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Original Article

Comparison of results of laparoscopic and open surgical techniques in adrenal masses larger than 6 cm

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Abstract

Aim: In this study, we aimed to compare the results of conventional and laparoscopic adrenalectomy in patients with adrenal masses greater than 6 cm.
Material and Methods: Thirty-six patients with tumor size greater than 6 cm who underwent adrenalectomy between January 2011 and January 2018 were included in the study. Patients were divided into two groups as Group 1 conventional and Group 2 Laparoscopic surgery. The two groups were retrospectively compared in terms of age, sex, mass localization, mass size, duration of operation, amount of bleeding, duration of hospitalization, duration of onset of food intake, perioperative mortality, early period complications and re-admission to the hospital within 90 days. P<0.05 was considered statistically significant.
Results: There were 13 patients in Group 1 and 23 patients in Group 2. There was no statistically significant difference between the groups in terms of age, sex, tumor localization, tumor size, indications for operation, postoperative complications, perioperative mortality and readmission within 90 days. Duration of operation (min), amount of bleeding (ml), duration of oral intake (day) and duration of hospitalization (day) were higher in Group 1 and statistically significant.
Conclusion: Laparoscopic adrenalectomy has demonstrated advantages in patients with a mass greater than 6 cm compared to conventional surgery, such as short operation duration, less blood loss, early onset of oral food intake and shorter hospital stay. It can be safely used in patients with a mass larger than 6 cm.

Keywords: Surrenal; laparoscopy; minimally invasive surgery.

INTRODUCTION

Laparoscopic adrenalectomy has become the preferred technique in adrenal surgery because of its rapid recovery, short hospitalization duration, less pain, and better cosmetic results since its inception in 1992 (1,2).

The first surgery for an adrenal cyst was performed by Pawlik in 1894. The first pheochromocytoma surgery was performed in 1923 (3). Laparoscopic adrenalectomy (LA) was first performed by Gagner et al. in 1992. Marcan et al. described the retroperitoneal laparoscopic adrenalectomy technique in 1995. In recent years, indications have been expanded by emphasizing that large adrenal masses and metastases can also be removed laparoscopically (1,4,5).

Many authors have suggested that size is an important criterion when choosing the best surgical method for adrenal tumor patients. There is an ongoing discussion in the literature about tumor size. Although many studies have shown that large tumors are no longer a contraindication to laparoscopic adrenalectomy (2,6-8), some authors report that laparoscopic approach is not appropriate, especially for large tumors that infiltrate the surrounding tissue (6-9).

The aim of this study was to compare the results of laparoscopic or conventional surgery in patients with adrenal masses greater than 6 cm, operated on in our clinic. In this study, we wanted to review the results of the studies in the literature based on our own results and emphasize the importance of a minimally invasive approach.

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MATERIAL and METHODS

Of the patients who underwent adrenalectomy at the Department of General Surgery Cukurova University Faculty of Medicine between January 2011 and January 2018, with tumor size greater than 6 cm determined by preoperative imaging methods, were included in the study. Our study was conducted in accordance with the Helsinki declaration. Informed consent could not be obtained from the patients because of the retrospective design of the study.

A prospective database was created with patient files and hospital information system records, and examined retrospectively. Information about the latest status of the patients was obtained by telephone. Patients under the age of 18, whose information could not be reached, underwent emergency surgery and Patients with a tumor diameter greater than 9 cm were excluded from the study to equalize the largest tumor diameter in the groups . A total of 36 patients were included in the study. The patients were divided into two groups as conventional approach and laparoscopic approach. The surgical approach was based on the preference and experience of the surgeon. Conventional surgery was preferred in patients with a history of previous upper abdominal surgery.

Demographic characteristics, Body mass index (BMI) American Society of Anesthesiologists (ASA) score , localization, size and hormone activity status, duration of operation, amount of intraoperative bleeding, postoperative complications, postoperative oral intake onset, postoperative hospital stay, perioperative mortality, re-admission within 90 days and reasons for converting to conventional surgery were analyzed.

