



Laparoscopic Bilateral Adrenalectomy with the Transabdominal Lateral Approach

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Abstract

Background: Laparoscopic adrenalectomy (LA) is a widely accepted method for most adrenal lesions. However, bilateral LA is performed less often than unilateral adrenalectomy. The most common indication for bilateral LA is adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome, including persistent Cushing's disease following unsuccessful transsphenoidal surgery and ectopic ACTH syndrome.

Objectives: This retrospective study was conducted to assess the indications, safety, efficacy, and outcomes for bilateral LA with the transabdominal lateral approach.

Methods: This retrospective study was conducted between January 2004 and February 2022. During the study period, transperitoneal LA was performed on 279 patients, among whom, 258 cases were unilateral LA. Therefore, our analysis included 21 consecutive patients who underwent laparoscopic bilateral LA with the transabdominal lateral approach. The surgery indication, tumor side and weight, operation time, conversion to open surgery, need for an additional trocar, complications, hospital stay, and follow-up information were analyzed.

Results: Indications of bilateral LA were refractory Cushing's disease (n=14), occult ectopic primary bilateral macronodular adrenal hyperplasia (n=5), ACTH secretion (n=1), and bilateral pheochromocytoma (n=1). The mean operative time was 207.8±21.3 min, including repositioning time. Intraoperative and postoperative complications were seen in 3 (14%) and 4 (19%) patients, respectively. No conversion to open surgery was observed. Median hospital stay was 7 (range, 5-10) days and median follow-up was 81 (range, 55-94.5) months. Three patients died at 62, 64, and 88 months after adrenalectomy due to heart failure, renal failure, and myocardial infarction, respectively. No adrenal insufficiency or signs of recurrent hypercortisolism was observed.

Conclusion: Our results demonstrated that laparoscopic bilateral LA was safe and effective, allowing acceptable morbidity and hospital stay. The most common surgical indication was ACTH-dependent Cushing's syndrome, followed by ACTH-independent Cushing's syndrome. The lateral transperitoneal approach obtains an excellent anatomical view. In our series, operative time and conversion to open surgery rate were in line with the literature.

Keywords: Adrenal, Bilateral adrenalectomy, Cushing's syndrome, Laparoscopy

1. Background

Laparoscopic surgery has been accepted as the gold standard for treating benign adrenal tumors since Gagner's first laparoscopic adrenalectomy (LA) (1, 2). Laparoscopic surgery offers several advantages, including less postoperative pain and blood loss, better cosmetic appearance, and early recovery of patients' daily activities (3). There are few indications of bilateral LA. The most common indication for bilateral LA is adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome, including persistent Cushing's disease following unsuccessful transsphenoidal surgery and ectopic ACTH syndrome (4, 5). Other indications include bilateral adrenocortical adenomas, adrenocortical hyperplasia, and bilateral pheochromocytomas in patients with multiple endocrine neoplasia type 2 (6-8). Both transperitoneal and retroperitoneal endoscopic approaches are currently used for bilateral LA (9, 10). The lateral transperitoneal is the most popular approach. This method has various benefits, such as easy recognition of anatomical

landmarks and early adrenal vein (11). The current guidelines recommend that surgeons should select a method that provides optimal patient outcomes, for which they are most experienced and have received training (2).

2. Objectives

Our retrospective study aimed to assess the indications, safety, efficacy, and results for bilateral LA with the transabdominal lateral approach.

3. Methods

3.1. Study design and participants

This retrospective study was conducted at our institution between January 2004 and February 2022. During the study period, transperitoneal LA was performed on 279 patients, among whom 258 cases were unilateral LA. Therefore, our analysis included 21 consecutive patients who underwent laparoscopic bilateral LA with the transabdominal lateral approach. All patients were evaluated

preoperatively by the endocrine unit and decided for surgical indication at the endocrine tumor board. Surgical indications were considered in patients with persistent Cushing's disease after an unsuccessful pituitary surgery or ectopic ACTH secretion, bilateral adrenocortical adenomas, and bilateral pheochromocytoma. The preoperative evaluation measured serum cortisol levels, aldosterone to renin ratio, 24-hour urinary cortisol level, ACTH, 24-hour urinary metanephrine, normetanephrine, and vanilyl-mandelic acid levels. The history and physical examination were considered. Complete blood count, biochemistry, and coagulation parameters were examined. The study flow diagram is shown in Figure 1. Patients with Cushing's syndrome were divided into two groups based on the etiology, namely ACTH-dependent Cushing's patients and non-ACTH-dependent patients.

