

Theoretically, in the final pathological report, around 75% of adrenal tumors larger than 6 cm will be benign. Therefore, patients with a likely benign condition will not be able to benefit from the minimally invasive approach if a tumor size greater than 6 cm is considered a contraindication to LA[6].

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Furthermore, early experience with LA revealed that, in the absence of suspicious radiological signs, the endoscopic removal of large adrenal lesions (up to 10 cm in maximum diameter) was safe and achievable in competent hands[7].

However, open adrenalectomy (OA) is still the preferred treatment for invasive adrenocortical carcinoma (ACC)[8].

The widespread use of minimally invasive adrenalectomy increased the number of referrals to surgery for adrenal incidentaloma, increasing the probability of an unexpected pathological diagnosis of ACC after endoscopic adrenalectomy. In fact, the reported frequency of ACC in patients operated for adrenal incidentaloma approaches 10% in some series[9].

However, in the absence of radiological worrisome features (invasion of surrounding structures, lymph node or distant metastases, intravenous thrombus), it may be difficult to detect malignancy pre- and even intraoperatively[10].

PATIENTS AND METHODS:

This is a case-control study conducted as a collaboration between Endocrine Surgery Unit in University college of London hospitals, UK and Head and Neck and Endocrine Surgery unit, Faculty of Medicine, Alexandria University, Egypt. The study was done in the period between February 2020 and April 2023 and included twenty patients having large adrenal tumors measuring 6 cm or more in diameter treated with lateral transperitoneal LA (group I) and another twenty patients as a control group having tumors measuring less than 6 cm in diameter (group II) with matching demographic data and clinico-radiologic criteria and were treated with the same procedure by the same group of surgeons.

Indications for LA were:

(a) Functioning adrenal lesions (pheochromocytoma, Conn's syndrome, and Cushing's syndrome) regardless of the size.

(b) Nonfunctioning adrenal lesions greater than or equal to 4 cm in diameter.

(c) Nonfunctioning adrenal lesions less than 4 cm with increasing diameter during follow-up.

Patients with preoperative evidence of malignant tumor with local tumor infiltration, lymphadenopathy or distant metastasis were excluded from the study as they are indicated for OA.

All patients in the study were subjected to detailed history taking including the presenting complain and any history of previous abdominal surgeries, detailed physical examination including measuring the blood pressure, weight and height measurement and calculating the BMI, laboratory investigations [plasma and urinary metanephrines, 24 h urinary cortisol, overnight low dose dexamethasone suppression test, adrenocorticotropic hormone (ACTH), aldosterone: renin ratio, serum sodium (Na), potassium (K), calcium (Ca), phosphorus (P) and parathormone (PTH)]. Computed tomography (CT) scan of the abdomen was done for all patients for accurate measurement of the size of the adrenal mass and its relations with the surrounding structures and blood vessels.

All patients were evaluated by an endocrinologist and patients with pheochromocytoma received appropriate alpha-adrenergic blockade and, in selected cases, beta-adrenergic blocking agents.

Surgical techniques

Laparoscopic trans peritoneal lateral adrenalectomy was done in all patients under general anesthesia with muscle relaxation and controlled ventilation. The patient should be placed initially in a supine position for induction of anesthesia. An orogastric tube for gastric decompression (mainly helpful in left-sided adrenalectomy). The patient is then positioned in the lateral position with adjusting the anterior border of the patient's body near the edge of the bed. The surgical table is flexed with the center of the break in the table is adjusted approximately at the midpoint between the costal margin and the iliac crest to allow the best exposure. The right/left arm is elevated and secured on an elevated arm board. The patient is secured to the table with a belt, an axillary roll is placed, and all pressure points are protected.

The region that should be exposed is the one that runs from the umbilicus to the spine and from the nipple to the superior anterior iliac crest. The surgeons face the monitor at the patient's head while standing on the patient's abdominal side. Using an optical access trocar, first peritoneal access is obtained 2 cm inferior to the right/left costal edge in the anterior axillary line. a pressure of 12–14 mmhg is generally used for carbon dioxide (CO_2) insufflation.

Right adrenalectomy

The four port sites are marked along the right costal margin from the xiphoid to the midaxillary line (Fig. 1). The right triangular ligament is cut with a harmonic scalpel or LigaSure after a fan retractor retracts the liver's right lobe in a medial orientation. The retroperitoneum next to the adrenal gland is revealed by the superior and anterior retraction of the right lobe of the liver made possible by this mobilization. (Fig. 2).

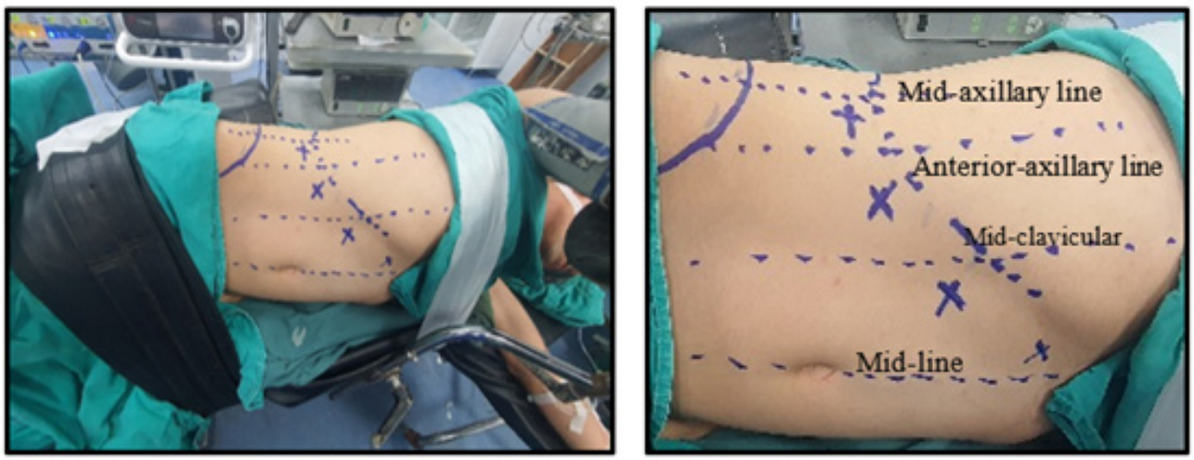

Fig. 1: Position and trocar sites for right laparoscopic adrenalectomy.