Wound infection was defined as superficial or deep surgical site infection occurring on the surgical incision according to the definition of the Centers for Disease Control (CDC) (10). The operations were performed by surgeons who completed the laparoscopic surgical learning curve. Unplanned hospitalization within the first 90 days after discharge was accepted as unplanned re-admission to hospital. Mortality occurring within 30 days postoperatively or during the hospital stay was defined as perioperative mortality.

Preoperative preparation and indications for the operations
Endocrinology and Metabolism Clinic evaluated whether the adrenal mass was functional or not. For the diagnosis of pheochromocytoma, metanephrine and normetanephrine were studied in 24-hour urine, and in some cases vanilmandelic acid was also studied. Alpha blocker (doxazosin 2x4 mg) and beta blocker (propranolol 1x40 mg or metoprolol succinate 2x50 mg) were given to the patients who will be operated on with a diagnosis pheochromocytoma, for the hypertensive crisis that would occur during the surgery, starting from at least 2 weeks before the operation.

Baseline plasma adrenocorticotropic hormone (ACTH) and cortisol levels were evaluated at 08:00 for Cushing's syndrome. Subsequently, 1 mg dexamethasone suppression test (DST) was applied. Cushing syndrome was not considered in patients whose cortisol levels were suppressed (<1.8 mcgr / dL) after DST. In patients whose cortisol levels were not suppressed, 2 mg DST was performed for 2 days for differential diagnosis of pseudo-Cushing. Cushing's syndrome was diagnosed in patients whose cortisol was not suppressed and morning cortisol was higher than 1.8 mcgr/dL. In order to determine the source of hypercortisolemia, 8 mg DST was performed. Cushing's syndrome was accepted as adrenal origin in cases whose cortisol level was not suppressed by more than 50% compared to the basal value at 8:00 am, after 8 mg dexamethasone application at 23:00, and who had a lower baseline ACTH value.

Plasma aldosterone and renin levels and aldosterone/renin ratio were evaluated in patients with hypopotassemia and hypertension to investigate primary hyperaldosteronism. NaCl loading test was applied to cases with a high ratio (>30) and primary hyperaldosteronism was diagnosed in cases with high aldosterone (11,12). In the preoperative examination, we performed ultrasound and computed tomography in all patients. We also added MRI to patients with suspected malignancy.

Surgical Technique
Varicose stockings for prophylaxis of deep venous thrombosis and prophylactic 1 gr Cefazolin was used. 30º modified flank position was given under general anesthesia. The umbilical area was coincided with the breaking point of the table and the table was broken and flexed from this area with the aid of the kidney pillow. CO2 insufflation with a Veress needle was made (LapraSurge®, France) with an entry approximately 6-8 cm lateral of the umbilicus (junction point with the anterior clavicular line and lateral to the m. rectus abdominis) and 3-4 cm superior through the abdomen, creating a pneumoperitoneum with a pressure of 12 mmHg. A 12 mm trocar (Versaport®, Covidien Health Care, USA) was inserted into the abdomen from the point entered with a Veress needle. The camera was placed, a second 12 mm working trocar was placed approximately 2 cm inferior to the junction of the mid clavicular line and the 12th rib, and a third 12 mm working trocar was placed at the junction of the mid clavicular line and iliaca anterior superior, at the cranial direction of the umbilicus. In the right transperitoneal laparoscopic adrenalectomy cases, a 10 mm 4th trocar was placed on the middle clavicular line, at 2 cm inferolateral to the xiphoid, to be used for placement of a 10 mm fan retractor (Endoretract®, Covidien Health Care, USA) for the liver. 450 lenses (Hopkins®, Karl Storz, Germany) were used in all operations. In the transperitoneal left laparoscopic adrenalectomy technique, first the sharp dissection was performed, the Toldt ligament and then the splenic flexura and descending colon were released in order and moved medially. The splenocholic and splenorenal ligaments were then cut using 5 mm monopolar scissors (Endo Shears ®, Covidien Health Care, USA) or 5 mm LigaSure (Covidien Health Care, USA). The suprarenal fossa was entered and

