Open Adrenalectomy versus Laparoscopic Adrenalectomy in the Management of Benign Adrenal Tumors

Mohamed Mahmoud El Sayed Ibrahim,[1] Wael Omar,[2] Ahmed Elhofy[3]
[1,3]Department of General Surgery, Ain Shams University, Egypt
[2]Department of General Surgery, Helwan University, Egypt

Objective: The aim of this study was to compare the outcome of open adrenalectomy (OA) to laparoscopic adrenalectomy (LA) performed for benign adrenal tumors.

Patints and methodes: The study was a prospective, randomized comparative study that included 32 patients with unilateral adrenal tumors who underwent adrenalectomy either open or laparoscopic in Ain Shams University Hospitals and Helwan University hospital between May 2015 and May 2017. Patients were divided into 2 groups: 16 patients underwent laparoscopic adrenalectomy (Group A) and 16 patients underwent open adrenalectomy (Group B). Patients with suspected malignancy were excluded from our study. Parameters including demographics, perioperative evaluation of patients, and postoperative pathological data were analyzed.

Results: The study included 32 patients who underwent adrenalectomy either laparoscopically or by open surgery, it was done for pheochromocytoma (16 patients) and cortical adenomas (16 patients) (nine cases Cushing's syndrome and seven Conn's syndrome). There was one conversion to open technique in the laparoscopic group and no mortalities recorded in both groups. By comparing the 2 groups it was found that the mean operative time was longer in the laparoscopic group 162.63 min versus 146.50 in open group ($p=0.019$); with less intraoperative bleeding 86 ml vs 400 ml in open group ($p<0.001$), but shorter postoperative recovery. Earlier toleration of diet (1.6 vs 3.5 days), shorter hospital stays (2.69 vs 5.44 days) and earlier return to normal activity (7.5 vs 13 days), ($p<0.001$ for all) and less analgesic use (10 vs 30mg) ($p<0.001$) in the laparoscopic group.

Conclusion: Laparoscopic adrenalectomy for adrenal tumors is an effective and safe technique that is associated with significantly earlier toleration of diet, shorter hospital stays and earlier return to normal activity with less post-operative pain and complications, in spite of the fact that it could be a longer procedure.

Key words: Laparoscopic, open, adrenalectomy, benign adrenal tumors.

Introduction

The adrenal gland is a retroperitoneal organ which is located beneath the diaphragm. The adrenal tumors are not rare and their incidence increased after the use of Computerize Tomography (CT). The incidence of adrenal tumours found on pelviabdominal CT scans is between 0.6% and 1.3%. The incidence of these tumours on all CT scans, including thoracic, abdominal, and pelvic, is between 0.4% and 4.4%. The incidence of adrenal tumours in patients who had no evidence of adrenal disease is between 1.4% and 9%.[1]

Open surgery is difficult and is associated with possible complications and prolonged recovery. Not that only, but no other surgical procedure than open adrenalectomy shows a greater difference between the small size of the organ to be removed and the extent of the skin incision needed.[1]

Since the first report on laparoscopic adrenalectomy (LA) by Gagner et al in 1992,[2] the laparoscopic approach has become the preferred technique to remove tumors of the adrenal gland. Subsequently, the operation has been performed with increasing frequency in specialist endocrine surgical units.

Hypothesis

The aim of this study was to report our experience and the benefits of minimally invasive techniques in adrenalectomy and compare it to open adrenalectomy.

Patients and methods

Patients

This study was conducted in the Endocrine-Surgery Unit of Ain-Shams University Hospital and Helwan University hospital. The study was a prospective, randomized comparative study that included 32 patients with adrenal tumors who underwent adrenalectomy between May 2015 and March 2017.