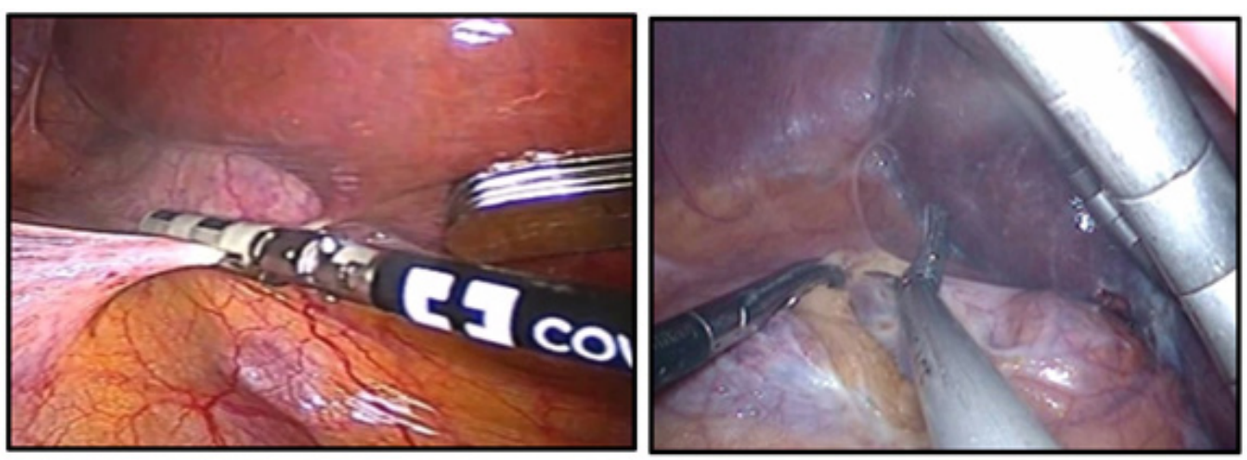

Fig. 2: Division of the triangular ligament and mobilization of the liver.

The superolateral margin of the periadrenal fat is where we start the dissection. This exposes the diaphragm posteriorly, and the dissection is done along the superior boundary of the periadrenal fat in a medial direction. The inferior vena cava (IVC) should be approached carefully using blunt graspers while dissecting the area close to the super medial border of the periadrenal fat (Fig. 3). The adrenal vein is normally located in the upper third of this medial border, approaching the IVC at a right angle. After clip ligation of the adrenal vein, this medial plane of dissection widens dramatically, and the adrenal gland is separated from the upper pole of the kidney (Fig. 4).

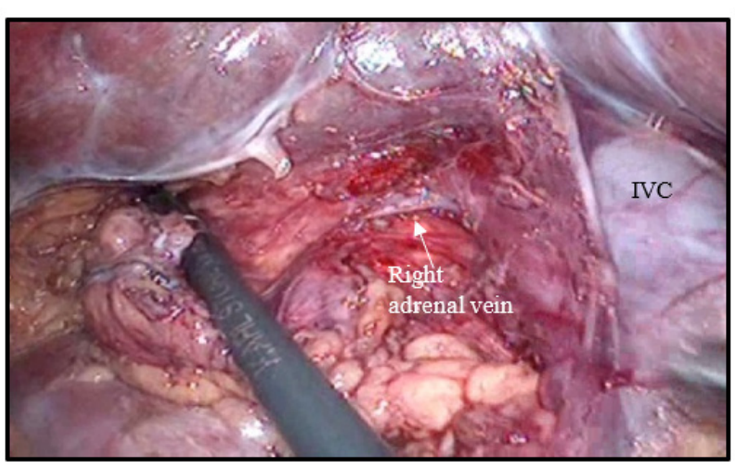

Fig. 3: Dissection of the superior lateral border of the adrenal mass and identification of the adrenal vein and inferior vena cava.

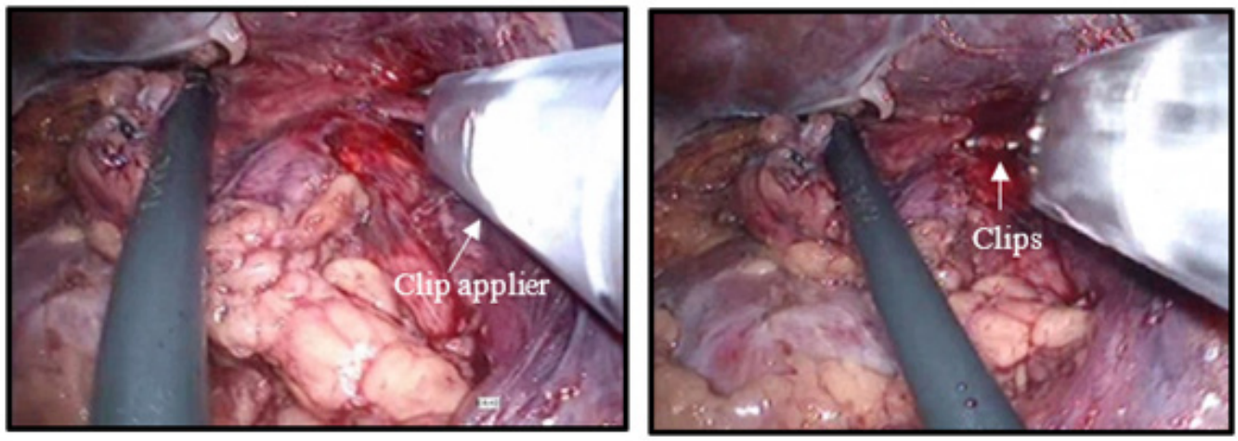

Fig. 4: Clipping of the right adrenal vein.

Left adrenalectomy

Sometimes the fourth port is not needed. The splenic flexure of the colon is dissected and taken down (Fig. 5). The splenoparietal ligament is subsequently dissected in order to mobilize the spleen. This ligament is easily exposed in the lateral decubitus position. Up till the diaphragm, the dissection is carried out to the point where the stomach fundus and the left crus of the diaphragm are visible (Fig. 6).