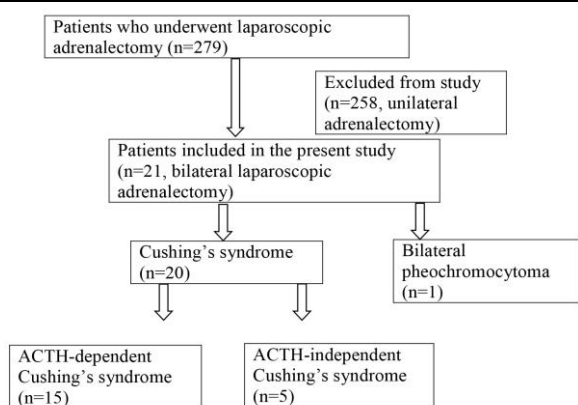


Figure 1. Study flow diagram

3.2. Data collection

Data were collected from the patient's medical records. The patients' age, gender, body mass index

(BMI), American Society of Anesthesiologists (ASA) score, previous surgery history, surgery indication, tumor side and weight, operation time, conversion, need for an additional trocar, complications, hospital stay, and follow-up information were analyzed.

3.3. Surgical technique

Experienced endocrine surgeons with similar learning curves performed all adrenalectomies under general anesthesia. Antibiotic and antithrombotic prophylactic treatments were given to all patients. All laparoscopic bilateral adrenalectomies were performed simultaneously by a lateral transperitoneal approach. Left or right lateral decubitus positions were used for surgical procedures (Figures 2a,b). The operation duration was considered the time interval between surgical incision and wound dressing. L-Hook monopolar cautery along LigaSure™ vessel sealing system (Tyco, Boulder, Colorado, USA) or Harmonic® ultrasonic scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, USA) was used during the dissections. Three instruments were utilized for the adrenal vein ligation method: metal clip (Figures 3a,b) or Hem-o-loc polymer ligation system, and LigaSure.

After insufflation, a 10 mm camera trocar was inserted in the anterior axillary line on both sides, 2-3 cm below the costal border for right and left adrenalectomies. For the right side, 10 mm and 5 mm working trocars were entered from the midaxillary and midclavicular lines, respectively (Figure 2a). For the left side, 5 mm and 10 mm working trocars were entered from the midaxillary and midclavicular lines, respectively (Figure 2b). Additional trocars were placed subxiphoid in the epigastrium for the left side. The retractor was used for the left side and provided retraction of the pancreas and spleen with an additional trocar. The specimens were removed using an endo bag (Figure 2c).

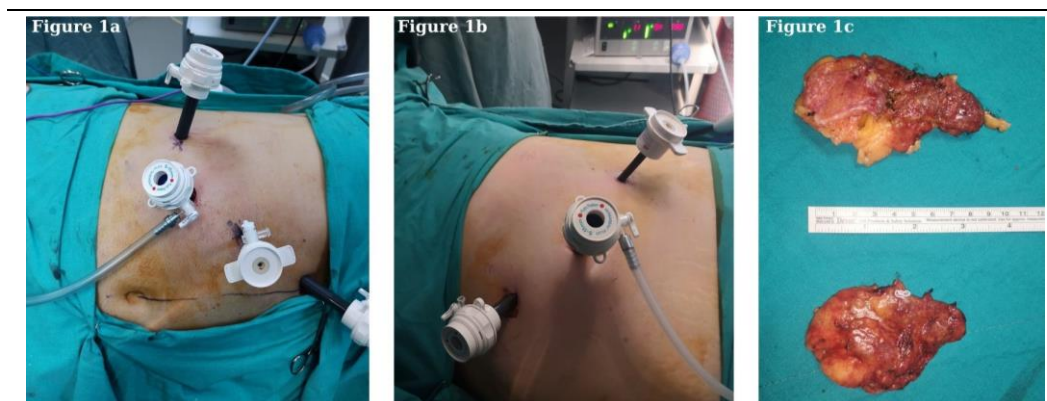


Figure 2. Trocar replacement and position for the right side (a) and left side (b), specimen (c)

3.4. Outcomes

The primary outcome was to evaluate the results of laparoscopic bilateral LA. The secondary outcome was to compare the clinical outcomes of ACTH-dependent

Cushing's patients (n=15) with those of non-ACTH-dependent patients (n=5). The postoperative complications in 30 days were classified according to the Clavien-Dindo classification (12). Postoperative

follow-up of the patients was performed regularly by endocrinologists.