We included cases with a tumor size of 2 to 10 cm. With no contraindication for laparoscopic surgery. We excluded any case with suspected preoperative malignant criteria using multiphasic CT - adrenal protocol. We excluded any case with attenuation value of >10 HU on pre-contrast film, heterogeneous enhancement on contrast injection, or washout at 10 minutes of <50%. 16 patients who underwent laparoscopic adrenalectomy were assigned to Group A and 16 patients who underwent open adrenalectomy were assigned to Group B. The randomization method

was the closed envelop method. Written informed consent was obtained from all patients before being assigned to surgery.

Preoperative

The surgical details and complications of both procedures was discussed in detail with the patients. We recorded the data from both groups and analyzed: age, sex, body mass index, co-morbidity, American Society of Anesthesiologists (ASA) Score, indication for surgery, previous surgery, length of procedure, histological diagnosis, specimen size, complications, blood loss, rate of conversion, and length of hospital stay (LOS), analgesia needed postoperatively, and time to return to normal activity and work. The preoperative laboratory tests included routine blood tests, electrolytes (Na+and K+), vanillyl mandelic acid (VMA), serum cortisole (am and pm) and aldosterone.

Workup included also chest X-ray and electrocardiogram (ECG). Evaluation of tumor size and extension was done by using ultrasonography, CT, and magnetic resonance imaging (MRI). Preoperative preparation for pheochromocytoma cases included the use of alpha adrenergic antagonists, beta-adrenergic antagonists and IV fluid therapy until optimal level of preoperative control of blood pressure and heart rate was achieved.

Preoperative preparation for Cushing cases included ketoconazole for three consecutive days and continued until the morning of the surgery.

Operative

The study was conducted in Ain-Shams University Hospital – Demerdash Hospital, all cases were operated on by consultant surgeon of the Endocrine Surgery Unit.

In Group A (laparscopic adrenalectomy), the patients were placed in a lateral position, with the operating table bridge elevated to maximum extension to widen the space between rib cage and pelvis to the maximum. Three 10–12-mm ports for the left-sided tumors (one camera trocar and two working trocars) and four 10–12-mm ports were used for the right-sided ones (to allow retraction of the liver). Port positioning and size of ports varried and were surgeon-dependent. The camera port was placed in the subcostal region at the anterior axillary line, a 12-mm trocar in the subcostal region at the midclavicular line, a 5-mm trocar in the subcostal region just to the right of the umbilicus on the right adrenalectomy for liver retraction and a 5-mm trocar in the posterior axillary line subcostally.

For right lateral adrenalectomy, a pneumoperitoneum was established using an open technique up to 12–15 mmHg in pressure and a 30-degree laparoscope which was used in all cases. Then the triangular ligament was dissected to mobilize the liver, which was then retracted medially exposing the inferior vena cava(IVC). The adrenal vein was identified first by dissection along the IVC until the adrenal vein was exposed, doubleclipped, and divided **(Figures 1,2)**. Then dissection was continued, first toward the superior pole of the adrenal gland, then laterally, and finally to the inferior pole of the adrenal gland.

For left lateral adrenalectomy, the retroperitoneal space was opened between the spleen and the lateral part of the abdominal wall. The gravity caused the spleen to be retracted medially. In the presence of small adrenal tumors, the adrenal and the renal veins were identified, and the latter was divided above its origin. Retraction of the adrenal gland medially exposed the middle suprarenal artery, which is then divided. Next the superior and inferior pole vessels were divided. At the end of the procedure, the specimen was always extracted as one piece using one of the commercially available bags **(Figure 3)**.