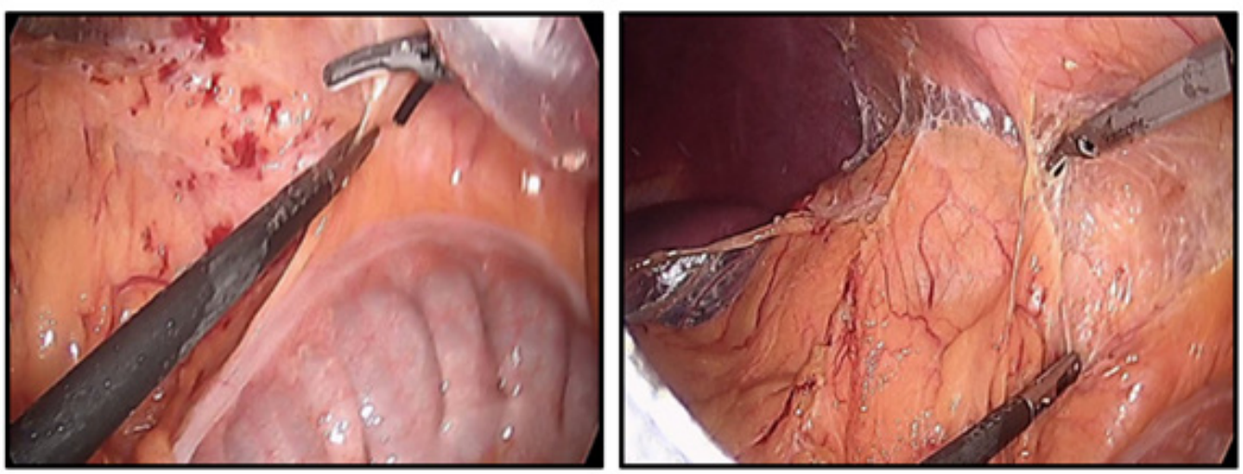

Fig. 5: Mobilization of the splenic flexure of the colon.

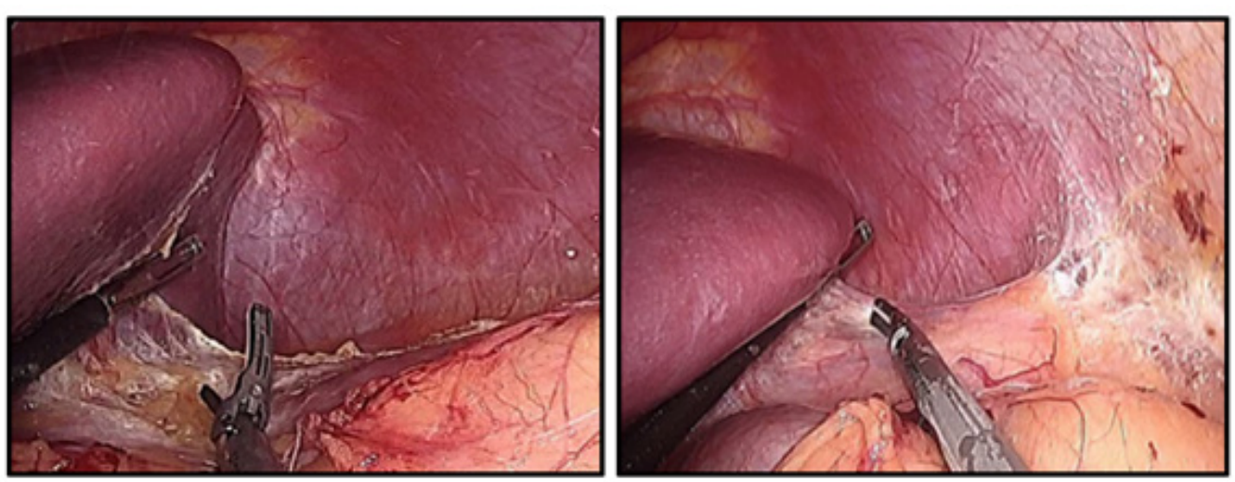

Fig. 6: Mobilization of the spleen by dissecting the splenoparietal ligament.

Between the spleen and the superior border of the adrenal gland, the dissection continues. This plane of dissection is often where the splenic vessels are located. The inferior phrenic vein and the tail of the pancreas are usually visible once the superior- medial corner is reached (Fig. 7). The pancreatico-splenic bloc is allowed to fall infero-medially by the effect of gravity after division of the spleno-parietal ligament exposing the upper pole of the kidney and adrenal region.

The left adrenal vein is often located in infer medial portion of the dissection. After adrenal vein is clipped (Fig. 8), the dissection continues along the inferior border between the adrenal gland and the kidney.

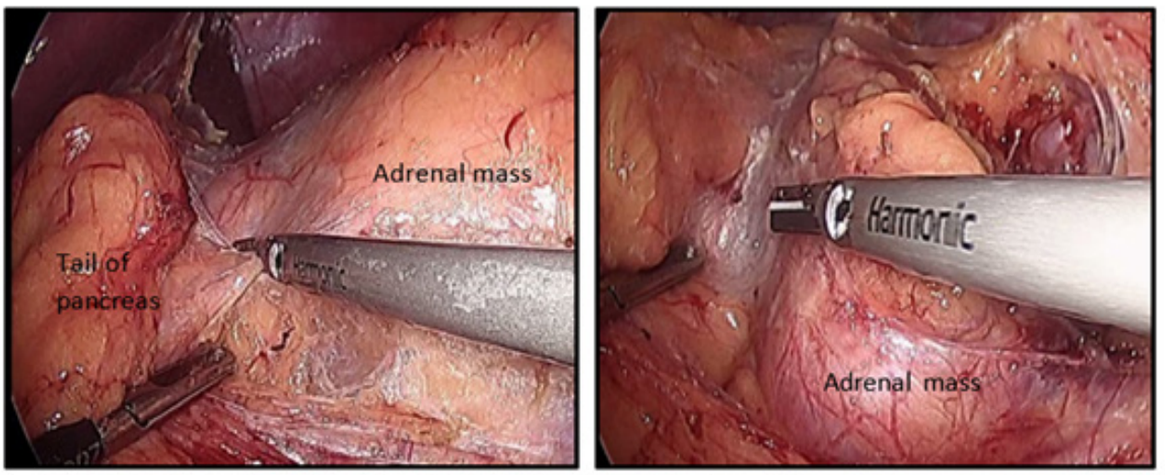

Fig. 7: Dissecting the adrenal mass from the tail of the pancreas.

