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Should Laparoscopic Surgical Approach be Offered for Large and Potentially Malignant Adrenal Tumors?

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Introduction: Since Gagner et al., described the first laparoscopic adrenalectomy (LA), this minimally invasive approach has almost replaced the open adrenalectomy in the management of small and medium-sized adrenal lesions. However, the increasing experience with the endoscopic adrenalectomy produced the broadening of the indications to this approach, proposing it also for large and potentially malignant adrenal tumors. The findings presented in this paper has evaluated our experience with laparoscopic adrenalectomy in relatively small adrenal masses less than 60 mm in size and large adrenal masses larger than 60 mm performed in our surgical unit.

Methodology: Our data come from a retrospective analysis of 25 patients who underwent consecutive transperitoneal laparoscopic adrenalectomies for relatively medium sized adrenal tumors ≥ 4 – < 6 cm [Group A] and large adrenal tumors ≥ 6 cm [Group B] between May 2021 and May 2023. These procedures were carried out at Urology department at the National cancer institute (NCI), Cairo University (CU). Perioperative data including demographics, medical comorbidities, characteristics of the adrenal masses, the operative details, and follow-up were analysed using the statistical package for the Social Sciences (SPSS) version 28. Patients provided informed consent and had follow-up appointments and imaging.

Results: The study included 25 patients with adrenal masses ≥ 4 cm who underwent transperitoneal laparoscopic adrenalectomy at the National cancer institute (NCI), Cairo University (CU). The study consists of 18 females (72.0%) and 7 males (28.0%) leading to a female to male ratio of 2.5:1 with a mean age of 36.40 ± 16.90 years. The preoperative biochemical work up and the histologic results showed 7 patients (28.0%) with functioning tumours, while 18 patients (72.0%) revealed non-functioning adrenocortical tumours. The cases were divided into two groups according to the size; 11 patients (44 %) had tumours

less than 60 mm [Group A] while 14 patients (56%) showed adrenal tumours larger than 60 mm [Group B]. Conversion to open approach occurred in 4 patients of group B, while no conversion to open approach occurred in any of the cases of group A.
Conclusion: In the absence of evidence of local invasion to surrounding structures; a comparative study between patients with adrenal tumors ≥ 6 cm and those with tumors < 6 cm revealed no major impact on the oncologic outcome provided that the laparoscopic resection is performed with experienced hands to assure the surgery to be feasible and safe.

1. Introduction

Since Gagner et al., had described the first laparoscopic adrenalectomy (LA), this minimally invasive surgical approach has almost replaced the open adrenalectomy approach in the management of small and medium-sized adrenal lesions [1]. The advantages of LA include shorter hospital stays, decreased postoperative pain, improved recovery times, and better cosmetic results. In addition, difficulty with open surgical exposure of the adrenal gland make this organ particularly amenable to a minimally invasive technique [2]. Endoscopic adrenalectomy is the gold standard treatment for small to medium-sized (≤6 cm) benign adrenal tumors, both functioning and non-functioning [3]. However, the increasing experience with the endoscopic adrenalectomy produced the broadening of the indications to this approach, proposing it also for large and potentially malignant adrenal tumors [4].

Despite tumor size is usually considered a parameter predicting the malignancy of the adrenal lesion, it remains relatively insensitive and nonspecific [4]. Indeed, the role of tumor size as a limiting factor for the choice of the surgical approach for adrenalectomy, seems unimportant for some surgeons [5]. In general, about 75% of suprarenal masses measuring more than 6 cm will be mostly benign at the final pathological examination report [5]. However, in the case of invasive adrenocortical carcinoma (ACC), open adrenalectomy remains the procedure of choice [6].

Indeed, the reported frequency of ACC in patients underwent surgery for adrenal incidentaloma reaches 10% in some series. However, in absence of radiological suspicious findings (invasion of surrounding structures, lymph node or distant metastases, intravenous thrombus), it may difficult to predict malignancy pre-and even intra-operatively [7].

The aim of the present study was to compare the outcomes of two groups of LA for adrenal tumors < 6 cm with those ≥ 6 cm. The contraindications to the laparoscopic approach, in our study, were radiological suspicious malignant locally advanced adrenal tumors that may necessitate enbloc resection of adjacent organs or cases with serious medical conditions that may preclude the laparoscopic surgery.

2. Materials And Methods

Between May 2021 and May 2023, 25 transperitoneal laparoscopic adrenalectomy were performed at the National cancer institute (NCI), Cairo University (CU) for adrenal tumors

larger than 4 cm in size. A retrospective analysis of the data including demographic, medical comorbidities, pre-operative, intra-operative, post-operative, pathologic, and follow-up data were collected and compared among 2 groups. Groups were designed according to the adrenal tumor size as estimated by the maximum diameter of the pathologic specimen and divided into: group A for relatively medium sized adrenal tumors ≥ 4 – < 6 cm (n = 11), and group B for large adrenal tumors ≥ 6 cm (n = 14).