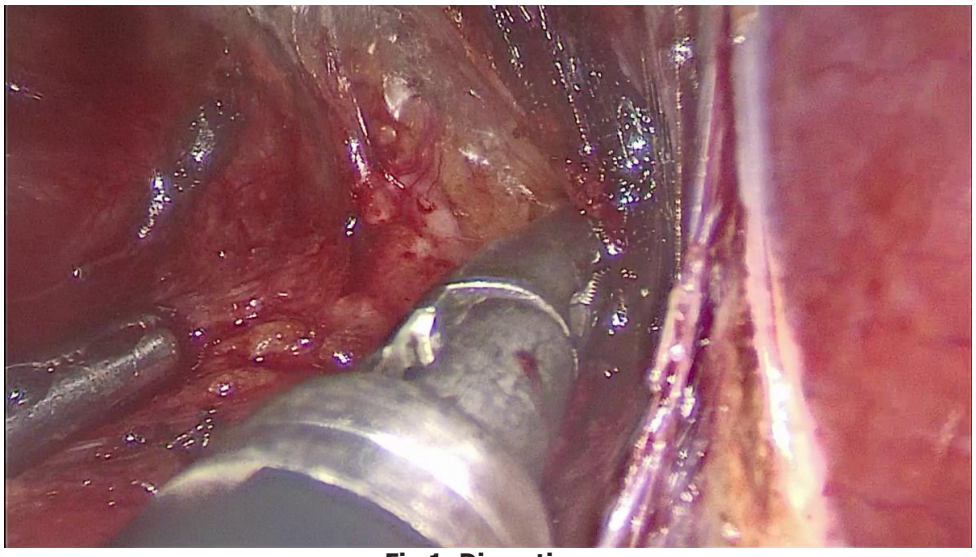

Fig 1: Dissection.

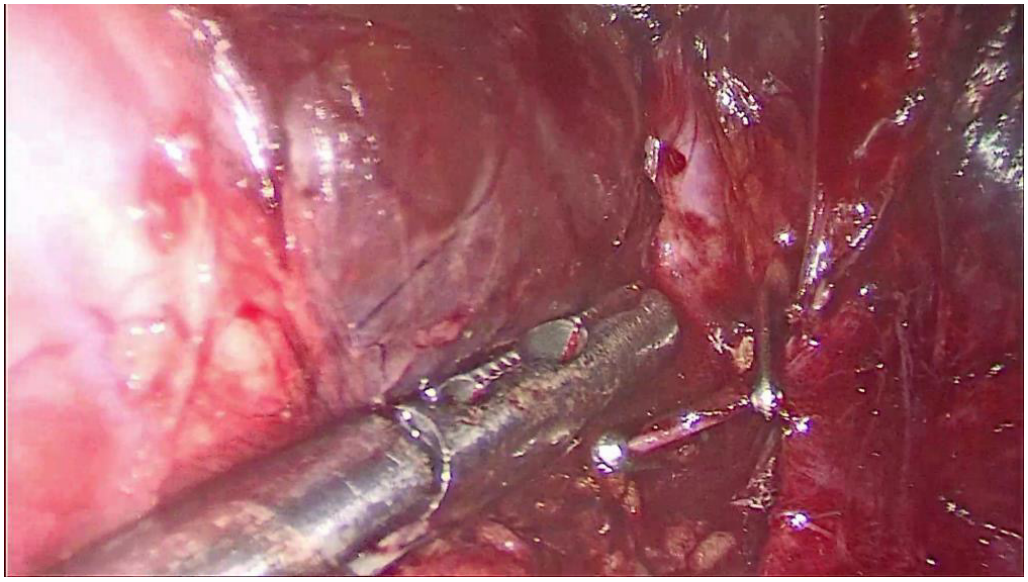

Fig 2: Right adrenal vein.

On the other hand, the open surgical procedure in Group B was initiated with the patient supine and the subcostal incision was made two fingerbreadths below the costal margin. This was extended across the midline if necessary or extended to a full chevron if access to both adrenals was warranted. The rectus muscle and fascia were divided medially, and the external oblique, internal oblique, and transversus abdominis were divided with their fascia laterally. The falciform ligament was identified in the right hemiabdomen and ligated after sharp incision of the peritoneum. The colon was then identified and reflected medially by sharp dissection. On the left open adrenalectomy, the spleen was mobilized off the colon and kidney on the left by incising the ligamentous attachments, and the liver was retracted superolaterally after ligamentous attachments were divided on the right. Care was taken on the right to identify and protect the duodenum and on the left to identify and protect the tail of the pancreas. Both of these structures were reflected medially with appropriate mobilization when necessary. The adrenal gland was then mobilized from medial to lateral, with care taken to ligate vascular branches when encountered and to mobilize the kidney for inferior traction when necessary. The wound was then closed in layers.

