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LAPAROSCOPIC SURGICAL TREATMENT FOR ADRENAL TUMORS, A RETROSPECTIVE ANALYSIS

Abstract

Objective. Laparoscopic adrenalectomy has rapidly replaced open adrenalectomy as the procedure of choice for benign adrenal tumors. The aim of this study was to evaluate the long-term results of 105 consecutive laparoscopic and open adrenalectomies performed during a period of 14.5 years at the University Clinic of Urology in Skopje. We aimed to present our experience with this procedure. In addition, we compare the clinical outcomes of laparoscopic (LA) vs. the open adrenalectomies (OA) performed at our institution.

Patients and methods: A retrospective analysis of patients operated on for adrenal tumors was conducted. From May 2005 to August 2020, one hundred adrenalectomies were performed on 105 patients since laparoscopic adrenal surgery was introduced in our country. There were 48 men and 57 women, aged 23 to 73 years. All patients were assessed regarding their demographic data, hormonal status, operative time, estimated blood loss,

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complications, size of the tumor, number of patients requiring blood transfusion, hospital stay and conversion to open surgery for LA.

Results: In 93 patients, the laparoscopic procedure was completed successfully. In 12 cases, the laparoscopic procedure was converted to an open one. Operative time for laparoscopic adrenalectomies ranged from 45 to 120 minutes. The average postoperative hospital stays for laparoscopic adrenalectomy ranged from 1 to 2 days (1.5 days), versus 5 to 20 days for patients who underwent the open or converted procedure. LA proved superior to OA, resulting in less estimated blood loss, shorter operating time, shorter time to resumption of oral intake, shorter postoperative hospital stay and less analgesic requirements. During the follow-up of 3 to 96 months, no tumor recurrence and/or metastasis developed.

Conclusions: Laparoscopic adrenalectomy should be the treatment of choice for all benign adrenal tumors. Laparoscopic resection of large adrenal tumors necessitates experience in open and advanced laparoscopic surgery. Our results concur with other retrospective reviews comparing laparoscopic and open adrenalectomy, demonstrating unequivocal advantages in terms of reduced length of hospital stay, blood loss, return of bowel function, functional recovery, and post-operative morbidity

Keywords: Adrenal tumors, Laparoscopic adrenalectomy, Laparoscopy

Introduction

The surgical approach to the adrenal gland varies widely according to the size and the endocrine nature of the tumor, with the anterior transperitoneal, posterior and flank extraperitoneal and thoracoabdominal approaches being preferable in individual cases. The incision of open adrenalectomy is quite large, leading to significant postoperative pain that may necessitate the use of epidural catheters, with consequent increased wound morbidities, cosmetic defect, and longer hospital stay [1, 2]. Morbidity after open adrenalectomy has been reported to be as high as 40%, with the mortality rate in the range of 2% to 4% [1]. However, the small size of the adrenal gland, the benign nature of most adrenal tumors, and the difficulty of gaining access to the organ by open surgery, together with the improvement

of cross-sectional imaging (CT and MRI) to define the lesion preoperatively, make the laparoscopic approach particularly suitable for adrenalectomy [3].

Twenty two years ago, Gagner et al. [4] reported their first experience with the transperitoneal laparoscopic adrenalectomy (LA) in three cases of benign adrenal pathology. In the early 1990s, the indications for LA included small benign lesions [5], with larger lesions or phaeochromocytomas being approached very cautiously, with malignancy being considered an absolute contraindication. The indications included various pathological conditions, e.g. aldosterone-producing adenoma, Cushing's disease, nonfunctioning adenoma and other rare pathologies (adrenal cyst and myelolipoma). The groups in favor of laparoscopic surgery were gaining experience rapidly and many early contraindications (e.g. obesity, phaeochromocytoma, large adrenal lesions, previous abdominal surgery and malignancy) proved not to be absolute, but rather related to the team's surgical skills [6].

This type of operation is presently considered to be the ‘standard of care’ for most adrenal diseases requiring surgery because of its functional efficacy and all the typical advantages inherent in minimally invasive surgery. More than 20 years after the initial description of this surgical procedure we present one of the first LA experiences in the Balkan region, with a particular focus on the indications, results, and complications. We compare these data with those from open surgeries performed in our Institution. In addition, we present a case of giant splenic artery aneurism mimicking adrenal tumor, treated successfully by the laparoscopic approach.

Patients and methods

During the study period, one hundred and five consecutive patients, aged from 23 to 73 (an average age of 55 years) underwent unilateral LA adrenalectomy in our institution, including 65 right and 40 left sided. Abdominal CT and ultrasound were the radiologic tools used for diagnosing the adrenal masses, unless otherwise indicated. There were 31 OA performed mostly in the period before LA was introduced. The LA procedures

were performed by a few surgeons at the University Clinic of Urology. All patients were assessed regarding their demographic data, complete endocrinological status, operative time, estimated blood loss, complications, size of the tumor, number of patients requiring blood transfusion, hospital stay, and conversion to open surgery for LA. The postoperative course was carefully reported, especially concerning the time of initial eating and ambulation, as well as any postoperative complications and the length of the hospital stay.

