SCIENTIFIC PAPER

Laparoscopic Adrenalectomy for Pheochromocytoma Versus Other Surgical Indications

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ABSTRACT

Objective: Laparoscopic adrenalectomy is widely recognized as the preferred technique for surgical removal of adrenal masses. This study aimed to evaluate the outcomes of consecutive laparoscopic adrenalectomies performed at a high-volume referral center and compare operative results for pheochromocytomas with that of other adrenal diseases.

Materials and Methods: We retrospectively reviewed a single surgeon's experience with laparoscopic adrenalectomy performed between July 2002 and June 2007. Patient records were analyzed in regards to demographics, pathology diagnoses, operative time, postoperative complications, tumor size, hospital stay, among others.

Results: Seventy-two consecutive laparoscopic adrenalectomies were performed on 70 patients, including 2 bilateral adrenalectomies and one partial adrenalectomy. Surgical indications included pheochromocytoma (n=11), aldosteronoma (n=26), malignant adrenal disease (n=4), nonfunctioning adenomas (n=17), Cushing's disease (n=6), and other adrenal disease (n=8). No mortality was observed. Perioperative complications occurred in 7 cases (9.7%). When a comparison between pathological diagnosis groups was made, no statistical differences were seen between pheochromocytomas and other adrenal neoplasms with respect to estimated blood loss, open conversion rate, length of stay, preoperative and postoperative hemoglobin values, blood transfusion rates, perioperative complication occurrence, tumor size, and ASA class.

Conclusion: Laparoscopic adrenalectomy is a safe and appropriate surgical technique for most adrenal lesions, including pheochromocytomas.

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This study was supported by NIH T32 CA111198 (MJM).

Key Words: Adrenal tumor, Adrenal adenoma, Adrenocortical carcinoma, Laparoscopic adrenalectomy, Hypertension, Aldosteronoma, Pheochromocytoma.

INTRODUCTION

Since its first report in 1992, laparoscopic adrenalectomy (LA) has increasingly become the preferred operative approach for adrenal disease.[1] Difficulty with open surgical exposure and the small size of the adrenal gland make this organ particularly amenable to a minimally invasive approach.[2] Additionally, numerous studies have demonstrated clear advantages to this technique in regards to decreased intraoperative blood loss, shorter operative times and hospital stays, reduced narcotic requirements, and earlier return to normal activity and diet.[3–6] Current widely accepted indications for LA include aldosteronoma, nonfunctioning adenomas, bilateral adrenal hyperplasia, and less common cysts and myelolipomas.[7] Though initially there was debate regarding the use of LA for pheochromocytoma because of concerns for hemodynamic instability due to catecholamine release during tumor manipulation, the laparoscopic approach has now been adopted for most pheochromocytomas today.[8,9] The aim of this study was to assess the contemporary outcomes of LA for an individual surgeon at a high-volume referral center. Further, we compare the safety and efficacy of this procedure for pheochromocytomas with other adrenal tumors.

MATERIALS AND METHODS

Study Design

A retrospective analysis was performed of all patients who underwent laparoscopic adrenalectomy by the author (CS) at the Indiana University Medical Center from July 2002 through June 2007 after institutional review board approval. Medical records were reviewed to include data regarding patient demographics, disease cause, operative details, postoperative complications, length of stay, pathologic analysis, and follow-up information.

Preoperative Evaluation

Adrenal masses were localized by computed tomography or magnetic resonance imaging. Preoperative endocrine assessment included laboratory testing, history and physical examination, biochemical screening for urinary and serum catecholamine or metanephrine expression. All pheochromocytomas were treated preoperatively with a selective alpha-receptor blocker. Beta-receptor blocking agents were also used in those patients with tachyarrhymia under concurrent alpha blockade.

