Safety of Minimally Invasive Surgical Techniques in Large Adrenal Lesions: A Single-Centre Study

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ABSTRACT

Objective: To compare perioperative outcomes of minimally invasive surgery for ≥5 cm and <5 cm adrenal lesions.
Study Design: Retrospective cohort study.
Place and Duration of Study: Hacettepe University School of Medicine, Ankara, Turkey, between October 2007 and September 2019.
Methodology: Data of 83 patients operated for adrenal lesions was collected retrospectively. Patients were categorized into two groups based on the size of the adrenal gland as <5 cm and ≥5 cm. The groups were compared in terms of perioperative outcomes.
Results: The median age of the patients was 51 (41-60) years, with a female-to-male ratio of 27/56. The median follow-up period was 27 (11.5-91) months. Of 83 adrenal masses, 60 (72.3%) were in the <5 cm group and 23 (27.7%) were in the ≥5 cm group. Fifteen (18.1%) patients underwent adrenalectomy for lung cancer metastasis, whereas three (3.6%) for renal cell carcinoma metastasis. The overall rate of post-operative complications was 10.8%. Post-operative complication rates were similar in each group (p=0.433). Operation time was found to be significantly higher in patients with large adrenal masses (p=0.003).
Conclusion: Minimally invasive surgical techniques have the same perioperative results in the group with adrenal lesions ≥5 cm compared to <5 cm and may be safely employed in this group of patients.

Key Words: *Laparoscopy, Robotic assisted laparoscopy, Adrenalectomy, Metastasectomy, Adrenal gland neoplasms.*

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INTRODUCTION

Laparoscopic adrenalectomy has rapidly gained popularity among urologists and endocrine surgeons since its first description in 1992 by Gagner *et al*.[1] Currently, laparoscopic surgery is the standard of care for benign adrenal lesions.[2] Laparoscopy is considered less suitable for larger adrenal tumours, when suspicion of local invasion is present and in adrenocortical tumours. The main concern in this setting is the risk of inadequate resection.[3,4] At the same time, there is an evident trend in favour of minimally invasive surgery for adrenocortical carcinomas.[5]

While the adoption of minimally invasive techniques in clinical practice has increased, the threshold value for laparoscopy has remained a constant topic of discussion. Various study groups accepted threshold values of 5, 6 and 8 cm for large adrenal lesions and reported promising results.[6-12] In this study, we present our experience with adrenal masses ≥5 cm treated with standard laparoscopic and robotic techniques.

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METHODOLOGY

The study was designed as a retrospective cohort study. The Institutional Review Board approval was obtained from the Hacettepe University Faculty of Medicine prior to the study (Approval No. GO 20/593). We included and analysed the institutional data of 83 patients who underwent adrenalectomy with minimally invasive surgical techniques (MIS; trans-peritoneal laparoscopy or robotic-assisted laparoscopy) from October 2007 to September 2019. Indications for adrenalectomy included hormone-secreting tumours, non-functional tumours >4 cm or metastatic lesions. Open adrenalectomies and patients missing perioperative data were excluded from this study. All adrenal masses were approached as malignant regardless size until proven otherwise on final pathological investigation. Specimens were routinely extracted from the abdomen in a specimen bag avoiding fragmentation.

Patients were classified into two groups based on the size of the adrenal gland in preoperative imaging as <5 cm and ≥5 cm. The groups were compared in terms of gender, age, body mass index (BMI), lesion side, American Society of Anaesthesiologists (ASA) score, operation time (min), estimated blood loss (mL), operation technique (laparoscopic or robotic), postoperative haemoglobin drop (g/dL), drain removal time (day), length of hospital stay (day), postoperative complications, pathological diagnosis and surgical margin positivity. The Clavien-Dindo

classification was used to assess 30-day postoperative complications.[13]

All statistical analyses were performed with the SPSS 24.0 (IBM Corp., Chicago) software for Windows. Chi-square Test was used for nominal data, the Mann-Whitney U-test was used for non-parametric variables, and T test was used for parametric variables. Kolmogorov-Smirnov test was used to assess normality. Mean ± standard deviation was used for parametric variables, while the median and interquartile range were used for non-parametric variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