Surgical Technique

All cases were performed through transperitoneal laparoscopic approach and trocars insertion positions varied according to the tumor side. For the left sided masses, three trocars were inserted: a 12-mm trocar at the lateral border of the rectus abdominis just above the level of the umbilicus to accommodate the camera, a second 5-mm trocar in the midclavicular line about 3 cm below the costal margin, and a third 5-mm trocar in the anterior axillary line (Fig. 1).

Figure 1: Planned positions for post site insertion for left sided adrenalectomy

Initially the spleno-colic ligament is divided, reflecting the splenic angle of the colon. Then spleen and the pancreatic tail are mobilized medially exposing the adrenal gland. Once the adrenal gland had been exposed, adrenal vessels were identified, clipped, and divided. In cases of pheochromocytoma it is preferred to be identified, clipped, and divided first if applicable to avoid intra-operative blood pressure shooting (Figure 2).

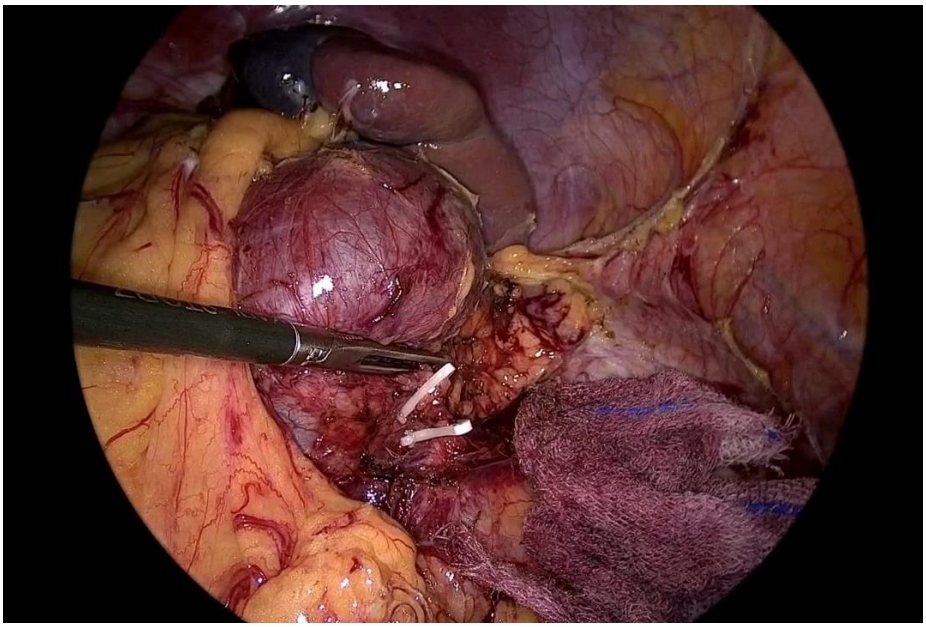

Figure 2: The adrenal vein is first identified, clipped, and divided in a case of left adrenal pheochromocytoma.

For the right sided adrenal masses, a fourth 5-mm trocar is usually added in the epigastrium to insert a liver retractor. The line of Toldt is subsequently dissected caudally, exposing the upper pole of the kidney and the inferior vena cava. Once the adrenal gland had been exposed, adrenal vessels were identified, clipped, and divided. Care must be taken for the short right adrenal vein carrying a major risk of iatrogenic injury and bleeding.

3. Results

The study included a total of 25 patients presented with adrenal masses ≥ 4 cm who performed laparoscopic transperitoneal adrenalectomy. The cases divided into 2 groups according to the adrenal tumor size: group A for relatively medium sized adrenal tumors ≥ 4 – < 6 cm (n = 11), and group B for large adrenal tumors ≥ 6 cm (n = 14). The majority of the cases in both groups were females (n=18) while males (n=7). The majority of the patients were non-smokers with no serious medical comorbidities that may preclude the laparoscopic procedure. Details of the patients baseline demographics have been illustrated in (Table 1).