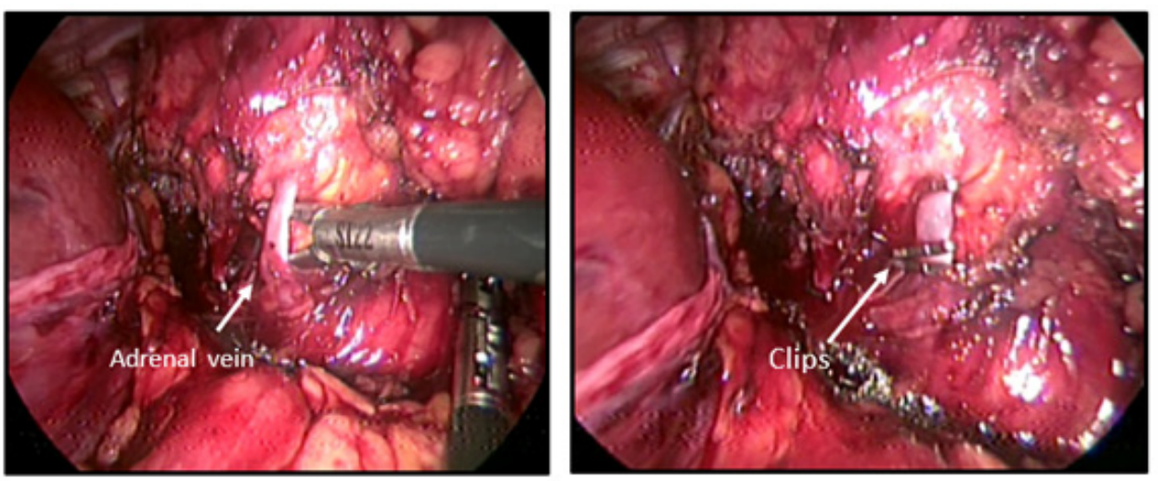

Fig. 8: Clipping of the left adrenal vein.

In both sides, once all attachments are divided, the gland is placed into an endoscopic bag for removal through a 10–12 mm trocar. Trocar sites can be slightly enlarged if needed.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp).Qualitative data were described using number and percent. The Kolmogorov–Smirnov and Shapiro–Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were: χ^2 test for categorical variables, to compare between different groups, Fisher's Exact or Monte Carlo correction for correction for χ^2 when more than 20% of the cells have an expected count less than 5, Student t-test for normally distributed quantitative variables, to compare between two studied groups, Mann–Whitney test for abnormally distributed quantitative variables, to compare between two studied groups.

RESULTS:

The results showed that there was no statistically significant difference between the two studied groups according to demographic and clinico-radiological (*P>0.05*) as shown in (Table 1).

Table 1: Demographic and clinico-radiological data of the patients

Demographic and clinico-radiological data	Group I (*n*=20) *N* (%)	Group II (*n*=20) *N* (%)	Test of significance	*P*
Sex				
Male	10 (50.0)	8 (40.0)	χ^2=0.404	0.525
Female	10 (50.0)	12 (60.0)		
Age (years)				
Min–max	19.0–75.0	40.0–75.0	t=1.541	0.082
Mean±SD	54.74±14.46	60.33±9.17		
BMI (kg/m^2)				
Min–max	23.40–33.0	23.90–36.90	t=0.201	0.842
Mean±SD	28.86±3.50	29.10±4.04		
Side				
Right	10 (50.0)	11 (55.0)	χ^2=0.100	0.752
Left	10 (50.0)	9 (45.0)		
Size (cm)				
Min–max	6.0–13.0	1.0–4.30		
Mea±SD	7.17±1.58	2.85±1.06	U =0.00*	<0.001*
Median (IQR)	6.50 (6.4–7.35)	3.0 (2.0–3.70)		
Surgical history				
Free	16 (80.0)	17 (85.0	χ^2=0.173	^{FE}P=1.000
Positive	**4 (20.0)**	**3 (15.0)**		
Lap. Sleeve gastrectomy	1 (5.0)	0		
Laparoscopic appendectomy	0	1 (5.0)		
Laparoscopic washout for perforated diverticular disease	1 (5.0)	0		
Laparotomy due to uterine perforation from hysteroscope	1 (5.0)	0		
Open appendectomy	0	1 (5.0)		
Open cholecystectomy	0	1 (5.0)		
Splenectomy for thalassemia	1 (5.0)	0		

χ^2, Chi square test; t, Student t-test.
P: P value for comparing between group I and II.
*: Statistically significant at *P* less than or equal to 0.05.
IQR, Inter quartile range; SD, Standard deviation.

Regarding previous history of abdominal surgeries, it was recorded that four (20%) patients in group I had previous abdominal surgeries including laparoscopic sleeve gastrectomy, laparoscopic washout for perforated diverticular disease, laparotomy due to uterine perforation from hysteroscopy and splenectomy for thalassemia. In group II, there was three (15%) patients with a history of previous abdominal surgeries including laparoscopic appendectomy, open appendectomy, and open cholecystectomy. there was no statistically significant difference between the two studied groups according to surgical history (*P>0.05*).

Incidental discovery of the adrenal tumor was the main presentation in both groups with nine (45%) patients in group I and 13 (65%) patients in group II followed by hypertension in five (25%) patients and seven (35%) patients in group I and II, respectively.

Concerning the operation (Table 2), no drain was inserted in all patients in the two groups except for two (10%) patients in group I and it was removed after 24 h. conversion to open approach was done in only one (5%) case in group I, it was in a patient with a 13 cm diameter right sided tumor, the mass was displacing the liver and the kidney with complete overriding of the IVC, the mass was highly vascular and covered with large blood vessels, laparoscopically the mass was dissected from the liver with no problem, identified from the kidney and the IVC was identified, when there was breaching on the capsule of the mass the decision was made to convert to open approach through the right subcostal incision for fear of incomplete

resection of the tumor, after conversion it was found that the mass is encasing the IVC but without invasion, the upper pole was very high and it would probably be converted to open even if the capsule was not opened, the final tumor pathology was metastatic hepatocellular carcinoma.