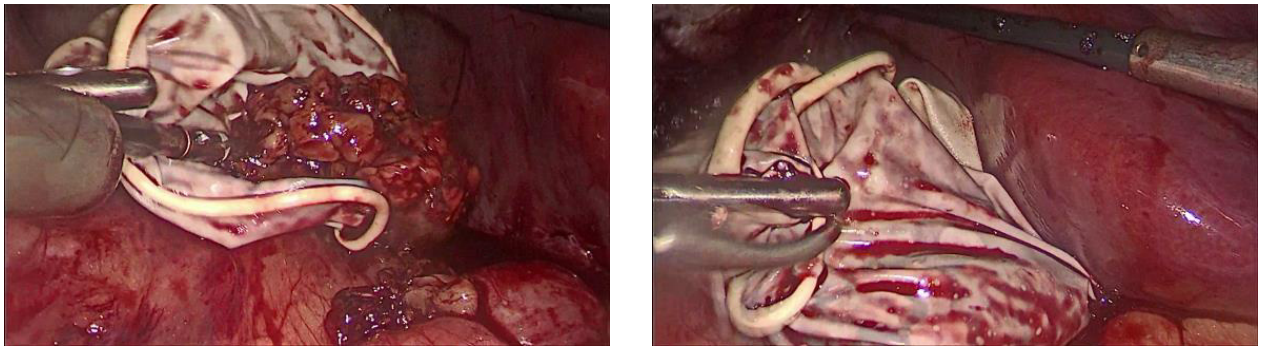

Fig 3: Specimen Retrival.

The operating time was recorded in laparoscopic operations as the time from insertion of the Veress needle for insufflation to skin closure and in open operations as the time from skin incision to completion of skin closure. Blood loss was estimated by swab weight and/or suction volume.

Postoperative

The postoperative care for pheochromocytoma cases included meticulous monitoring of blood pressure and plasma glucose level. Cushing cases received hydrocortisone postoperatively with tapering dose. Postoperative period for all patients was uneventful.

Statistical analysis

Continuous variables are expressed as mean and Standard Deviation. Categorical variables are expressed as frequencies and percents. Student t Test was used to assess the statistical significance of the difference between two study group mean. Chi square and

Fisher's exact test was used to examine the relationship between Categorical variables. A significance level of P < 0.05 was used in all tests. All statistical procedures were carried out using SPSS version 20 for Windows (SPSS Inc, Chicago, IL, USA).

Results

Thirty-two patients underwent adrenalectomy, of whom 16 underwent laparoscopic adrenalectomy (Group A) and 16 underwent open adrenalectomy (Group B), both groups were included over the same period of time, there were 19 males and 13 females, with mean age 48.44 years (38-65 years). The mean body mass index was 34.19 (27-40), with no significant difference between 2 groups, as shown in **Table 1**.

Only one case of the laparoscopic group required conversion to open, it was due to uncontrollable bleeding for 15 minutes.

Table 1: Demographic data of the patients

No. = 32		Total	Lap. Adrenalectomy	Open Adrenalectomy	Test value	P-value
		No. = 16	No. = 16			
Age	Mean±SD	48.44 ± 9.21	50.81 ± 9.27	46.06 ± 8.80	1.487•	0.147
	Range	38 – 65	38 – 65	38 – 65		
Gender	Males	19 (59.4%)	9 (56.3%)	10 (62.5%)	0.130*	0.719
	Females	13 (40.6%)	7 (43.8%)	6 (37.5%)		
Body mass index	Mean±SD	34.19 ± 2.84	34.00 ± 2.78	34.38 ± 2.99	-0.368•	0.716
	Range	27 – 40	28 – 39	27 – 40		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
*: Chi-square test; •: Independent t-test.