The transperitoneal approach for laparoscopic adrenalectomy was used in all cases of LA. The surgical technique was that described by Hamilton [7]. We routinely employ a 60° flank position, with the bed flexed, in order to elevate the surgical area and to widen the space between the costal arch and the iliac crest for adequate port placement. Figure 1 shows the exact placement of the trocars. We prefer this approach since the anatomic landmarks for a safe procedure are well visualized. Our primary target was early control of the main adrenal vein. This had two benefits: it avoided attacks of hypertension resulting from manipulation of the adrenal gland, and it facilitated complete mobilization of the gland, as the adrenal vein is the main structure anchoring the gland in place [2]. The exposure of the inferior vena cava (IVC) on the right side and the left renal vein on the left side was used for early control of the main adrenal vein. On the right side, after the liver has been lifted, the posterior peritoneum was incised to expose the inferior vena cava and the adrenal gland (Figure 2). Because of the small size of the adrenal vessels, vascular endoclips were sufficient for their control (Figure 3). The dissection progresses superomedially, laterally, posteriorly, and, finally, posteriorly. After the dissection of the adrenal mass was completed, it was entrapped in a plastic bag (Figure 4), then retrieved via an extended muscle-splitting portside incision. The left sided LA was performed mostly using 3 ports, whereas for the right-sided LA we used 4 ports.



Figure 1 – Flank semilateral position and exact placement of the trocars (left sided adrenalectomy)

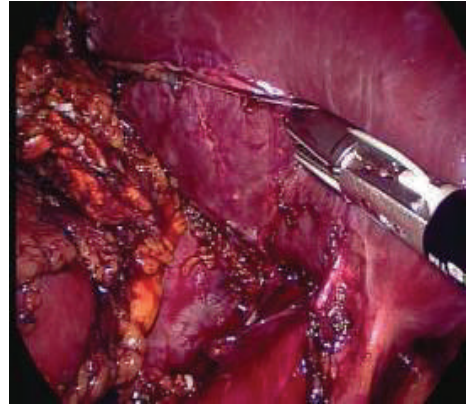


Figure 2 – Incision of the posterior peritoneum To expose the inferior vena cava and the adrenal gland

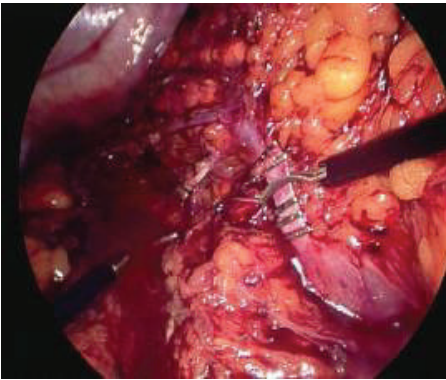


Figure 3 – Division of the adrenal vein after dissection and clipping

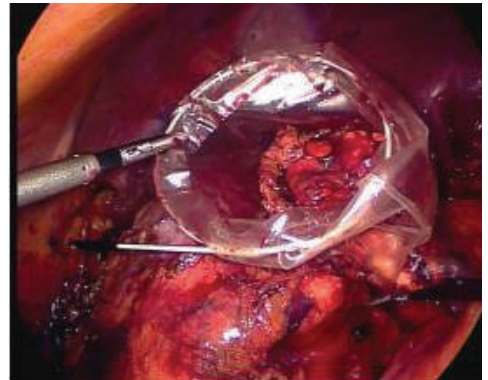


Figure 4 – Adrenal mass entrapped in a plastic bag

The laparoscopic procedure was successfully completed in all cases except in 12, which was converted to open surgery primarily for patient safety as well as better surgical efficacy.

Operative time for laparoscopic adrenalectomies ranged from 45 to 120 minutes (median 80 minutes). The average postoperative hospital stay for laparoscopic adrenalectomy ranged from 1 to 2 days (mean 1.5 days), versus 5 to 20 days in patients who underwent an open or converted

procedure. The definitive histopathological diagnosis for LA included: Conn's syndrome (17 patients), Cushing's syndrome (33 patients), pheochromocytoma (39 patients), incidentaloma (10 patients) and other tumors (6 patients). (Table 1). Another 31 cases were performed via transabdominal subcostal approach. The definitive histopathological diagnosis for OA were: Conn's syndrome (4 patients), Cushing's syndrome (10 patients), pheochromocytoma (4 patients), incidentaloma (7 patients), malignancy between one metastatic RCC (3 patients), suprarenal cyst (2 patients) and oncocytoma (1 patient) (Table 1).