firstly the left adrenal vein which pours into the left renal vein at the inferomedial of the adrenal gland, followed by the adrenal artery, was found and completely released with the aid of a 5 mm laparoscopic nut (Autosuture®, Covidien Health Care, USA), and then it was clipped and cut using a metal clip (Systems; Research Triangle park, NC). Dissection was continued sharply and bluntly from the posterior of the adrenal gland and then from the neighboring kidney. After adrenalectomy, specimen was taken out of body with a 10 cm bag (Endocatch, Covidien Health Care, USA).

In transperitoneal laparoscopic right adrenalectomy, the right colon and duodenum were released and medialized by entering the retroperitoneal area through the Toldt line. The triangular ligament of the liver was released and moved to the superior with the aid of a 10 mm fan retractor (Endoretract®, Covidien Health Care, USA). Vena Cava Inferior (VCI) was anatomically revealed. The right adrenal vein was clipped on the posterolateral of the VCI, followed by the adrenal artery, and cut with the aid of ligature. After the structure of the adrenal gland was defined, it was released from the posterior and then from the neighboring kidney with sharp and blunt dissection and taken out of the body with a 10 cm specimen bag (Endocatch, Covidien Health Care, USA). In all operations, a 10 mm Jackson Pratt drain was placed on the surgical site.

Management of patients during the perioperative period

All procedures were performed with lateral transperitoneal approach under general anesthesia. Anesthesia was provided by sevoflurane (1%) and oxygen (50%) inhalation supplemented with remifentanil infusion. Muscle relaxation during the operation was maintained with rocuronium in accordance with the neuromuscular monitoring guide. In patients with pheochromocytoma, invasive arterial pressure was routinely monitored. Intraoperative hypertension was managed with nitroprusside (0.2-10 mg/kg/min) and short-acting beta-blockers (if necessary, intravenously with esmolol 50-300 mg/kg/min; if necessary, at a dose of 0.2-0.7 mg/kg/min). Intravenous dexmedetomidine infusion was also added to the treatment in some patients to provide hemodynamic control.

Postoperative management

Patients who underwent bilateral adrenalectomy and had hemodynamic instability were followed up in the intensive care unit postoperatively. Patients with cortisol-secreting adenoma were treated with intravenous stress doses of hydrocortisone (1-2 mg/kg) or prednisolone (25 mg) for three doses on the first day of operation. After the first postoperative day, steroid replacement therapy was administered orally with hydrocortisone or prednisolone tablets (a dose of 10 mg in the morning and a dose of 5 mg in the evening).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 24 (IBM Corp, Armonk NY, USA). Categorical measurements were summarized as numbers and percentages, and continuous measurements were summarized as mean and standard deviation (median and minimum-maximum where necessary). In the comparison of continuous measurements between groups, distributions were controlled and Student T test was used for parameters showing normal distribution according to the number of variables. Statistical significance level was taken as 0.05 in all tests.

RESULTS

Thirty-six patients were included in our study. Group 1 conventional surgery (CS) had 13 patients and Group 2 LA had 23 patients. The mean age was 50.62+13.30 in Group 1 and 46.83+13.65 in Group 2 (p=0.431). 53.8% of Group 1 and 54.2 % of Group 2 were female (p=0.599). Body mass indexes were 28.03+5.45 in Group 1 and 27.26+4.95 in Group 2 (p=0.699). Distribution of ASA scores were similar in the two groups (p=0.196). 47.8% of patients undergoing LA and 0% of undergoing CS were hormone active and this was statistically significant (p=0.002). Tumor diameter was larger in patients who underwent CS (CS:7.17+1.20 cm; LA:6.70+0.65 cm) (p=0.177) (Table 1).

The most common surgical indications in the CS (most common carcinoma metastasis) and LA (most common incidentaloma) groups were incidentaloma and metastatic masses (p=0.286). Other operation indications are shown in Table 2.

