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Can Laparoscopic Adrenalectomy Be A Reliable Method for Adrenal Masses Larger than 4 Cm?: Our Clinical Outcomes

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What's known on the subject? and What does the study add?

Adrenal masses are now a common pathology in urology clinics, found incidentally or managed under endocrinological guidance. Adrenalectomy is the preferred approach for masses larger than 4 cm in individuals where surgery is considered acceptable. The most crucial factor in surgical selection is the experience of the surgeon. However, considering criteria such as hospital stay, intraoperative complications, cost, postoperative pain, and wound infection, the gold standard in adrenalectomy is laparoscopic adrenalectomy. We hope that this study will contribute to the literature by demonstrating the safe and effective use of laparoscopic adrenalectomy for large adrenal masses.

Abstract

Objective: The laparoscopic approach to large adrenal masses is becoming increasingly common. Our study aims to investigate the reliability and effectiveness of adrenalectomy performed with laparoscopic surgery in adrenal masses larger than 4 cm.

Materials and Methods: Fifty-two patients who underwent transperitoneal laparoscopic adrenalectomy in our clinic between January 2014 and July 2022 were evaluated retrospectively. Each patient's age, gender, hormonal activity status, tumor size and side, hospital stay, amount of bleeding, operation time, complication rates (Clavian classification), pathology results, and surgical margin positivity were evaluated. Thirty patients with tumor size over 4 cm and 22 patients under 4 cm were compared separately.

Results: There was no statistically significant difference between the two groups regarding hospital stay (p=0.11). When the operation time and bleeding amount were compared, no statistically significant difference was found between these two groups (p=0.392, p=0.761; respectively). Although slightly more complications were seen in patients with tumors smaller than 4 cm, no statistical difference was observed (p>0.05). Surgical margin positivity was detected only in one of the patients with a tumor size of less than 4 cm, and this patient was reported to have adenoma. All operations were completed laparoscopically. No complications occurred in Clavien class 3 or above in any of the patients.

Conclusion: Our study and experience unequivocally demonstrate that transperitoneal laparoscopic adrenalectomy is not only effective but also remarkably safe for large (>4 cm) adrenal masses.

Keywords: Laparoscopy, adrenal, large mass

Introduction

Adrenal masses are now a common pathology in urology clinics, incidentally or under endocrinology's guidance. Recently, with the widespread use of radiological imaging, there has been a significant increase in the incidence of adrenal masses. Adrenal masses require a detailed evaluation because they may present with different clinical, laboratory, and radiological features (1). Adrenal masses are hormonally active or inactive; oncologically, they can be benign or malignant. Asymptomatic masses larger than 1 cm that are detected incidentally are called incidentalomas. These masses are generally benign. Its incidence is between 1.5% and 8.5% (2,3). Ten percent of adrenal masses are hormonally active. Hormonally active masses

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are generally symptomatic. They can cause conditions such as Conn syndrome, Cushing syndrome, pheochromocytoma, hypercortisolism, hyperandrogenism, and hyperaldosteronism. From an oncological perspective, 94% of adrenal masses are benign. As the size of the mass increases, the possibility of malignancy and hormonal activity also increases (1,4).

Adrenalectomy is recommended for masses that show malignant characteristics on imaging or for hormonally active masses. Masses that are under 4 cm and non-functional can be monitored since the likelihood of malignancy is low. However, masses larger than 6 cm should be considered malignant and treated surgically. If there is no radiological evidence of malignancy in adrenal tumors between 4-6 cm, follow-up with intermittent imaging can be considered as an option. However, adrenalectomy is still recommended for masses that grow during follow-up. Adrenalectomy is a more recommended approach for masses larger than 4 cm in individuals for whom surgery is deemed appropriate, and the risk of anesthesia is not high (3,5,6).

Adrenalectomy can be performed openly, laparoscopically, or robotically. The most crucial factor in surgical selection is the experience of the surgeon. However, considering criteria such as hospital stay, intraoperative complications, cost, postoperative pain, and wound infection, the gold standard in adrenalectomy stands out as laparoscopic adrenalectomy (7).