3.5. Ethical considerations

The study protocol was approved by the Ethics Committee of the University of Erziyes University, Faculty of Medicine, Kayseri, Turkey (Decision No: 2022/749).

3.6. Statistical analysis

The data were analyzed in Jmp® 16.2.0 software. Descriptive statistical techniques were applied to the data to calculate the number, percentage, mean, and standard deviation. The Shapiro-Wilk test was used to obtain the normal distribution. Based on the distribution, the data were represented as mean, standard deviation, or median (interquartile range 25-75). Comparing categorical variables was done using Fisher's exact or Chi-square. The t-test/Wilcoxon signed-rank test was utilized to compare quantitative and ordinal variables. A statistically significant level was accepted as a p-value of < 0.05.

4. Results

Twenty-one patients who underwent laparoscopic adrenalectomy were enrolled in this study at our institution. All patients were subjected to simultaneous bilateral operations. Patients' characteristics are presented in Table 1. Bilateral laparoscopic adrenalectomy indications are tabulated in Table 2.

Patients with Cushing's syndrome were divided into two groups based on etiology. We compared the clinical outcomes of ACTH-dependent Cushing's patients (n=15) with those of non-ACTH-dependent patients (n=5) (Table 3). There is no statistical difference between the groups regarding age, gender, ASA score, co-existing morbidity, previous abdominal surgery, hospital stay, operative time, and mortality. In non-ACTH-dependent Cushing's patients, the left-side specimen weight was significantly greater (P=0.02); however, it was not significant on the right side. Finally, histology was adrenal hyperplasia (n=14), pheochromocytoma (n=1), and primary pigmented nodular adrenal hyperplasia (n=1).

Table 1. Patients characteristics

Patient characteristics	n=21
Age (mean) (years)	41.2±13.2
Gender, (n) (male/female)	8/13
BMI, mean (kg/m ²)	35.4±4.5
Coexisting morbidity (%)	8 (38%)
ASA score (n)	3 (2-4)
Previous radiation therapy (n)	2
Previous pituitary surgery (n)	14
Previous abdominal surgery (n)	3
Operative time (minutes)	207.8±21.3
Left side (minutes)	89±10.9
Right side (minutes)	93.3±14.5
Weight of adrenal glands, mean (g)	
Right	17.7±12.6
Left	18.6.1±14
Intraoperative complications (n)	3 (14.2%)
Liver capsular laceration (n)	2
Vascular injury (n)	1
Postoperative complications (n)	4 (19%)
Atelectasis (Clavien-Dindo grade I) (n)	2
Respiratory failure Atelectasis (Clavien-Dindo grade IV) (n)	2
Conversion to open surgery (n)	0
Hospital stay, median (range) (days)	7 (5-10)
Mortality (%)	0
Follow-up, median (range), (month)	81 (55-94.5)

BMI: Body mass index; ASA: American Society of Anesthesiologists

Table 2. Indications for bilateral laparoscopic adrenalectomy

Patient groups	n=21
ACTH-dependent Cushing's Syndrome	15 (71.4%)
Pituitary	14 (66.6%)
Ectopic ACTH	1 (4.8%)
ACTH-independent Cushing's Syndrome	6 (28.6%)
Primary pigmented nodular adrenal hyperplasia	4 (19%)
Primary bilateral macronodular adrenal hyperplasia	1 (4.8%)
Bilateral pheochromocytoma	1 (4.8%)

ACTH: Adrenocorticotrophic hormone

Table 3. Comparison of ACTH-dependent Cushing's syndrome patient outcomes with ACTH-independent Cushing's syndrome patient outcomes

Patient characteristics	ACTH-dependent Cushing's syndrome (n=15)	ACTH-independent Cushing's syndrome (n=5)	P-value
Age, median (range) (years)	45 (24-52)	49 (28-51)	0.965 ^a
Gender (%) (male/female)	6 (75%)/8 (72.7)	2 (25%)/3 (27.3)	0.703 ^c
BMI, mean (n)	36±4.4	35±5.2	0.701 ^d
Coexisting morbidity	5 (33%)	2 (40%)	
ASA score, n (%)			0.826 ^c
II	5 (33.3%)	2 (40%)	
III	9 (60%)	3 (60%)	
IV	1 (6.7%)	0	
Previous abdominal surgery (n)	-	3 (20%)	0.278 ^b
Operative time, mean (minutes)	204.3±22.1	219±19.1	0.202 ^d
Weight of adrenal glands, mean (g)			
Right	14.2±2	13.4±3.5	0.831 ^d
Left	14.3±8.4	30.8±1	0.02 ^d
Intraoperative complications (n)	2	1	0.717 ^b
Postoperative complications (n)	2	2	0.196 ^b
Hospital stay, median (range), (days)	8 (6-10)	6 (5-10)	0.373 ^a