The median age of the patients at the time of surgery was 51 (41-60) years, with a female-to-male ratio of 27/56. Median follow-up period was 27 (11.5-91) months. Nine patients (10.8%) had a history of abdominal surgery. Two patients (2.4%) underwent the same session bilateral adrenalectomy, whereas the robotic approach was used in seven patients (8.4%). Forty-nine (59%) patients presented with hypertension and nine (10.8%) with diabetes. Fifteen (18.1%) patients underwent adrenalectomy for lung cancer metastasis and three (3.6%) for renal cell carcinoma metastasis. Out of 83 adrenal masses, 60 (72.3%) were in the <5 cm group and 23 (27.7%) were in the ≥5 cm group. The median time to surgical drain removal was 1 (1-1) day, whereas the median duration of hospitalisation was 2 (1-3) days. The median size of the tumours was 30 (17-51) mm and 40 (22.25-61.75) mm for preoperative imaging and pathology specimen, respectively. The median size of the gross pathological specimen in the greatest dimension was 80 (70-100) mm and median weight was 49 (28.5-83.5) gr. The capsular/vascular invasion was reported on microscopic investigation in 6 (9.2%) patients with primary adrenal tumours. The surgical margin positivity was reported in 6 (9.2%) patients with primary adrenal tumours. The median estimated blood loss was 20 (0-20) mL with a median operation time of 105 (85-120) minutes. The most common pathology was adrenal adenoma (41%), followed by metastasis (21.7%) and pheochromocytoma (12%). Table I illustrates the demographic and preoperative characteristics.

Median hospitalisation time, estimated blood loss, drain removal time and mean haemoglobin decrease were similar across groups (p=0.417, p=0.924, p=0.461 and p=0.766, respectively). Operation time was found to be significantly higher in patients with large adrenal masses (p=0.003). The surgical technique, pathological histology and surgical margin positivity were similar between the groups (p=0.089, p=0.644 and p=0.682, respectively). The details are described in Table I.

The number of patients with clavien grade 1, 3, 4 and 5 complications were 4 (4.8%), 3 (3.6%), 1 (1.2%) and 1 (1.2%), respectively. The most common Grade 1 complication was potassium replacement requirement, which occurred in 3 patients (3.6%). One patient (1.2%) was readmitted to the hospital for retroperitoneal collection in the second week following surgery and was treated conservatively. Among the Grade 3 complications, 2 patients (2.4%) required a drainage catheter and 1 patient (1.2%) underwent laparotomy due to small intestine perforation. One patient (1.2%) had to be hospitalized in the intensive care unit due to multiple-organ failure during the postoperative period. One patient (1.2%) died following bilateral adrenalectomy. Only one patient received five units of blood transfusion in the peri-operative period (Table II).

DISCUSSION

Trends in the surgical approach to adrenalectomy have shifted towards laparoscopy with increased application of MIS in urology. The primary reason is that MIS has an advantage over open surgery in terms of postoperative morbidity and length of hospital stay.[14] After the widespread adoption of robotic laparoscopic systems in mainly reconstructive urological procedures, the accumulated data on robotic adrenalectomy has facilitated its further use in urological procedures.[15] Consequently, robotic adrenalectomy has emerged as a technique of choice in MIS for larger adrenal lesions over the past few years.[6,16] The shortening of the operative time and reduced bleeding as well as the increased comfort of the surgeon appear to be the main reason for such a choice.

In this study, the operative time was statistically higher in ≥5 cm lesions compared to smaller lesions. These findings appear logical and are consistent with the literature.[17,18] The relatively higher rate of robotic procedures in ≥5 cm group may have also contributed to prolonged operation time. The robotic cases in our series were carried out by surgeons experienced in standard laparoscopy at the beginning of their robotic learning curve.

In this series, the robotic approach was preferred more frequently in ≥5 cm lesions, although the difference was not statistically significant. This result may be due to the small number of patients in the robotic group. Our findings are consistent with the study of Sforza et al., in which they report preference in favour of robotics in larger lesions. The estimated blood loss was also found to be significantly less in robotic patients.[16] In a recent retrospective propensity score matched study by Wang *et al*. MIS was reported to be superior to open approach for ≥6 cm lesions in terms of estimated blood loss and length of hospital stay, but inferior in terms of financial burden. Tumour rupture rates were found to be lower in the MIS group, although statistically not significant. It was also reported that MIS was superior in pheochromocytoma lesions with shorter operative time, lower blood loss and shorter hospital stay with a comparable intraoperative blood pressure course.[8]

Table I: Comparison of demographics pre-operative and perioperative features between the groups.