While there continues to be uncertainty about which method is more suitable for large masses, this study aimed to investigate the safety and effectiveness of laparoscopic adrenalectomy in adrenal masses >4 cm with respect to complications, operation time, hospital stay, and bleeding volume.

Materials and Methods

Approval was received from the Düzce University Non-invasive Health Research Ethics Committee on 06.09.2021 with decision number 2021/184. A total of 52 patients who had undergone transperitoneal laparoscopic adrenalectomy for the treatment of an adrenal mass at the Düzce University Urology Clinic between January 2014 and July 2022, were retrospectively evaluated and included in the study. The study excluded patients with incomplete observation files, those lost to follow-up, and those who underwent retroperitoneal adrenalectomy, open adrenalectomy, or adrenalectomy during radical nephrectomy.

The two groups, 30 patients with tumor size over 4 cm and 22 under 4 cm, were compared separately. In the endocrinological evaluation, metanephrine, homovanillic acid, 5-hydroxy indole acetic acid, vanillylmandelic acid, adrenaline, noradrenaline, levels were measured in 24-hour urine. Dopamine levels, aldosterone levels, adrenocorticotropic hormone levels, cortisol levels, norepinephrine levels, and epinephrine levels, and complete blood count were also measured with serum tests. Each patient had abdominal computed tomography or magnetic resonance imaging. Decisions about surgery for the patients were made in a multidisciplinary council. Detailed verbal and written consent was obtained from each patient before surgery. In patients with diagnosed or suspected pheochromocytoma, alpha-blocker (doxazosin 4 mg 2x1), and beta-blocker (propranolol hydrochloride 40 mg 1x1), treatment was started with the recommendation of the preoperative endocrinology department. Intravenous fluid replacement was performed before surgery. Ceftriaxone 1 g was administered for prophylaxis before surgery.

All patients underwent laparoscopic adrenalectomy using the transperitoneal method in the lateral decubitus position under general anesthesia. The pneumoperitoneum was created with the help of a Veres needle. A 10 mm trocar was placed 3 cm lateral to the umbilicus. Two more trocars, measuring 5 mm and 10 mm, were placed to form a triangle in relation to each other. In patients who underwent right adrenalectomy, an additional 5 mm trocar was placed for liver retraction. Adrenal vein control was performed with the help of Hem-o-lock or metal clips. A 21f silicone drain was placed in the operation area after the masses were removed with an endo bag.

Each patient's age, sex, hormonal activity status, tumor side and size, hospital stay, amount of bleeding, operation time, complication rates, pathology results, and surgical margin status were recorded. Complications were evaluated with the Clavien-Dindo classification (8).

Statistical Analysis

Statistical analyses were performed using SPSS (version 16). In comparison between groups, continuous variables were evaluated using Mann-Whitney U test or Independent Samples t-test, depending on the data distribution. Categorical variables were examined with appropriate cross-tab statistics. A comparison of qualitative variables was made using chi-square and McNemar tests. The results were evaluated at the 95% confidence interval, and the significance level was $p<0.05$.

Results

The demographic characteristics of the two groups and operation-related data are summarized in Table 1. In the <4 cm group, 17 patients had tumors on the right side, while 5 patients had tumors on the left. In the >4 cm group, 4 patients had tumors on the right side, and 26 patients had tumors on the left. The average tumor size of the <4 cm group was 24.47 mm, and that of the >4 cm group was 67.09 mm. The average ages of the <4 cm group and >4 cm group were 57 and 53.2 years.

Table 1. Demographic characteristics of patients and operation-related data

	<4 cm group	>4 cm group	p-value
Number of patients	22	30	
Age (years)	57 (29-68)	53.2 (39-79)	p=0.731
Gender (female/male)	13/9	16/14	
Side (right/left)	17/5	4/26	
Hospitalization period (days)	3.63±1.25 (2-7)	4.35±1.61 (2-7)	p=0.11
Tumor size (millimeters)	24.47±7.40 (12-35)	67.09±28.96 (41-140)	p<0.05
Surgery time (minutes)	192.42±60.47 (60-285)	207.57±51.06 (122-315)	p=0.392
Bleeding amount (mL)	75.78±45.03 (30-200)	80.43±53.04 (20-230)	p=0.761
Hormonal activity (active/inactive)	19/3	17/13	
Complications (none/clavian 1/clavian 2)	16/3/3	23/4/4	p>0.05
Surgical margin positivity (negative/positive)	21/1	30/0	p>0.05
Pathology result	20 Adrenocortical adenoma 1 Pheochromocytoma 1 Metastatic carcinoma	14 Adrenocortical adenoma 3 Adrenocortical hyperplasia 4 Pheochromocytoma 3 Myelolipoma 2 Adrenocortical carcinoma 1 Metastasic carcinoma 2 Pseudocyst 1 Adrenal endothelial cyst	