Estimated blood loss (EBL) in group I ranged from 100.0–400.0 ml with a mean value 180.0±95.15 and in group II ranged from 100.0–300.0 ml with a mean value 147.50±71.59.

Operative time in group I ranged from 1–3 h with a mean value 2.04±0.50 and in group II ranged from 1.08–2.25 h with a mean value 1.67±0.31. There was no statistically significant difference between the two studied groups according to drain insertion, conversion to open approach, and blood loss (*P> 0.05*) while there was a statistically significant difference regarding time (*P< 0.05*). Where the operative time was longer in group I than group II.

Table 2: Comparison between the two studied groups according to intraoperative data

Operation	Group I (*n*=20) *N* (%)	Group II (*n*=20) *N* (%)	Test of significance	*P*
Side				
Right	10 (50.0)	11 (55.0)	c^2=0.100	0.752
Left	10 (50.0)	9 (45.0)		
Drain				
No	18 (90.0)	20 (100.0)	c^2=2.105	^{FE}P=0.487
Yes	2 (10.0)	0		
Conversion				
No	19 (95.0)	20 (100.0)	c^2=1.026	^{FE}P=1.000
Yes	1 (5.0)	0		
Blood loss (ml)				
Min–max	100.0–400.0	100.0–300.0	U=168.50	0.398
Mean±SD	180.0±95.15	147.50±71.59		
Median (IQR)	150.0 (100.0 250.0–)	100.0 (100.0 150.0–)		
Time (h)				
Min–max	1.0–3.0	1.08–2.25	U=114.0*	0.020*
Mean±SD	2.04±0.50	1.67±0.31		
Median (IQR)	1.92 (1.75–2.31)	1.75 (1.42–1.92)		

χ^2, Chi square test; FE, Fisher Exact; U, Mann–Whitney test.
P, P value for comparing between group I and II.
*: Statistically significant at *P* less than or equal to 0.05.
IQR, inter quartile range; SD: standard deviation.

Regarding intra and postoperative complications, wound infection was recorded in only one (5%) patient in group I, the infection was at the trocar site where the specimen was removed, and it was treated by frequent dressings. Injury to intraabdominal organs occurred in one (5%) patient in group II where two small injuries in the splenic capsule happened likely related to trocar site with minimal blood oozing, it was successfully stopped by compression with Surgicel for a few minutes. No significant intra or postoperative bleeding was recorded in both groups. There was no statistically significant difference between the two studied groups according to intra and postoperative complications (*P> 0.05*).

The postoperative tumor histopathology results showed that adrenal cortical adenoma was the most common tumor in both groups, it was diagnosed in seven (35%) patients in group I and in 13 (65%) patients in group II. Pheochromocytoma was the second common tumor, it was diagnosed in six (30%) patients in group I and in four (20%) patients in group II as shown in (Table 3).

According to the pheochromocytoma of the adrenal gland scaled score (PASS score) which is a score used to separate tumors with a potential for biologically aggressive behavior (PASS > or =4) from tumors that behave in a benign fashion (PASS <4) according to specific histologic features, two patients in group I had pass score 8 and 9 while one patients in group II had pass score 7 suggesting that these patients had malignant pheochromocytoma.

It is worth mentioning that most (80%) of the tumors in group I (16 patients) were found to be benign after excision. The malignant tumors in this group were pheochromocytoma (two cases), metastatic hepatocellular carcinoma, and peripheral neuroblastic tumor.

Table 3: Comparison between the two studied groups according to final tumor pathology

Pathology	Group I (*n*=20) *N* (%)	Group II (*n*=20) *N* (%)
Adrenal cortical adenoma	7 (35.0)	13 (65.0)
Pheochromocytoma	6 (30.0)	4 (20.0)
Adrenocortical tumor	2 (10.0)	2 (10.0)
Cavernous hemangioma	0	1 (5.0)
Cortico-medullary adenoma	1 (5.0)	0
Metastatic hepatocellular carcinoma	1 (5.0)	0
Myelolipoma	1 (5.0)	0
Peripheral neuroblastic tumor	1 (5.0)	0
Simple epithelial cyst	1 (5.0)	0

The operative time was correlated with other parameters including side, size of the tumor, previous abdominal surgical history, and BMI. The results showed that in group I, the operative time for right-sided tumors ranged from 1 to 3 h while in left sided tumors it ranged from 1 h and 40 min to 2 h and 55 min. The operative time in patients with no previous history of abdominal surgeries ranged from 1 to 3 h while in patients with positive history of abdominal surgeries, it ranged from 1 h and 30 min to 2 h and 15 min. In group II the operative time for right-sided tumors ranged from 1 h and 5 min to 2 h and 15 min while in left side tumors it ranged from 1 h and 20 min to 2 h. The operative time in patients with free surgical history ranged from 1 h and 5 min to 2 h while in patients with previous history of abdominal surgery it ranged from 1 h and 50 min to 2 h and 15 min. The results showed that among these parameters, the size of the tumor was the only parameter affecting the length of the operation significantly (Tables 4 and 5).

Table 4: Relation between time of surgery (hours) and different parameters in each group

	Time of surgery (hours)					
	N	Min–max	Mean±SD	Median	U	*P*
Group I (*n*=20)						
Side						
Right	**10**	1.0–3.0	1.93±0.56	1.83	41.0	0.529
Left	**10**	1.67–2.92	2.14±0.44	2.08		
Surgical history						
Free	**16**	1.0–3.0	2.09±0.54	2.0	21.0	0.335
Positive	**4**	1.50–2.25	1.83±0.31	1.79		
Group II (*n*=20)						
Side						
Right	**11**	1.08–2.25	1.73±0.35	1.83	36.50	0.331
Left	**9**	1.33–2.0	1.60±0.26	1.50		
Surgical history						
Free	**17**	1.08–2.0	1.61±0.29	1.50	8.50	0.072
Positive	**3**	1.83–2.25	2.0±0.22	1.92		

U: Mann–Whitney test.
P: P value for comparing between different categories SD: Standard deviation.