Parameters		<5 cm	≥5 cm	p
Gender, N (%)	Female	20 (33.3)	7 (30.4)	0.801*
	Male	40 (66.7)	16 (69.6)	
Age, year, Median (IQR)		53.5 (19)	48 (18)	0.144**
BMI, kg/m^2, Median (IQR)		26.40 (6.18)	26.30 (8.37)	0.919**
Surgical side, N (%)	Right	29 (48.3)	12 (52.2)	0.665*
	Left	29 (48.3)	11 (47.8)	
	Bilateral	2 (3.3)	0 (0)	
ASA score, N (%)	1	5 (8.3)	3 (13)	0.622*
	2	43 (71.7)	14 (60.9)	
	3	12 (20)	6 (26.1)	
Hypertension, N (%)		38 (63.3)	11 (47.8)	0.199*
Diabetes, N (%)		5 (8.3)	4 (17.4)	0.254*
Operation time, min, Median (IQR)		100 (45)	120 (55)	*0.003**
Estimated blood loss, mL, Median (IQR)		20 (20)	20 (20)	0.924*
Operation technique, N (%)	Laparoscopic	57 (95)	19 (82.6)	0.089**
	Robotic	3 (5)	4 (17.4)	
Haemoglobin drop, g/dL, Mean (SD)		1.19 (1.06)	1.10 (0.53)	0.766***
Drain removal time, day, Median (IQR)		1 (0)	1 (1)	0.461*
Length of hospital stay, day, Median (IQR)		2 (2)	2 (2)	0.417*
Postoperative complications, N (%)		8 (13.3)	1 (4.3)	0.433**
Histology, N (%)	Benign	44 (73.3)	18 (78.3)	0.644**
	Malignant	16 (26.7)	5 (21.7)	
Surgical margin positivity, N (%) †		10 (62.5)	2 (40)	0.682**

*ASA, American Society of Anaesthesiologists; BMI, Body mass index; IQR, Interquartile range. *Chi-square Test; IQR, Interquartile range; SD, Standard deviation; † Percentage of patients with malign pathology; *Mann-Whitney U-test; **Chi-square Test; ***T-test*

Table II: Distribution of intra-operative and post-operative complications.

Parameters		N (%)
Intraoperative complications		1 (1.2)
Splenectomy		1 (1.2)
Postoperative complications		9 (10.8)
Clavien 1	Potassium replacement	3 (3.6)
	Prolonged hospitalization	1 (1.2)
Clavien 2	-	0 (0)
Clavien 3a	Drainage catheter placement	2 (2.4)
Clavien 3b	Re-operation	1 (1.2)
Clavien 4	Intensive care unit admission	1 (1.2)
Clavien 5	Exitus	1 (1.2)

Larger lesions are also associated with increased blood loss and potential damage to adjacent organs. Nevertheless, patients treated with MIS outperform those treated with the open approach.[17] In this series, no significant differences were observed in terms of blood loss, post-operative complication rates and length of hospital stay between the smaller and the larger lesions. Therefore, we conclude that the robotic approach is a good option along with the standard laparoscopy, particularly in presumably benign ≥5 cm lesions. The robotic approach will be preferred more frequently in the future with a further decrease in procedure costs.[19]

The increase in the size of the adrenal lesion is associated with an increase in the likelihood of malignancy.[20,21] Capsular disruption and positive surgical margins are the key concerns in this context. Accurate assessment of pathological specimen characteristics such as tumour size, immunohistochemistry properties, surgical margin status, local aggression degree etc. is critical in discrimination between benign and malignant lesions.[22] Considering the large difference in clinical behaviour of malignant tumours, integrity of specimen should be preserved to allow optimal pathological evaluation. Although occurs rarely, surgeon should not hesitate to convert to open surgery whenever tumour disruption risk arises to avoid possible complications. The median size of the gross specimen was larger when compared to the median lesion size in our study. Such difference can be explained by wide surgical margins deliberately carried out during the dissection, mostly including big bulks of Gerota's fascia.

Our results show no significant difference for malignant lesions in terms of positive surgical margins between <5 and ≥5 cm group, but both groups had a high positive margin rate. Therefore, an open approach may be considered to achieve better oncological outcomes in patients with suspected malignant adrenal lesions. On the other hand, 78.3% of ≥5 cm lesions were reported as benign on the final pathology. This finding is consistent with the literature.[23] Therefore, patients should not be denied a less morbid surgical approach based solely on the size of a lesion. MIS should be offered to patients with high suspicion of benign disease.

The main shortcomings of this study are its retrospective design and a relatively small number of patients. Further randomised controlled studies are required to investigate the benefits of MIS in larger adrenal lesions.

CONCLUSION

Adrenal masses ≥5 cm treated with MIS are associated with a longer operative time. MIS techniques have the same peri-

operative outcomes in adrenal lesions ≥5 cm and can be safely applied in this group of patients.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
SY, MA, HBH, AG, CYB: Study concept and design.
MA, TM, HBH: Data acquisition.
HBH, MA, SY: Data analysis and interpretation.
MA, HBH, SY, TM: Drafting of the manuscript.
SY, MA, HBH, TM, AG, CYB: Critical revision and final approval of the manuscript.
All authors approved the final version of the manuscript to be published.
SY, MA: Both authors contributed equally to the manuscript.

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