The average hospitalization day was 3.63 days in the >4 cm group and 4.35 days in the <4 cm group. There was no statistically significant difference between these two groups (p=0.11). The average operation time was 207.57 minutes in the >4 cm group and 192.42 minutes in the <4 cm group. The difference between these two groups was not statistically significant (p=0.392). The average amount of bleeding was found to be 80.43 mL in the >4 cm group 75.78 mL in the <4 cm group, and this difference was not statistically significant (p=0.761).

In the <4 cm group, Clavien class 2 complications were observed in 3 patients, and Clavien class 1 complications were observed in 3 patients. In the >4 cm group, Clavien class 1 complications were reported in 4 patients, and Clavien class 2 complications were reported in 4 patients. However, no significant difference was found between these two groups regarding complications (p>0.05). No complications occurred in any of the patients with Clavien 3 or higher.

As noted in the classification above, postoperative low saturation was detected in 1 patient and improved with triflow exercise. One patient received one unit of an erythrocyte suspension transfusion. One patient was extubated postoperatively, and then intubated again due to low saturation and taken to intensive care, but later their saturation improved spontaneously. One patient developed atrioventricular block during surgery, and improved later. One patient had mild postoperative chest pain, but no problem was detected in the examinations performed afterwards, and it improved spontaneously. A few patients used analgesics due to pain during their postoperative hospitalization. Hypertensive attacks were observed during the operation in two cases diagnosed with pheochromocytoma. Both attacks occurred during maneuvers applied to the adrenal tissue while releasing the surrounding tissue. In one case with a diameter of 42 mm, the session had to be interrupted three times for approximately 30 minutes each due to hypertensive attacks. Anesthesiologists controlled hypertensive episodes intraoperatively.

In a patient with a 2 cm tumor, the pathology of which was reported as adrenocortical adenoma surgical margin positivity was detected. No positive surgical margins were detected in any of the other 51 patients. All surgeries were completed laparoscopically. In a follow-up of at least 2 years of patients, with malignancy detected in their pathology, port site metastasis, which is considered a feared complication in malignant adrenal masses, was not detected in any patient. No intraoperative or postoperative blood transfusion was performed in either group.

Discussion

Laparoscopic adrenalectomy is currently the preferred surgical method for most patients with adrenal tumors. The laparoscopic method has many advantages compared to open surgery, such as fewer complications, less analgesic need, less blood loss, earlier mobilization, quicker nutritional recovery of the patient, and shorter hospital stay.

The size of the incision made to remove the tumor is proportional to its size. The disadvantages of a large tumor diameter are wound infection due to the lengthening of the incision, delay in wound healing, and a higher risk of incisional hernia. However, no wound infection, evisceration, or incisional hernia was detected in our patients during the 1-year follow-up. However, because this incision will be much more prominent in open surgery, laparoscopic surgery clearly reduces the incision size in large masses (9).

It is stated that approximately 20-40 cases are needed to complete the learning curve for laparoscopic adrenalectomy. On the other hand, high volume surgeons are defined as those who perform 6 or more cases of adrenalectomy per year (10). While National Comprehensive Cancer Network recommends the open method in adrenocortical carcinomas, regardless of size, European Society of Endocrine Surgeons recommends (weak recommendation) laparoscopic adrenalectomy only in high-volume centers and high-volume surgeons in lesions with suspected adrenocortical carcinoma under 6 cm and without suspicion of invasion. However, adrenocortical cancer does not contraindicate laparoscopic adrenalectomy. In our study, no recurrence was detected in the 3-year follow-up of 2 patients with tumor sizes of 6.5 cm and 7 cm who underwent laparoscopic adrenalectomy, and whose pathology was reported as adrenocortical carcinoma (11,12).