Table 1

Postoperative histopathological diagnosis

Histopathology	Laparoscopic adrenalectomy	Open adrenalectomy
Conn's syndrome	17	4
Cushing syndrome	33	10
Pheochromocytoma	39	4
Incidentaloma	10	7
Malignancy (one metastatic)	x	3
Suprarenal cyst	x	2
Oncocytoma	x	1

Table 2

Demographic and operative data

	Laparoscopic	Open adrenalectomy	p
Number	105	31	
Female/male	57/48	17/14	
Size of the tumor (cm) range	4.6 ± 0.4	6.1 ± 0.7	p < 0.5
Mean surgical time (hours)	1.5 ± 0.9	3.7 ± 0.3	p = NS
Blood loss avg (ml)	120 (50–350)	371 (150–450)	p < 0.01
Time to resumption of oral intake (days)	1.9	4.4	p < 0.001
Postoperative hospital stay (days)	1,5 ± 0.5	8.7 ± 1.5	p = 0.01

Discussion

In the present study we present our initial experience with LA, with a particular focus on the indications, results, and complications, comparing these data with those from the open surgery performed at the University Clinic of Urology. At present, LA should be considered the 'platinum standard' for the treatment of the vast majority of adrenal diseases, including malignancy that is confined to the organ [8]. In addition, LA can be performed safely and efficiently in patients with significant comorbidities and in patients with large adrenal tumors [9]. In the early series, the operative times were prolonged, but it quickly became clear that the operation was a safe and feasible procedure. Several large single-surgeon and single-institution studies demonstrated excellent results beyond the initial learning curve. For example, Suzuki and associates in 1999 reported 24 complications among 75 consecutive patients (32%). Five patients (6.6%) were converted to open surgery. The operative time was 227 minutes on the left and 210 minutes on the right with minimal blood loss [10]. Lezoche and colleagues have just recently reported their experience with 214 consecutive cases of laparoscopic transperitoneal adrenalectomy with a mean operating time of 80 minutes and a mean hospital stay of 2.5 days [6]. There were no deaths, 2% of the patient had complications, and 6% underwent conversion to open surgery. In our series, the conversion rate (11.42%) is in accordance with the literature. The hospitalization period in the first half of our series was 2.2 ± 0.3 days. Many of our patients leave the hospital within 2 days after successful LA. Likewise, the average surgical time for LA procedures was longer in the first half of series than in the later operations ($p < 0.03$).

Our results concur with other retrospective reviews comparing laparoscopic and open adrenalectomy, demonstrating unequivocal advantages in terms of reduced length of hospital stay, blood loss, return of bowel function functional recovery and post-operative morbidity. In contrast, we did not achieve any cost savings in the laparoscopic approach; in fact, the charges were higher in this group. However, the operative and hospitalization costs represent only a fraction of the overall costs attributable to the medical care of these patients. Cost savings result from a quicker return to normal activities, shorter disability, and rapid return to society as compared to open

procedures. These savings may be more difficult to quantitate, however. From a technical standpoint, large adrenal masses are difficult to dissect laparoscopically. Several authors limit the laparoscopic adrenalectomy to lesions less than 6 cm in size, whereas others perform laparoscopic adrenalectomy on tumors up to 13 cm in diameter, with no morbidity. Extensive experience in advanced laparoscopic techniques and in open adrenal surgery are mandatory to manipulate and excise large tumors with a laparoscopic approach.

At present, laparoscopic adrenalectomy for invasive malignant tumors is contraindicated. En bloc extensive resections as nephrectomy, hepatectomy, and splenectomy are not well suited to the laparoscopic technique. Several cases of laparoscopic adrenalectomy for malignant tumors, followed by local recurrence and disseminated abdominal carcinomatosis within a few months, have been published. Although most institutions perform open procedures for adrenal cancer, the number of laparoscopic adrenalectomies carried out for malignant tumors is a notable phenomenon over the past few years.

In conclusion, LA is not easier, quicker or cheaper; nor does it avoid the need for general anesthesia. It has taken considerable time and effort in the operating room to develop a safe and effective operation procedure. Early ligation of the central adrenal vein to facilitate pharmacologic control in pheochromocytoma has been emphasized in reports and textbooks. One of our patients with an 6 cm pheochromocytoma developed hypertension during laparoscopic adrenalectomy, and was successfully treated with hydralazine. An extensive search of the literature showed that hemodynamic instability during surgery has been successfully treated. Other investigators suggest that the laparoscopic approach to pheochromocytoma decreases the intraoperative release of catecholamines compared to the open technique, thereby minimizing the risk of a hypertensive crisis. Laparoscopic adrenalectomy is currently the gold standard for all benign adrenal diseases. Our series confirms that laparoscopic adrenalectomy is a safe and effective procedure associated with low morbidity, short hospital stay, and recovery. However, the procedure necessitates experience in open adrenal surgery, advanced laparoscopic techniques, and familiarization with new technologies. Careful

preoperative planning and support from the endocrinology team minimize the occurrence of intraoperative or postoperative complications.