BMI: body mass index; ASA: American Society of Anesthesiologists; ACTH: Adrenocorticotropic Hormone

^aWilcoxon signed-rank test

^bFisher's exact test, n (%)

^cChi-square, n (%),

^dStudent's t-test, mean±SD

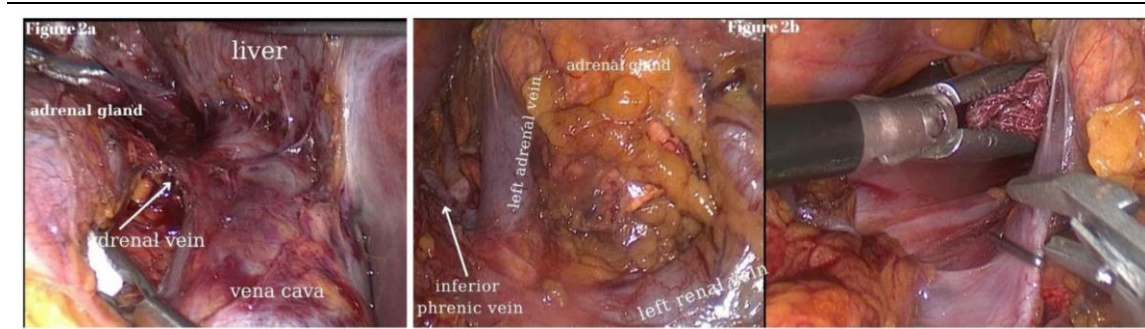


Figure 3. Adrenal vein ligation for right side (a) and left side (b)

The mean operative time was 207.8±21.3 min, including repositioning time. The mean repositioning time was 25 (20-35) min. The operative time for the left side was 89±10.9 min, while it was 93.3±14.5 min for the right side, excluding repositioning time (P=0.287).

No blood transfusion was required in the intraoperative period. One patient required a blood transfusion on the seventh postoperative day due to upper gastrointestinal bleeding. All patients with bilateral total adrenalectomy needed to receive hydrocortisone and fludrocortisone in physiological doses. Intraoperative complications occurred in 3 (14%) patients, including liver capsular lacerations in two patients and bleeding due to one vascular injury controlled by electrocautery, hemostatic agent, and clipping, respectively. Postoperative complications were observed in 4 (19%) patients: atelectasis (Clavien-Dindo grade I) in two patients and respiratory failure requiring mechanical ventilation (Clavien-Dindo grade IV) in two patients with a diagnosis of chronic obstructive pulmonary disease. One of these patients also received a heparin infusion due to heart valve disease, and upper gastrointestinal

bleeding occurred on the seventh postoperative day. Endoscopy revealed erosive gastritis. A blood transfusion was needed due to low hemoglobin.

Following surgery, three patients were lost entirely to follow-up. Eleven patients had diabetes before surgery, of which, ten patients were eligible for ongoing assessment. After surgery, five of them experienced good glycemic control within the first year. Two patients were not followed up despite repeated calls. In our work, three patients died at 62, 64, and 88 months after adrenalectomy. The causes of death of the patients were heart failure, renal failure, and myocardial infarction, respectively. No adrenal insufficiency or signs of recurrent hypercortisolism were observed

5. Discussion

The results of our study demonstrated that laparoscopic bilateral LA with the transabdominal lateral approach was safe, effective, and technically feasible, with no conversion. In our research, there were no cases of mortality and the need for perioperative blood transfusion.

Based on the findings of numerous studies, LA is associated with a reduced postoperative hospital stay, early recovery, and reduced operative time than open adrenalectomy (13, 14). Four approaches are available for LA, namely the lateral and anterior transperitoneal, the lateral and posterior retroperitoneal, and none of them outweighed the other one (2). The lateral transabdominal approach is the most common technique adopted for laparoscopic adrenal surgery (3). At our institution, we presented our experience with this approach (15). The disadvantage of this procedure is the need to reposition the patient for bilateral LA (16); however, it allows the exploration of the abdominal cavity for accompanying abdominal pathology (3, 7).

Miccoli et al. (17) compared lateral transperitoneal and retroperitoneal approaches in 20 patients who performed bilateral LA. They reported that both techniques were feasible, safe, and effective, with similar results. Gozen et al. (9) aimed to compare synchronous bilateral transperitoneal and posterior retroperitoneal LA. Although the operation time was longer in the transperitoneal approach, intraoperative and postoperative complications were similar. The reported operative times for the lateral approach range from 189 to 330 min (4, 5, 11). The operative time in our study was 207.8 ± 21.3 min, which was similar to the literature. This difference may be due to different patient characteristics.