The risk of port metastasis or local recurrence after laparoscopic adrenalectomy in large masses with malignant potential is not fully known, but port site metastasis has rarely been reported. Port site metastases appear to be more common in adrenalectomy performed for metastatic masses. In the study conducted by Micali et al. (13), laparoscopic adrenalectomy was performed on 330 patients, and port site metastases were detected in 4 of these patients. Three of these four metastases had metastatic adrenal masses with a primary origin in another organ. In our study, no port site metastasis was detected in at least a 2-year follow-up of a total of 4 patients diagnosed with adrenocortical carcinoma and with metastatic masses.

The laparoscopic method is generally recommended for adrenal masses under 4 to 5 cm in diameter. Open adrenalectomy is recommended in patients with suspected or known invasion, vein thrombus, or positive surgical margins. However, many publications have shown that laparoscopic adrenalectomy is a safe and effective method for large adrenal masses (>4-5 cm) (14-18). Novitsky et al. (19) reported in their study that laparoscopic adrenalectomy for masses larger than 5 cm is equally effective and safe for both right and left-located tumors. However, it is also suggested that laparotomy may be more effective in locally invasive tumors, and hand-assisted laparoscopy may be considered (9). Although no complications related to the incision site developed in our case series, considering the incision required for specimen removal in large masses (>10 cm), hand-assisted laparoscopy may also be considered as an option in these patients.

Agrusa et al. (20) found that laparoscopic adrenalectomy showed better surgical results compared to open adrenalectomy. However, they stated that it is still controversial whether this technique is safe and applicable for large adrenal masses due to the increased risk of malignant lesions. The study argues that laparoscopic adrenalectomy is safe and appropriate for adrenal masses larger than 5-6 cm, but open surgery should be considered in cases of suspected malignant invasion (20).

Young and Thompson (21) argued that the 3.6% conversion rate to open surgery in laparoscopic adrenalectomy, means the surgeon should be knowledgeable about open adrenalectomy even if they use the laparoscopic method. Therefore, any surgeon who performs laparoscopic adrenalectomy should also be familiar with the open surgical approach. This will make the surgery safer and more effective, and will allow the surgeon to perform it more comfortably.

Study Limitations

The complication rates encountered in this study were lower in both large and small masses compared to the literature. However, more accurate comparisons can be made as the number of patients increases. A limitation of our study is the small number of cases. A larger number of patients would have increased the sample size and therefore the reliability of the study.

Although many complications, such as injuries to the spleen, pancreas, colon, duodenum, kidney, and vascular injuries, have been reported in the literature, there was no organ injury or significant vascular injury in any of our cases (16,17,22-26). This situation suggests that surgeons who have completed the learning curve can perform laparoscopic adrenalectomy on large adrenal masses as safely and effectively as on small adrenal masses.

It is important to acknowledge the limitations of our study. Firstly, it was retrospective and conducted at a single center. Secondly, the sample size was relatively small. Thirdly, the follow-up period was less than three years.

Conclusion

Recently, there has been a trend towards minimally invasive surgery, especially in urology. While open adrenalectomy was previously performed, today the majority of adrenal surgeries are performed laparoscopically or robotically. Considering the cost of robotic surgery, laparoscopic adrenalectomy has an essential place in adrenal gland surgery. Although there is an opinion that laparoscopic adrenalectomy surgery would be complicated in cases of large masses, our study found that the laparoscopic approach for masses larger than 4 cm and below 4 cm had similar effectiveness and surgical reliability results. However, studies with more patients are needed to support this reliability and effectiveness.

Ethics

Ethics Committee Approval: Approval was received from the Düzce University Non-invasive Health Research Ethics Committee on 06.09.2021 with decision number 2021/184.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.Ş., A.T., Concept: Y.Ş., A.Y.B., Design: Y.Ş., A.Y.B., Data Collection or Processing: A.Y.B., D.B., A.T.T., Analysis or Interpretation: Y.Ş., A.Y.B., Literature Search: A.T.T., E.B., Writing: Y.Ş., A.Y.B., D.B.

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