REFERENCES

1. McLeod MK. Complications following adrenal surgery. *J Natl Med Assoc.* 1991; 83: 161–164.
2. El-Kappany HA, Shoma AM, El-Tabey NA, et al. Laparoscopic adrenalectomy: a single-center experience of 43 cases. *J Endourol.* 2005; 19: 1170–1173.
3. Lezoche E, Guerrieri M, Feliciotti F, et al. Anterior, lateral, and posterior retroperitoneal approaches in endoscopic adrenalectomy. *Surg Endosc.* 2002; 16: 96–99.
4. Popov Z, Jankulovski N, Stankov O, Stavridis S, Saidi S, Kuzmanoski M, Chipurovski I, Banev S, Krstevska B, Ivanovski O, Dimitrovski C. Laparoscopic Adrenalectomy: First Single-Center Experience in the Balkans. *Pril (Makedon Akad Nauk Umet Odd Med Nauki).* 2015; 36(3): 27-33. doi: 10.1515/prilozi-2015-0075. PMID: 27442393.
5. Gagner M, Lacroix A, Bolte E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med.* 1992; 327: 1033.
6. Gagner M, Lacroix A, Prinz RA, et al. Early experience with laparoscopic approach for adrenalectomy. *Surgery.* 1993; 114: 1120–1124; discussion 1124–1125.
7. Lezoche E, Guerrieri M, Crosta F, et al. Perioperative results of 214 laparoscopic adrenalectomies by anterior transperitoneal approach. *Surg Endosc.* 2008; 22: 522–526.
8. Hamilton BD. Transperitoneal laparoscopic adrenalectomy. *Urol Clin North Am.* 2001; 28: 61–70.
9. Cobb WS, Kercher KW, Sing RF, et al. Laparoscopic adrenalectomy for malignancy. *Am J Surg.* 2005; 189: 405–411.
10. Chan JE, Meneghetti AT, Meloche RM, et al. Prospective comparison of early and late experience with laparoscopic adrenalectomy. *Am J Surg.* 2006; 191: 682–686.
11. Suzuki K, Ushiyama T, Ihara H, et al. Complications of laparoscopic adrenalectomy in 75 patients treated by the same surgeon. *Eur Urol.* 1999; 36: 40–47.

12. Castilho LN, Mitre AI, Arap S. Laparoscopic adrenal surgery in a Brazilian center. *J Endourol.* 2003; 17: 11–18.
13. Popov Z, Ivanovski N, Cakalaroski K, et al. [Co-elioscopic renal prelevation on living donor. The first four cases in Republic of Macedonia]. *Prog Urol.* 2005; 15: 1227–1228.
14. Saw EC, Ku W, Ramachandra S. Laparoscopic resection of a splenic artery aneurysm. *J Laparoendosc Surg.* 1993; 3: 167–171.
15. Watanabe Y, Sato M, Abe Y, et al. Three-dimensional arterial computed tomography and laparoscope-assisted splenectomy as a minimally invasive examination and treatment of splenic aneurysms. *J Laparoendosc Adv Surg Tech A.* 1997; 7: 183–186.
16. Leung KL, Kwong KH, Tam YH, et al. Laparoscopic resection of splenic artery aneurysm. *Surg Endosc.* 1998; 12: 53.
17. Meinke AK, Floch NR, Dicorato MP. Laparoscopic options in the treatment of splenic artery aneurysms. *Surg Endosc.* 2002; 16: 1107.
18. Reardon PR, Otah E, Craig ES, et al. Laparoscopic resection of splenic artery aneurysms. *Surg Endosc.* 2005; 19: 488–493.
19. Gagner M, Lacroix A, Bolte E, 1992 Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med.* 327: 1033.
20. Thomson GB, Grant CS, van Heerden J, et al, 1997 Laparoscopic versus open posterior adrenalectomy: a case-control study of 100 patients. *Surgery.* 6: 132-136.
20. Schell SR, Talamin MA, Udelsman R, 1998 Laparoscopic adrenalectomy. In: *Advances in surgery.* Mosby-year book Inc. 32: 333-350.
21. Lezoche E, Guerrini M, Paganini AM, et al, 2000 Laparoscopic adrenalectomy by the anterior transperitoneal approach: results of 108 operations in unselected cases. *Surg Endosc.* 14: 920-925.
22. Ramacciato G, Mercantini P, Pietromaria A, et al, 2005 Ten years of laparoscopic adrenalectomy: Lessons learned from 104 procedures. *Am Surg.* 71: 321-325.