Table 5: Correlation between time of surgery (hours) and different parameters in each group

	Time of surgery (h)	
	r_s	*P*
Group I (*n*=20)		
BMI (kg/m^2)	0.286	0.221
Size	0.523*	0.018*

Group II (n=20)		
BMI (kg/m^2)	0.113	0.634
Size	0.221	0.349

rs: Spearman coefficient.
*: Statistically significant at P less than or equal to 0.05.

DISCUSSION

Since it was initially described in 1992, LA has gained a lot of popularity[11]. Less perioperative morbidity, a shorter hospital stay, a smaller incision, less intraoperative blood loss, and a quicker return of the patient's strength are all benefits of LA. Furthermore, the laparoscope's magnification offers a clear view of the anatomic region; in fact, a LA allows access to a location that would otherwise need a large amount of transperitoneal exposure, minimizing damage associated with access. For this reason LA has quickly replaced the 'open' approach[12].

Due to the technical issues, most surgeons are concerned about incomplete resection and local recurrence caused by probable capsular rupture in bigger adrenal tumors. However, other authors reported successful treatment of large adrenal tumors laparoscopically, even those exceeding 10 cm[13].

An increasing risk of malignancy is linked to an increase in the size of nonfunctioning adrenal lesions. The incidence of ACC in adrenal incidentaloma is 1% for tumors of less than 4 cm, 6% for tumors of 4-6 cm, and 20% for tumors of greater than 6 cm. Although ACC is rare, it is a highly aggressive tumor. Therefore, the benefits of minimally invasive surgery must be weighed with the risk of incomplete resection and capsular perforation which can worsen the oncological outcomes[14]. In a study by Abdel-Aziz and colleagues on 37 patients with adrenocortical tumors greater than 8 cm, ACC was diagnosed in 84% of the patients. In cortical tumors greater than 8 cm, there was a six fold increase in malignancy when compared with benign tumors. In this study the three patients who were treated by LA had disease recurrence after 6 (3-14) months compared with 33 (5-65) months with open surgical approach[15].

However, an infrequent invasive malignancy will still be seen even using the 6 cm size cut-off for LA, as recommended by most studies. Therefore, in every LA, it is imperative to adhere to oncologic surgical principles. When there is no local invasion or vascular infiltration, researchers have had some success treating suspected adrenocortical cancers with LA. Notably, they argue that a bad outcome is likely to arise from insufficient surgery, regardless of whether the procedure is open or laparoscopic[16].

In one of the largest and most recent studies in the United States on the use of minimally invasive surgery (MIS) including a laparoscopic or robotic approach for resectable ACC, Among the 1183 total patients with tumors greater than 6 cm, 420 (35.5%) were large tumors (6-9.9 cm) and 763 (64.5%) were giant ACC tumors (>10 cm). Of the 420 patients with large ACCs, 191 (45.5%) underwent MIS resection while 229 (54.5%) underwent OA. Among patients with giant ACCs, 143 (18.7%) underwent MIS resection while 620 (81.3%) received an open operation. The results did not find any significant statistical difference in survival between recipients of MIS resection versus open resection in patients with large or giant ACC. The study concluded that tumor size is less important than tumor invasion with respect to survival[17].

However, this analysis has some limitations. Because of its retrospective nature, it is subject to significant selection bias by the surgeon. Patients who had MIS for ACC resection were more likely to have less disease burden than those who were selected for open technique. The study was unable to determine if the intent of the procedure was for malignant or benign disease at the start and given that guidelines recommend open surgery for known or suspected ACC, it is likely that surgeons using MIS did not suspect ACC before surgery. The observation that MIS surgery was frequently performed for tumors greater than 6 cm in size despite guideline recommendations, together with the finding that survival was equivalent independent of size or approach, suggests that appropriate selection by surgeons likely plays a significant role. Another drawback of this study is the lack of data about local or peritoneal recurrence in the study group and the lack of information about tumor capsule spillage during MIS approach[17].

A systematic review of literature by Machado and colleagues on LA for large ACC included 10 articles addressing LA versus OA and included 844 patients eligible for this review. Of these, 206 had undergone LA, and the remaining 638 had undergone OA. The mean size of tumors in patients who underwent LA (7.1 cm) compared with (11.2 cm) in patients who underwent OA. Among these 10 studies, five noted no statistically significant difference between the two groups in the oncological outcomes of recurrence and disease-free survival, whereas the remaining five reported inferior outcomes in the LA group[18].

Conflicting data regarding the relative risks and benefits of an MIS versus open approach for ACC is highlighted by the variation in guideline recommendations concerning the surgical approach. The National Comprehensive Cancer Network (NCCN) states there may be an increased risk of local recurrence and peritoneal spread with an MIS approach. They suggest open resection for suspected, resectable ACC and that an MIS approach may be considered based on 'tumor size and degree of concern regarding potential malignancy, and local surgical experience[19]. The American Association of Endocrine Surgeons/ American Association of Clinical Endocrinologists (AACE) guidelines recommend open resection for all cases of ACC, irrespective of tumor size[20].

Based on reports that had shown comparable results between laparoscopic and open approaches for resection of large adrenal tumors, the European Society of Endocrine Surgeons has revisited its guidelines with the suggestion that LA can be considered for stage I and II ACC with tumors less than 10 cm in size[21].

With the advancements in technology, it is becoming more frequent to diagnose larger adrenal incidentalomas using imaging techniques. Large adrenal lesions are regarded uncommon, with incidence rates ranging from 8.6 to 38.6%[22].

Here in this study, we explore laparoscopy for large adrenal tumors using transperitoneal laparoscopic technique.

The results of our study confirmed matching groups' demographics including age, sex, and BMI. The two groups were matched without significant differences. Also, the clinical and laboratory findings in the two groups were not significantly different, these results were important to eliminate the effect of basic demographic and clinical data on the net results of the study and the only variable factor was the size of tumor.

According to the postoperative histopathology results of the excised tumors in our study, the most common pathology in both groups was adrenal cortical adenoma (35%) and (65%) in groups I and II, respectively, followed by pheochromocytoma which was higher in large tumor group I (30%) than small tumor group II (20%). It was found that 80% of the tumors in group I were benign after excision. This means that if the size of the tumor is the only factor that determines whether to use the laparoscopic approach or not, most of the patients with adrenal tumors measuring 6 cm or more would have been deprived from the advantages of the laparoscopic technique.