While there was no difference between the localization of lesions in LA, left adrenal location (76.9%) was higher in the CS group (p=0.134). Duration of operation was calculated as 163.85+56.64 minutes and 111.3+21.59 minutes for CS and LA patients, respectively (p=0.000). Intraoperative hemorrhage was also higher and statistically significant with 157.69+103.77 ml in the CS group compared to 56.65+23.41 ml in the LA group (p=0.000). The time until oral intake and hospitalization duration were significantly higher in CS patients (p=0.00; p=0.019). There was no difference between postoperative complication rates (p=0.395).

The most common complications were wound infection and collection in the operation area. Among the LA patients, perioperative mortality developed in 2 patients. One patient died due to hemorrhagic shock and one patient died due to cardiac causes. Conversion to conventional surgery was made in 2 patients due to difficulty in exploration and in 1 patient due to hemorrhage. Re-admission rates within 90 days were similar between groups (p=0.291). They were hypotension and pleural effusion in CS, and wound infection in the area where the specimen was removed in LA (Table 3.)

DISCUSSION

Contraindications to LA are suspected or proven malignant mass, locally advanced cancer, or large tumor size. Especially thanks to new dissection and vascular sealing devices, LA can now be applied to large adrenal masses as well (13,14).

Table 1. Demographic and clinical data

Parameter		Conventional Surgery, n (%)	Laparoscopic, n (%)	p
Age (min-max) ± sd		50.62±13.30 (27-68)	46,83±13.91 (19-70)	0.431
Sex	Male	6 (46.2)	11 (47.8)	0.599
	Female	7 (53.8)	12 (52.2)	
BMI (min-max) ± sd		28.03± 5.45 (19-37)	27.26± 4.95 (22-38)	0.669
ASA Score	1	9 (69.2)	14 (60.9)	0.196
	2	1 (7.7)	7 (30.4)	
	3-4	3 (23.1)	2 (8.7)	
Hormone active	Yes	0 (0,0)	11 (47.8)	0.002
	No	13 (100.0)	12 (52.2)	
Tumor diameter (min-max)±sd		7.17± 1.20 6-9)	6.70± 0.86 (6-9)	0.177

Table 2. Operation indications

Parameter	Conventional Surgery, n (%)	Laparoscopic, n (%)	p
Conn syndrome	0 (0.0)	2 (8.7)	
Cushing	0 (0.0)	2 (8.7)	
Pheochromocytoma	0 (0.0)	4 (17.4)	
Incidentaloma	4 (30.8)	6 (26.1)	
Carcinoma metastasis	5 (38.5)	5 (21.7)	0.286
Cyst	2 (15.4)	1 (4.3)	
Cortical hyperplasia	0 (0.0)	2 (8.7)	
Cortical neoplasia	1 (7.7)	0 (0.0)	
Nonfunctional adenoma	1 (7.7)	1 (4.2)	

Table 3. Intraoperative and Postoperative Characteristics

Parameter		Conventional Surgery, n (%)	Laparoscopic, n (%)	p
Localization	Left	10 (76.9)	12 (52.2)	0.134
	Right	3 (23.1)	11 (47.8)	
Operation duration, min (min-max)±sd		163.85±56.64 (100-300)	111.3±21.59 (60-150)	0.000
Intraoperative bleeding, ml (min-max) ±sd		157.69±103.77 (50-400)	56.65±23.41 (25-100)	0.000
Oral intake onset (min-max) ±sd		2.54±1.05 (1-4)	1.13±0.34 (1-2)	0.000
Hospitalization duration (min-max) ±sd		5.62±3.40 (2-14)	3.39±2.01 (1-8)	0.019
Postoperative complication	Yes	1(7.7)	4(17.4)	0.395
Perioperative mortality	Yes	0(0.0)	1(4.3)	0.639
90-day hospital readmission	Yes	2(15.4)	1(4.3)	0.291

Malignancy rate is higher in large adrenal masses. Most of the past researchers do not recommend laparoscopic surgery because of the frequent occurrence of peripheral tissue invasion in these tumors, and the risk of perforation of the tumor which may cause local recurrence or implants in the trocar sites. In recent studies, it has been reported that surgical approach does not affect oncologic outcomes in adrenocortical carcinoma. In the literature, when LA and CS were compared, R0 resection rates, general and local recurrence rates, disease-free survival and mean survival times were similar in local or locally advanced primary adrenocortical carcinoma. LA seems to be equivalent to CS (15,16).