Table 2, shows the patients' comorbidities, as regard DM, HTN, Asthma and ISHD and **Table 3** shows the ASA classifications of patients, both show no significant difference between the two groups. 50% of patients (16 patients) included in this study were pheochromocytoma, and all of them were hypertensive patients with 10 patients with severe uncontrollable hypertension.

Table 2: Patients' comorbidities

Co morbidity No.		Total		Lap. Adrenalectomy		Open Adrenalectomy		Test value*	P-value
		%	No.	%	No.	%			
DM	No	17	53.1%	10	62.5%	7	43.8%	1.129	0.288
	Yes	15	46.9%	6	37.5%	9	56.3%		
HTN	No	10	31.3%	4	25.0%	6	37.5%	0.582	0.446
	Yes	22	68.8%	12	75.0%	10	62.5%		
Asthmatic	No	29	90.6%	14	87.5%	15	93.8%	0.368	0.544
	Yes	3	9.4%	2	12.5%	1	6.3%		
ISHD	No	28	87.5%	13	81.3%	15	93.8%	1.143	0.285
	Yes	4	12.5%	3	18.8%	1	6.3%		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
*: Chi-square test.

Table 3: ASA classification

ASA	Total		Lap. Adrenalectomy		Open Adrenalectomy		Test value*	P-value
	No.	%	No.	%	No.	%		
2	9	28.1%	3	18.8%	6	37.5%		
3	13	40.6%	5	31.3%	8	50.0%	5.292	0.071
4	10	31.3%	8	50.0%	2	12.5%		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
*: Chi-square test.

2 patients of Group A (Laparoscopic Adrenalectomy) underwent previous abdominal surgery, one underwent laparoscopic cholecystectomy and the other one underwent open appendectomy, both underwent left laparoscopic adrenalectomy and there were no obstacles. On the other hand, 4 patients of Group B (Open Adrenalectomy) underwent previous abdominal surgery, one underwent open cholecystectomy, another patient laparoscopic cholecystectomy and the other two underwent open appendectomy, the patients who underwent open cholecystectomy underwent right open adrenalectomy and there were adhesions at the site of surgery which required adhesiolysis and it prolonged the duration of the operation, without any additional comorbidity on the patient, **Table 4**.

Table 4: Previous surgical history

Previous abdominal surgery	Total		Lap. Adrenalectomy		Open Adrenalectomy		Test value*	P-value
	No.	No.	%	No.	%	No.		
No	26	81.3%	14	87.5%	12	75.0%	0.821	0.365
Yes	6	18.8%	2	12.5%	4	25.0%		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
*: Chi-square test.

The indications for surgery included 16 phechromocytomas, 12 cortical adenomas (nine cases Cushing's syndrome and seven cases Conn's syndrome) with mostly equal distribution between the 2 groups as shown in **Table 5**. Postoperative pathological analysis confirmed benign disease in all patients.

By comparing the 2 groups as shown in **Table 6**, we found significant difference in the length of the procedure as the mean time of laparoscopic adrenalectomy (162.63±23.97 minutes) was longer than that of open adrenalectomy (146.50±10.25 minutes), in spite of the fact that there was 5 laparoscopic operations with less time than the mean operative time of open adrenalectomy (range 120-145, with mean 135 min) as shown in **Table 7**. These 5 operations were the last 5 operations which reflect the learning curve.