Variables		Group A	Group B
Number of cases		11	14
Age/years		30.50 ± 16.20	41.10 ± 16.50
Sex: n (%)	Males	2 (18.18%)	5 (35.7%)
	Females	9 (81.8%)	9 (64.2%)
Smoking: n (%)	No	10 (90.9%)	11 (78.5%)
	Yes	1 (9%)	3 (21.4%)

Hypertension: n (%)	No	7 (63.6%)	11 (78.5%)
	Yes	4 (36.3%)	3 (21.4%)
Diabetes: n (%)	No	9 (81.8%)	10 (71.4%)
	Yes	2 (18.18%)	4 (28.5%)
Laterality: n (%)	Right	8 (72.7%)	8 (57.1%)
	Left	3 (27.2%)	5 (35.7%)
	Bilateral	0	1 (7.1%)
Endocrine Functioning status (n) (%):	Functioning	3 (27.2%)	4 (28.5%)
	Non-functioning	8 (72.7%)	10 (71.4%)
Conversion to open	No	11 (100%)	10 (71.4%)
	Yes	0 (0%)	4 (28.5%)

TABLE 1: Details of the baseline demographics

The results revealed only one confirmed case of adrenocortical carcinoma in group B in a mass measuring 90 mm in its maximum diameter, while group A cases showed no pathologically proven malignant cases. Pathological variants of adrenal lesions in both groups have been illustrated in (Table 2). Follow-up of the cases in both groups for 18 months revealed no evidence of local recurrence or distant metastasis.

Pathology	Group A (N= 11) Tumor size ≥ 4–< 6 cm: n (%)	Group B (N= 14) Tumor size ≥ 6 cm: n (%)
Adrenocortical adenoma	2 (18.18%)	2 (14.28%)
Adrenocortical neoplasm of undetermined biologic behavior	2 (18.18%)	2 (14.28%)
Adrenocortical carcinoma	0 (0%)	1 (7.14%)
Angiomyolipoma	0 (0%)	2 (14.28%)
Ganglioneuroma	1 (9%)	0 (0%)
Myelolipoma	1 (9%)	2 (14.28%)
Mature benign cystic teratoma	1 (9%)	0 (0%)
Hemorrhagic cyst	0 (0%)	1 (7.14%)
Adrenal inflammatory pseudocyst	1 (9%)	0 (0%)
Pheochromocytoma of unpredicted biologic behavior	3 (27.27%)	4 (28.57 %)

TABLE 2: Details of pathological variants.

The endoscopic procedure was successful in all patients of group A; while 4 of the 14 cases of group B (28.5%) had to be converted into open approach due to intraoperative uncontrollable bleeding during dissection. No early or delayed post-operative complications were detected in group A; however, group B revealed post-operative early complication in one case, in the form of uncontrolled hypertension that led to stroke and acute kidney injury that necessitated post-operative 2 sessions of hemodialysis. Delayed complications occurred in 3 cases of group B,

in the form of incisional hernia.

4. Discussion

Endoscopic adrenalectomy is the gold standard modality of resection for small and medium sized suprarenal masses measuring less than 6 cm in their maximum diameter [3]. However, with the ongoing increasing experience wuth the endoscopic techniques, resulted in broadening the applicability of this approach for the large adrenal masses [4].

Moreover, the early experiences with laparoscopic adrenalectomy reported that with experienced hands the endoscopic resection of the large adrenal masses upto 10 cm in maximum diameter, in absence of evidence of local infiltration of surrounding structures, was feasible and safe [4].

Our retrospective study has been conducted at the National Cancer Institute(NCI), Cairo University, over a period between May 2021 and May 2023, aiming at assessment of the feasibility and outcomes of transperitoneal adrenalectomy in large adrenal tumors more than 6 cm in maximum diameter in 25 patients , divided into 2 groups; group A for relatively medium sized adrenal tumors ≥ 4 – < 6 cm (n = 11), and group B for large adrenal tumors ≥ 6 cm (n = 14).

In this study, the frequency of adrenal malignancy was not clearly related to tumor size. No detected malignant adrenal tumors among 11 patients included in group A with tumors ≥ 4 – < 6 cm in maximum diameter, however, 7 cases was confirmed as benign, 2 cases showed adrenocortical neoplasm of unpredicted biologic behavior, and 3 cases showed pheochromocytoma of unpredicted biologic behavior. Among 14 patients presented in group B for large adrenal tumors ≥ 6 cm, only one case was confirmed to be malignant, however, 6 cases were confirmed as benign tumors, 2 cases revealed adrenocortical neoplasm with unpredicted biologic behavior, and 4 cases showed pheochromocytoma of unpredicted biologic behavior with no evidence of local recurrence or distant metastasis in any case during the follow-up period. Hence, if size would be the only criterion on which the operative approach should be based, many benign suprarenal tumors would have an unnecessary open adrenalectomy, which may result in increasing morbidity, post-operative pain, post-operative hospital stay and recovery period.

The number of functioning tumors showed slight difference between the two groups, with three cases of functioning tumors in group A, as compared with group B that included 4 cases of functioning tumors.