The results of this study showed that the operative data including side of the tumor, conversion rate to open approach, EBL) showed insignificant difference between the two studied groups while there was a significant difference between the two groups regarding the operative time.

Öz and colleagues conducted a study comparing trans peritoneal LA in large (>6 cm) and small (<6 cm) adrenal tumors. The study included 33 patients in the large tumor (Lt) and 110 patients in the small tumor (St) group. The results showed that according to the conversion rate to open approach, it was about 6% (two patients) in the Lt group and 0.9% (one patient) in the St group. The reason for conversion was uncontrolled bleeding in one case and difficult dissection in the other two cases. There was no statistically significant difference between the two groups[23].

In the current study, the conversion rate was 5% (one patient) in group I and there was no conversion to open approach in group II. The conversion was in a 13 cm diameter right-sided tumor which was diagnosed postoperatively as metastatic hepatocellular carcinoma. The reason for conversion was difficult dissection and breaching on the capsule of the tumor so conversion was done to avoid treatment failure. There was no difference statistically between the two groups regarding conversion rates. Some studies reported that the conversion rate in large adrenal tumors ranged from 4.2 to 14.5% and in small tumors from 0.5 to 5.6%. This is consistent with our study as the conversion rate was 5% (one patient) in the large tumor group and no conversion in the small tumor group[24].

The operative EBL was higher in LA for large tumors but with no significant difference between both groups. Natkaniec *et al*. reported a significantly higher EBL and conversion rate in LA for large adrenal tumors more than 6 cm in a large comparative study conducted on 530 patients. The outcome of a study carried out by Bozkurt *et al*. comparing transperitoneal LA in large (n=16) and small (n=19) sized adrenal tumors showed that EBL was higher in the large tumors group, but the difference between the two groups did not reach a significant level[25].

Our study showed that the operative time was significantly longer in group I with a mean duration of 2.04±0.5 h while in group II was 1.67±0.31 h (*P=0.020*). When the operative time was correlated to other factors including the side, size of the tumor, previous abdominal surgical history, and BMI, the results showed that the only factor affecting the length of the operation significantly in group I was the size of the tumor.

In agreement with our study Balla and colleagues reported in a study comparing the outcomes of transperitoneal LA for lesions measuring greater than 6 cm versus less than 5.9 cm in diameter that the only significant difference noticed between the two groups of patients was the mean operative time which was significantly correlated with tumor size. In our study, operation time was longer in larger adrenal tumors (*P=0.0174*)[26]. In the study done by Natkaniec *et al*. using the lateral transperitoneal approach for LA, the mean operative time was longer in patients with large adrenal tumors greater than 6 cm than patients with lesions less than 6 cm in diameter (111.9±43.7 min vs. 86.6±35 min, respectively, *P <0.0001*)[27].

The increase in operative time can be attributed to greater attention being devoted to larger tumors, which have a wider surface to be dissected and richer vascularization, necessitating more care. Operative time seemed to be larger for right-side masses. This may be explained by the relatively difficult control of adrenal vein and need to mobilize the liver; also, large adrenal tumors often locate in the retrocaval space making dissection more tedious which prolongs the operative time.

Like our study, Gunseren *et al*.[28] and Kokorak *et al*.[29] reported that the right or left side of transperitoneal LA does not necessarily prolong the operation.

In this study, it was found that there was no significant difference between the two studied groups regarding the incidence of intra and post-operative complications. There was only one intraoperative complication reported which was a small splenic capsule laceration in a patient in group II mostly related to the trocar site, it was managed by compression with Surgicel for few minutes. We also reported only one case of postoperative complication in a patient in group I who developed a minor wound infection at the trocar site where the specimen was retrieved, it was managed with frequent dressings.

According to Chung *et al*., the complication rates were notable but did not differ significantly (33.3% vs. 18.5%). (*P=0.47*) in greater than or equal to 6 and less than 6 cm adrenal tumors, respectively. In addition, Natkaniec and colleagues reported no statistical difference in complication rates between greater than or equal to 6 and less than 6 cm adrenal lesion groups 15.7% versus 9.3% (*P=.069*). Also, Hobart *et al*. noticed higher but not significantly different postoperative complication rates for greater than 6 cm lesions[30].

The largest adrenal tumor that was removed by trans peritoneal LA in our study measured 9 cm in the largest diameter in a patient with left side pheochromocytoma. Abraham *et al*. reported successful removal of a 17 cm ganglioneuroma by LA and Bozkurt *et al*. treated a 15 cm myelolipoma by LA[31,32].

CONCLUSION

Our results showed that LA is effective, safe and technically feasible for excision of large adrenal tumors with no statistically significant difference from small tumors as regards conversion to open approach, intra and postoperative complications, EBL. However because the risk of malignancy increases with the size of the tumor, feasibility should not be the only consideration when deciding to use the laparoscopic approach, the main aim is to ensure complete tumor excision with clear surgical margins without tumor capsule rupture to reduce the risk of local recurrence if proven to be malignant thereafter. Multidisciplinary approach for large adrenal tumors in a specialized endocrine center is important to assess the risk of malignancy and to help in choosing the best approach and management plan for these tumors.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Gagner M, Lacroix A, Bolté E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 1992; 327:1033.

2. Bittner R, Bingener-Casey J, Dietz U, Fabian M, Ferzli GS, Fortelny RH, *et al*. Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society (IEHS)-part 1. Surg Endosc 2014; 28:2–29.

3. Lombardi CP, Raffaelli M, De Crea C, Sollazzi L, Perilli V, Cazzato MT, *et al*. Endoscopic adrenalectomy: Is there an optimal operative approach? Results of a single-center case-control study. Surgery 2008; 144:1008–14.

4. Lombardi CP, Raffaelli M, De Crea C, Bellantone R. Role of laparoscopy in the management of adrenal malignancies. J Surg Oncol 2006; 94:128–31.