Table 5: Final diagnosis

Indication for surgery	Total		Lap. Adrenalectomy		Open Adrenalectomy		Test value*	P-value
	No.	%	No.	%	No.	%		
Pheochromocytoma	16	50.0%	8	50.0%	8	50.0%		
Cushing 's syndrome	9	28.1%	5	31.3%	4	25.0%	0.343	0.952
Conn's syndrome	7	21.8%	3	18.7%	4	25.0%		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
*: Chi-square test.

Table 6: Intra-operative comparison between 2 groups

No. = 32		Total	Lap. Adrenalectomy	Open Adrenalectomy	Test value	P-value
		No. = 16	No. = 16			
Size of specimen	Mean±SD	4.06 ± 3.2	3.93 ± 3	4.18 ± 2.5	-0.383‡	0.761
	Range	2.5 – 8.5	2.50 – 7	3.00 – 8.50		
Length of procedure	Mean±SD	154.56 ± 19.90	162.63 ± 23.97	146.50 ± 10.25	2.473	0.019
	Range	120 – 210	120 – 210	126 – 160		
	Median(IQR)	220 (86 - 395)	86 (75 - 91.5)	395(387.5 - 408)	-4.829‡	0.000
Blood loss	Mean±SD	243.15 ± 166.98	86 ± 20.08	400.31 ± 67.31	-17.897	0.000
	Range	60 – 620	60 – 150	290 – 620		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
•: Independent t-test; ‡: Mann Whitney test.

In **Table 6**, we also compared the two groups as regard the size of specimens with little difference of the means as the mean size for all was 4.06 cm, while the mean sizes of specimens for laparoscopic adrenalectomy and open adrenalectomy were 3.93 cm and 4.18 cm respectively, and by comparing the means, there was no significant difference between the 2 groups p value = 0.761.

The intraoperative blood loss was calculated using the volume suctioned minus the saline used for irrgiation plus the difference in weight between the used and unused gauze and towels, and by comparing both groups we used the median first to exclude the effect of odd variable as there was one laparoscopic procedure and one open procedure with extensive bleeding, 150 ml and 620 ml respectively, and by comparing the 2 groups, it was found that there is highly significant difference between the 2 groups as regard the bleeding (p value = 0.000), the mean bleeding for the laparoscopic group was 86 ml and for the open group was 400ml as shown in **Table 6**. Only one patient of the open group needed postoperative blood transfusion of 1 PRBCs.

Although the length of laparoscopic adrenalectomy was longer but the postoperative recovery the length of time to tolerate regular diet, hospital stay and time to return to normal activity were shorter.

The mean time to tolerate regular diet for patients who underwent laparoscopic adrenalectomy was 1.63 ± 0.81 days in comparison to 3.5 ± 0.97 days with p value <0.001. Also, the mean length of hospital stay in patients with laparoscopic procedure was 2.69 ± 1.01 and 5.44 ± 1.09 in open procedure, with high significant (p value <0.001).

And as regard the time to return to normal activity which was calculated by asking the patients in follow-up visits and by telephone surveys, it was found that there was also highly significant difference between the 2 groups as the mean time in laparoscopic procedure was 7.5 ± 1.67 days and 13 ± 2.42 days in the open procedure, **Table 7**.

Table 7: Postoperative Recovery

Conversion rate No. = 32		Total	Lap. Adrenalectomy	Open Adrenalectomy	Test value•	P value
		No. = 16	No. = 16			
Time to tolerate regular diet (days)	Mean±SD	2.56 ± 1.29	1.63 ± 0.81	3.50 ± 0.97	-5.960	<0.001
	Range	1 – 6	1 – 4	2 – 6		
Length of hospital stay (days)	Mean±SD	4.06 ± 1.74	2.69 ± 1.01	5.44 ± 1.09	-7.374	<0.001
	Range	2 – 8	2 – 6	3 – 8		
Time to return to normal activity (days)	Mean±SD	10.25 ± 3.46	7.50 ± 1.67	13.00 ± 2.42	-7.473	<0.001
	Range	4 – 18	4 – 12	8 – 18		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
•: Independent t-test.