The endoscopic procedure was successful in all patients of group A; while 4 of the 14 cases of group B (28.5%) had to be converted into open approach due to intraoperative uncontrollable bleeding during dissection. All cases in group A were resected with an intact capsule; however, 2 cases of group B showed distorted capsule. The rate of complications was higher in group B (28.5%), in the form of incisional hernia that occurred in 3 cases due to relatively large incision done to extract the specimen, while one case had experienced an early post-operative complication in the form of uncontrolled hypertension that led to stroke and acute kidney injury that necessitated post-operative 2 sessions of hemodialysis. However, group A revealed no early or delayed post-operative complications. The total rate of complications in group B

was even higher as compared with the results of meta-analysis published by Brunt et al. [8], in which complication rate was reported as 10.9% in 1522 cases, however it could be contributed to the large scale of cases in the study.

In a study by Palazzo et al. [9], the authors found a mean hospital stay and a rate of 30-day re-admissions significantly higher in the low- versus high-volume adrenal surgeons. In this study, the mean postoperative stay was 2 days for group A, while the mean hospital stay was prolonged hospital stay for the 4 cases converted to open approach with a mean hospital stay 4 days, however, other cases of group B not converted to open approach showed no significant difference in post-operative hospital stay as compared to cases in group A.

The role of oncologic outcome after laparoscopic adrenalectomy in cases with malignant adrenal tumors was controversial, moreover, some authors as documented in a study done by Gonzalez et al. [10], had reported a 100% rate of local recurrence and peritoneal carcinomatosis according to laparoscopically treated malignant adrenal tumors. Other authors as shown by MacGillivary et al [5], showed no significant differences in outcome in long term follow-up. In our study, on the follow-up for all cases especially for the case that was pathologically proven as malignant in group B, patients showed no locoregional recurrence, no port site metastasis, and no distant metastases.

These data showed the feasibility of laparoscopic adrenalectomy for enbloc resection for even large adrenal tumors, that lack any evidence of invasion of surrounding structures.

5. Conclusions

Based on our study results, laparoscopic adrenalectomy is considered feasible and safe for resection of large adrenal tumors even cases larger than 6 cm in its maximum dimeter. Laparoscopic adrenalectomy carries the same benefits as other minimally invasive techniques in the form of reduced hospitalization, reduced post-operative pain, fewer post-operative complications and faster recovery time.

Endoscopic adrenal resection for the large adrenal tumors in the study showed no major impact on the oncologic outcome; moreover, according to the number of cases included in this study, the tumor size as a parameter predicting the malignancy of the adrenal lesion was relatively non-specific. However, we strongly recommend that endoscopic resection for the large adrenal masses to be performed with experienced hands to assure the surgery to be technically safe and feasible with no significant impact on the oncologic outcome.

References

1. Gagner, M., Lacroix, A., & Bolte, E. (1992). Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. The New England journal of medicine, 327(14).
2. Gill, I. S. (2001). The case for laparoscopic adrenalectomy. The Journal of urology, 166(2), 429-436.
3. Raffaelli, M., De Crea, C., & Bellantone, R. (2019). Laparoscopic adrenalectomy. Gland surgery, 8(Suppl 1), S41.
4. Henry, J. F., Sebag, F., Iacobone, M., & Mirallie, E. (2002). Results of laparoscopic adrenalectomy for large and potentially malignant tumors. World journal of surgery, 26(8), 1043-

1047.
5. MacGillivray, D. C., Whalen, G. F., Malchoff, C. D., Oppenheim, D. S., & Shichman, S. J. (2002). Laparoscopic resection of large adrenal tumors. Annals of surgical oncology, 9(5), 480-485.
6. Gaujoux, S., Mihai, R., Joint Working Group of ESES and ENSAT, Carnaille, B., Dousset, B., Fiori, C., ... & Donatini, G. (2017). European Society of Endocrine Surgeons (ESES) and European Network for the Study of Adrenal Tumours (ENSAT) recommendations for the surgical management of adrenocortical carcinoma. British Journal of Surgery, 104(4), 358-376.
7. O'Neill, C. J., Spence, A., Logan, B., Suliburk, J. W., Soon, P. S., Learoyd, D. L., ... & Sywak, M. S. (2010). Adrenal incidentalomas: risk of adrenocortical carcinoma and clinical outcomes. Journal of surgical oncology, 102(5), 450-453.
8. Brunt, LM, Halverson, JD. The Endocrine System. In: The Physiologic Basis of Surgery, O'Leary, JP (Eds), Lippincott, Philadelphia 2002. p.351.
9. Palazzo F, Dickinson A, Phillips B, et al. Adrenal surgery in England: better outcomes in high-volume practices. Clin Endocrinol (Oxf) 2016;85:17-20. 10.1111/cen.13021
10. Gonzalez, R. J., Shapiro, S., Sarlis, N., Vassilopoulou-Sellin, R., Perrier, N. D., Evans, D. B., & Lee, J. E. (2005). Laparoscopic resection of adrenal cortical carcinoma: a cautionary note. Surgery, 138(6), 1078-1086.