It is generally considered that tumors larger than 10 cm should be resected by open adrenalectomy. The reason behind this idea is considering how to manage potentially malignant tumors of 6-10 cm size, as there is currently no preoperative test to exclude malignancy (17).

Sturgeon et al. reported that the incidence of malignancy in adrenal lesions will increase as the diameter increases (<4cm=5%, 4cm=10% and 8cm=47%) (18). Humphrey et al. found that tumor diameter was higher in their patients undergoing open surgery (5 cm) compared to laparoscopic surgery (3.9 cm) (p= 0.01) (19). In our study, the mean tumor diameter was 7.17 cm in CS patients and 6.70 cm in LA patients (p=0.177). We think that this difference is due to the fact that we prefer conventional surgery in patients with a larger tumor size. Although isolated carcinoma metastasis does not affect our surgical approach, In isolated carcinoma metastasis, patient selection for LA is important. In the preoperative evaluation, open surgery should be preferred in cases of adjacent organ or periadrenal fat tissue invasion, lymphadenopathy, a tumor larger than 10 cm, and presence of thrombus in renal vein or inferior vena cava (20).

In the literature, the age range for LA and CS has been reported as 44-63 years and 43-65 years, respectively. BMI ranges from 24.7-34.1kg/m2 in CS and 25.5-35.0kg/m2 in LA (7,21-24). In our study, age, sex and BMI were consistent with the literature and no statistical difference was found between the groups. In accordance with the literature, there was no difference was found regarding the tumor localizations between the groups (p=0.286) (21,25). It has been reported that bilateral adrenalectomy can be performed safely by a laparoscopic approach (26).

The adrenal gland is also the site of metastatic spread for many tumors, mainly due to its rich sinusoidal blood supply (27). Large metastatic lesions are usually confined within the adrenal gland during presentation, thus making them an ideal tumor for laparoscopic approach (27). Adrenal metastases usually originate from a primary lung, colon, kidney, breast tumor or melanoma (28,29). While 46.2% of the patients in the CS group underwent surgery for malignant reasons, we found this rate to be 21.7% in the LA group. In the LA group, incidentaloma was the most common cause of surgery. In our series, hormonal activity in the LA group was higher than the CS group. Pheochromocytoma shows strong adhesions to surrounding tissues by a desmoplastic reaction (13). NCCN guidelines suggest that when safe and feasible, a laparoscopic approach is the preferred treatment, even if open surgery is recommended for tumors with a high risk of malignancy (30). The Endocrine Society 2014 guideline recommends an open surgical approach to tumors larger than 6 cm or for invasive pheochromocytomas, in order to achieve complete resection, to prevent tumor rupture and ultimately local recurrence (31). In our series, pheochromocytoma rates were higher in the LA group.

In daily practice, it was found that the duration of dissection in laparoscopic technique was dependent on tumor characteristics but not on tumor size (2). Oz B et al. found in their study grouping patients according to hormone activity, that the operation time was similar in hormone active and inactive tumors. In the same study, the duration of operation in hormone active tumors varied according to the characteristics of the tumor (32).

Soon PSH et al., in their study on adrenal tumors larger than 6 cm, found the operation time to be 194 minutes in the laparoscopic group and 140 minutes in the conventional group (p <0.003). Generally, in the literature, the duration of LA has been reported to be slightly longer than CS (18,24,33,34). However, laparoscopic surgery can be performed in a shorter time with the completion of the laparoscopic learning curve (22). In recent years, the number of publications indicating that they completed LA in a shorter time than open adrenalectomy has been increasing (23). Our mean operative time was 111 minutes in the LA group and 163 minutes in the CS group. This time difference was found to be statistically significant. This may be explained by the fact that open adrenalectomy is applied to large or invasive malignant tumors requiring complex surgery and increased laparoscopic surgical experience (35).