This highly significant difference in postoperative recovery is due to the difference in the post-operative pain as the pain in laparoscopic procedure was much less than that of the open procedure because of the big difference in the size of the wounds, which caused the severe pain and subsequent restriction in both respiration and mobility of the patient and then increased the time of hospital stay and the time needed to return to normal activity.

This was evident by the postoperative analgesic use as the median use of opioids after laparoscopic procedure was 50mg pethidine (meperidine) while the median use in open procedure was 150mg pethidine (meperidine) in the 1st postoperative day. Most of the laparoscopic patients continued NSAIDS with no need of opioids in the following days. On the other hand the open adrenalectomy patients needed more analgesics either in the 1st day postoperative or in the following days. Also, the open procedure was associated with postoperative ileus which was due to the surgical manipulation and manifested by the delay of passing flatus and delay in tolerating normal diet after the procedure, **Table 8**.

Table 8: Postoperative analgesic consumption

Postoperative analgesic consumption	Total	Lap. Adrenalectomy	Open Adrenalectomy	Test value‡	P-value
	No. = 32	No. = 16	No. = 16		
Median(IQR)	100 (0 - 300)	50 (0 - 150)	150 (100 - 300)	-4.430	0.000
Range	0 – 300	0 – 150	100 – 300		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value< 0.01: highly significant.
‡: Mann Whitney test.

Table 9 shows postoperative complications which collectively was less in the laparoscopic group and less serious than that of the open group. The most prevalent complications in the open the group were the atelectasis and the wound infection, the former was due to the painful wound and it decreased with the increase in analgesic consumption.

Table 9: Postoperative complications

Open Adrenalectomy		Lap. Adrenalectomy	
Atelectasis	8 (50%)	Peritoneal hematomas	1 (6%)
Pneumonia	1 (6%)	Parietal hematoma	1 (6%)
Wound infection	7 (44%)	Partial infarction of the spleen	1 (6%)
		DVT	1 (6%)

Discussion

Since its introduction in 1992, the laparoscopic adrenalectomy has gradually become the operative procedure of choice for adrenal tumors.[2.3]

In our study we compared morbidity and mortality rates of laparoscopic and open adrenalectomy for benign tumors.

For the laparoscopic adrenalectomy, we chose the lateral transperitoneal approach. This approach provides the best exposure and makes anatomical orientation easier, allows exploration of the abdominal cavity and better and easier manipulation of intraabdominal organs. Our initial experience indicates that this approach is highly satisfactory.

Literature have suggested 6 cm as an upper limit for the size of adrenal tumor in laparoscopic adrenalectomy, as there is increase in the incidence of malignant neoplasms in larger tumors as well as the technical difficulties encountered when removing large lesions.[4.5] However, Gagner et al. and De Canniere L have proposed that adrenal tumors with 12-15 cm are safely respectable by well-trained laparoscopic surgeons.[5.6] In our study, we set the size limit for tumors between 2 and 10 cm, however, the largest tumor size in laparscopic group was 7 cm, and the patient had a successful laparoscopic procedure.

As Elfenbein et al, found in their meta-analysis of 3100 patients[7] and similar to several other studies[5.8.8.10] of the laparoscopic vs the open approach which found significant benefits in terms of postoperative outcome and recovery as the earlier toleration of diet, the shorter hospital stays and the earlier return to normal activity with less post-operative pain and complications.

As would be expected, the respiratory complications in the open group were markedly higher than in the laparoscopic group (atelectasis and pneumonia), and the wound infection was a serious complication. Both limited the early ambulation and then delayed the oral intake and toleration.

Based on this comparative study we found that laparoscopic adrenalectomy for benign adrenal tumors is a safe and effective procedure with less pain, less operative time, less pulmonary and wound complications. Also, it reflects the learning curve associated with advanced laparoscopic surgery, as the results were better with advancement in laparoscopy.

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