Bilateral LA is usually the treatment option for patients with overt Cushing's syndrome due to bilateral macronodular adrenal hyperplasia. Therefore, it is not considered for patients with mild or subclinical hypercortisolism (18, 19). Bilateral LA effectively and immediately ameliorates hypercortisolism; nevertheless, this condition is prone to long-term adrenal insufficiency (20). The results of our study revealed no adrenal insufficiency or recurrent hypercortisolism during follow-up.

There was no conversion to open in our study. The conversion rate ranges from 0% to 14% (6, 7, 21). Some studies reported mortality due to sepsis and pulmonary embolism (8, 22), while others did not (16, 23). In our study, a patient received heparin infusion due to heart valve disease and upper gastrointestinal bleeding occurred on the seventh postoperative day after bilateral LA. This patient was managed non-operatively with blood transfusion and mechanical ventilation support in the intensive care unit (ICU). No mortality was observed. The rate of postoperative complications of laparoscopic bilateral LA with the transabdominal lateral approach is 10.3%-26% (4, 23, 24). Similar to the literature, 4 (19%) patients in our study experienced postoperative problems, two of whom were reported to suffer from Clavien-Dindo grade IV complications. Obesity is considered a risk factor for perioperative complications and conversion due to more difficult anatomy for visualization and dissection (21). The

mean BMI in our series was 35.4 ± 4.5 kg/m².

Most unilateral tumors are benign and nonfunctional (25). The etiology of bilateral adrenal masses often contains metastatic cancers, adrenal hyperplasia, adrenal adenoma hemorrhage, pheochromocytoma, Cushing's disease, and ectopic ACTH production (26). With our experience, the two main subgroups of patients requiring bilateral LA were patients with ACTH-independent Cushing's disease and (ACTH)-dependent Cushing's syndrome, most of whom had unsuccessful pituitary surgery.

There has not been a study comparing these patient groups in the literature. The ACTH-dependent Cushing's patients were compared with non-ACTH-dependent Cushing's patients. The preoperative and postoperative findings were similar. The only difference was that left-sided specimen weight, which was significantly higher in patients with non-ACTH-dependent Cushing's syndrome. Sheppard et al. (24) and Aggarwal et al. (11) reported that the mean weight of the two adrenal glands was 24.7 g and 42 g, respectively. The mean weight of the combined adrenal glands was 35 g in our study, which was in line with the above study.

An additional trocar may be required in left-sided adrenal tumors for LA as the spleen does not retract itself. In our study, we used an additional trocar to retract the spleen in 4 patients for the left side, which could facilitate superior medial dissection by improving counter traction. Cianci et al (27). suggested that transperitoneal left-side LA was more complex due to the difficulty of dissecting the tail of the pancreas and mobilization of the splenic flexure of the colon for better exposure and anatomical variations of the spleen. In contrast, others found that right and left transperitoneal LA results were similar (28, 29).

The limitations of the present study were its single-center nature, retrospective analysis design, and the lack of a control group. Moreover, long-term results still need to be obtained. Longer follow-up is necessary to confirm the efficacy of this procedure concerning the endocrinological evaluation of patients.

6. Conclusion

Our results demonstrated that laparoscopic bilateral LA was safe and effective, allowing acceptable morbidity and hospital stay. The most common surgical indication was ACTH-dependent Cushing's syndrome, followed by ACTH-independent Cushing syndrome. The clinical results of both groups were similar. Additionally, we found that the operation times on the right and left sides were comparable. In our series, operative time and conversion to open surgery rate were in agreement with the literature. The lateral transperitoneal approach obtains an excellent anatomical view. A

multidisciplinary team, including anesthesiologists, ICU specialists, and endocrinologists, is needed to manage patients for adequate perioperative and postoperative management.

Footnotes

Conflicts of Interest: The authors declare no conflict of interest among them.

Ethical Approval: The study protocol was approved by the Ethics Committee of the University of Erciyes University, Faculty of Medicine, Kayseri, Turkey (Decision No: 2022/749)

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Authors' contributions: BÖ and AA: Methodology, Data Analysis, Interpretation, Drafting the article, and Revising. ES, BÖ, and MG: Methodology and final revising of the manuscript. AA and BÖ: Critical review of the manuscript. All authors read and approved the final manuscript.

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