Another advantage of laparoscopic surgery is that the amount of intraoperative bleeding is less than open adrenalectomy. In the literature, it is stated that the fact that this surgery is performed for large and invasive malignant tumors may be effective on the amount of bleeding in open adrenalectomy (21). Hobart et al. found in their study comparing conventional and laparoscopic surgery in patients with an adrenal mass greater than 5 cm, that the amount of intraoperative bleeding was similar between the groups (p=0.12). Postoperative oral food intake time was significantly shorter in the laparoscopic group than in the conventional group (1.13 days vs 3.7 days; p=0.001). In the same study, postoperative hospital stay was significantly shorter in the laparoscopic group (2.4 days vs 7.7 days p=0.001) (7). In our series, similar to the studies in the literature, we demonstrated the advantages of laparoscopic surgery in tumors larger than 6 cm such as decreased intraoperative bleeding, early onset of oral intake and shorter hospital stay.

Conversion to open surgery in LA is reported to be approximately 5-14.3% in large adrenal masses

(7,17,28,36). The most common cause is bleeding from small venous structures. Vena cava or renal vein injuries, local or vascular invasion due to malignancy, abdominal adhesions, adjacent organ injuries, diaphragmatic injury, obesity, large liver, and large mass size are other causes (21). Our rate of conversion to open surgery was 13%. The most common causes were bleeding and difficulty in exploration.

Although laparoscopic adrenalectomy is accepted as a minimally invasive surgery, there is a risk of complications during this procedure. The most common perioperative complications are vascular, intestinal, spleen, pancreas, liver, kidney and diaphragm injuries (37,38). These complications are especially more common in right adrenalectomy cases and the overall incidence varies between 0.7% and 5.4% (37,38,39).

Eichhorn-Wharry et al., in their study comparing complication rates laparoscopic (n=1980) and open (n=592) adrenalectomy cases based on the Clavien classification system, determined the Clavien grade 4 and 5 complication rates in laparoscopic and open adrenalectomy cases to be 1.8% and 7.6%, respectively ($p<0.001$). In addition, the need for intensive care and mortality rate was reported to be 4.5 times higher in the open adrenalectomy group ($p<0.001$) (40). In our series, postoperative complication rates were similar between the groups. There were no complications specific to laparoscopy. Among the LA patients, perioperative mortality developed in 2 patients. One patient died due to hemorrhagic shock and one patient died due to cardiac causes.

Complications after discharge may be a reason for re-admission. The frequency of re-admissions varies depending on surgical discipline and the size of the surgery. This rate is between 5% and 15% after abdominal surgery (41). Beck et al. reported re-admission risk factors as high ASA score, diabetes, advanced age, surgery due to primary adrenal cancer, prolonged operative time, mode of operation and postoperative complications after adrenalectomy (42). In our series, re-admission to the hospital was found to be 15.4% in the open approach and 4.3% in the laparoscopic approach and the difference was not statistically significant ($p=0.291$). Reasons for reapplication were hypotension and pleural effusion in the open surgical approach, and wound infection in the area where the specimen was removed in the laparoscopic approach group.

Limitations of our study were its retrospective nature, the limited number of patients, and it being a single center study.

CONCLUSION

In conclusion, in our study, we also found advantages of LA compared to CS in adrenal masses larger than 6cm, such as short operation duration, short hospitalization time, decreased bleeding, and early oral food initiation. Laparoscopic adrenalectomy requires good knowledge of conventional adrenalectomy surgery and good laparoscopic surgical experience. Complications of LA can be avoided by surgeons with these experiences performing the operation and the advantages of minimally invasive surgery can be achieved. We believe that laparoscopic adrenalectomy is an effective and safe surgical procedure when performed by experienced surgeons in all eligible patients.

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