5. Carnaille B. Adrenocortical carcinoma: which surgical approach? Langenbecks Arch Surg 2012; 397:195–9.

6. Soon PS, Yeh MW, Delbridge LW, Bambach CP, Sywak MS, Robinson BG, *et al*. Laparoscopic surgery is safe for large adrenal lesions. Eur J Surg Oncol 2008; 34:67–70.

7. Brunt LM, Moley JF. Adrenal incidentaloma. World J Surg 2001; 25:905–13.

8. Miller BS, Doherty GM. Surgical management of adrenocortical tumours. Nat Rev Endocrinol 2014; 10:282–92.

9. Miller BS, Ammori JB, Gauger PG, Broome JT, Hammer GD, Doherty GM. Laparoscopic resection is inappropriate in patients with known or suspected adrenocortical carcinoma. World J Surg 2010; 34:1380–5.

10. Else T, Williams AR, Sabolch A, Jolly S, Miller BS, Hammer GD. Adjuvant therapies and patient and tumor characteristics associated with survival of adult patients with adrenocortical carcinoma. J Clin Endocrinol Metab 2014; 99:455–61.

11. Assalia A, Gagner M. Laparoscopic adrenalectomy. BMJ 2004; 91:1259–74.

12. Parnaby CN, Chong PS, Chisholm L, Farrow J, Connell JM, O'Dwyer PJ. The role of laparoscopic adrenalectomy for adrenal tumours of 6 cm or greater. Surg Endosc 2008; 22:617–21.

13. Maestroni U, Ziglioli F, Dinale F, Ferretti S, Frattini A, Cortellini P. Is laparoscopy contraindicated in giant adrenal masses? Surg Laparosc Endosc Percutan Tech 2010; 20:288–90.

14. Li L, Yang G, Zhao L, Dou J, Gu W, Lv Z, *et al*. Baseline demographic and clinical characteristics of patients with adrenal incidentaloma from a single center in China: a survey. Int J Endocrinol 2017; 2017:3093290.

15. Abdel-Aziz TE, Rajeev P, Sadler G, Weaver A, Mihai R. Risk of adrenocortical carcinoma in adrenal tumours greater than 8 cm. World J Surg 2014; 39:1268–73.

16. Arora E, Bhandarwar A, Wagh A, Gandhi S, Patel C, Gupta S, *et al*. Role of indo-cyanine green (ICG) fluorescence in laparoscopic adrenalectomy: a retrospective review of 55 Cases. Surg Endosc 2018; 32:4649–57.

17. Delman AM, Turner KM, Griffith A, Schepers E, Ammann AM, Holm TM. Minimally invasive surgery for resectable adrenocortical carcinoma: A nationwide analysis. J Surg Res 2022; 279:200–7.

18. Machado NO, Al Qadhi H, Al Wahaibi K, Rizvi SG. Laparoscopic Adrenalectomy for Large Adrenocortical Carcinoma. JSLS 2015; 19:e2015.00036.

19. Network NCC. NCCN guidelines version 3.2021 adrenal gland tumors; 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed July 12, 2021

20. Zeiger MA, Thompson GB, Duh QY, *et al*. The American association of clinical Endocrinologists and American association of endocrine surgeons medical guidelines for the management of adrenal incidentalomas. Endocr Pract 2009; 15(Suppl 1):1e20.

21. Henry J-F, Peix J-L, Kraimps J-L. Positional statement of the European Society of Endocrine Surgeons (ESES) on malignant adrenal tumors. Langenbeck's. Arch Surg 2011; 397:145–6.

22. Zhang Z, Wang L, Chen J, Li X, Liu D, Cao T, *et al*. Clinical analysis of adrenal lesions larger than 5 cm in diameter (an analysis of 251 cases). World J Surg Oncol 2019; 17:220.

23. Öz B, Cücük Ö, Gök M, Akcan A, Sözüer E. Laparoscopic transperitoneal adrenalectomy for adrenal tumours of 6 cm or greater: A single-centre experience. J Minim Access Surg 2024; 20:47–54.

24. Balla A, Palmieri L, Meoli F, Corallino D, Ortenzi M, Ursi P, *et al*. Are Adrenal Lesions of 6 cm or More in Diameter a Contraindication to Laparoscopic Adrenalectomy? A Case-Control Study. World J Surg 2020; 44:810–8.

25. Prakobpon T, Santi-Ngamkun A, Usawachintachit M, Ratchanon S, Sowanthip D, Panumatrassamee K. Laparoscopic transperitoneal adrenalectomy in the large adrenal tumor from single center experience. BMC Surg 2021; 21:68.

26. Balla A, Palmieri L, Meoli F, Corallino D, Ortenzi M, Ursi P, *et al*. Are Adrenal Lesions of 6 cm or More in Diameter a Contraindication to Laparoscopic Adrenalectomy? A Case-Control Study. World J Surg 2020; 44:810–8.

27. Natkaniec M, Pędziwiatr M, Wierdak M, Major P, Migaczewski M, Matłok M, *et al*. Laparoscopic Transperitoneal Lateral Adrenalectomy for Large Adrenal Tumors. Urol Int 2016; 97:165–72.

28. Gunseren KO, Cicek MC, Vuruskan H, Kordan Y, Yavascaoglu I. Challenging risk factors for right and left laparoscopic adrenalectomy: A single

centre experience with 272 cases. Int Braz J Urol 2019; 45:747–53.

29. Kokorak L, Soltes M, Vladovic P, Marko L. Laparoscopic left and right adrenalectomy from an anterior approach - is there any difference? Outcomes in 176 consecutive patients. Wideochir Inne Tech Maloinwazyjne 2016; 11:268–73.

30. Hobart MG, Gill IS, Schweizer D, Sung GT, Bravo EL. Laparoscopic adrenalectomy for large-volume (> or = 5 cm) adrenal masses. J Endourol 2000; 14:149–54.

31. Abraham GP, Siddaiah AT, Das K, Krishnamohan R, George DP, Abraham JJ, *et al*. Laparoscopic extirpation of giant adrenal ganglioneuroma. J Minim Access Surg 2014; 10:45–7.

32. Bozkurt IH, Arslan M, Yonguc T, Degirmenci T, Koras O, Gunlusoy B, *et al*. Laparoscopic adrenalectomy for large adrenal masses: Is it really more complicated? Kaohsiung J Med Sci 2015; 31:644–8.