Operative Technique

All patients for unilateral adrenalectomy underwent a transperitoneal lateral approach to laparoscopic adrenalectomy. After the patient was placed in a lateral decubitus position, two 5-mm trocars for the working instruments and a 12-mm trocar for the laparoscope were introduced. On the right side, a fourth 5-mm port was inserted in the epigastrium for liver retraction. Another 5-mm trocar was often used in the subcostal region at the anterior axillary line for lateral retraction. During left LA, the retroperitoneum was exposed by incising along the descending colon from the splenic flexure to below the kidney. For right-sided procedures, the retroperitoneum was accessed by incising the peritoneum just below the inferior liver edge and exposing the inferior vena cava. The duodenum was often mobilized. In each case, correct identification of the vasculature was confirmed prior to isolation and clipping of the adrenal vein. The crucial step of dividing the adrenal vein is always accomplished before gland dissection to avoid troublesome bleeding or catecholamine release. Ultrasonic shears and bipolar forceps were used for dissection and hemostasis. The medial and inferior adrenal dissections were initially accomplished. The adrenal gland was subsequently dissected free and placed in an Endopouch. The operative field was inspected for hemostasis, and the pneumoperitoneum was decompressed. The specimen was extracted via extension of the 12-mm port site.

Follow-up

All patients underwent short-term follow-up with an outpatient clinic visit 3 weeks to 4 weeks following hospital discharge. In addition, for those requiring long-term observation, annual office visits were scheduled, and in select patients, abdominal imaging was performed. Patients with functioning neoplasms were followed serially by their endocrinologist who routinely performed indicated laboratory analysis.

Statistical Analysis

The chi-square test was used to compare categorical data. It was used to compare categorical differences between LA groups based on pathological diagnosis. The Mann-Whitney test was used to compare LAs performed for pheochromocytomas versus other adrenal disease (OAD) as a whole. $P<0.05$ was considered statistically significant.

RESULTS

Between July 2002 and June 2007, a total of 72 consecutive transperitoneal laparoscopic adrenalectomies were performed. Patient demographics are displayed in **Table 1**. The mean age of all patients was 54 years (range, 27 to 77). The male to female ratio was approximately 1.33:1. Thirty-six LAs were performed on the left, 32 on the right, and 2 patients underwent bilateral adrenalectomies. No mortality was observed. Open conversion occurred in one patient (1.4%) secondary to adhesions from a previous laparotomy. In this case, significant blood loss or other

Table 1.
Patient Demographics

Patients	Pheochromocytoma	Adenoma	Conn's	Cushing's	Malignancy	Other
Total (n)	11	17	26	4	4	8
Female	4	11	6	2	1	6
Male	7	6	20	2	2	3
Mean Age (y, range)	57.3 (32–76)	54.8 (27–74)	52.8 (34–77)	60.3 (54–72)	45.3 (28–62)	49.6 (30–72)
Side						
Right	6	8	12	1	1	4
Left	5	9	14	1	3	4
Bilateral	0	0	0	2	0	0

complications did not occur, and the patient was discharged home on postoperative day 4. Also, one patient with symptoms of Conn's disease underwent right-sided partial LA. This was performed without complication, and the patient was discharged home the next day.

The results of the comparison between LA for pheochromocytomas versus OAD are shown in **Table 2**. Our study demonstrated no statistically significant differences between these groups with respect to operative time, EBL, open conversion rate, length of stay, preoperative and postoperative hemoglobin values, blood transfusion rates, perioperative complication occurrence, tumor size, and intraoperative average blood pressures and ASA class. Additionally, patients undergoing pheochromocytoma resections did not routinely receive intensive care unit (ICU) admission for blood pressure monitoring.

Perioperative complications occurred in 7 cases (9.7%). These are listed in **Table 3** and classified according to Clavien's modified scale.[10] A small transmural perforation of the descending colon occurred during a left LA for adrenocortical carcinoma diagnosed postoperatively. The injury was immediately recognized. An intraoperative general surgery consult was obtained, and the injury was repaired laparoscopically without complication. The adrenalectomy was completed, and the patient was discharged 5 days later. To date, there have been no oncologic recurrences. One individual with cystic fibrosis developed a severe pulmonary exacerbation requiring postoperative intubation and prolonged ICU stay after a right LA for an enlarging adrenal pseudocyst. A fifth patient underwent an unremarkable left adrenalectomy but developed a prolonged ileus and renal failure secondary to hypovolemia. After aggressive resuscitation, the patient's renal function returned to baseline, and he was discharged on POD 7 without sequelae. An additional 4 patients required one unit blood transfusions for symptomatic anemia. Otherwise, their hospital course was unremarkable, and no further intervention was required.

Table 2.
Comparison of Laparoscopic Adrenalectomy for Pheochromocytoma Versus Other Adrenal Diseases

	Pheo* (n=11)	OAD* (n=61)	P
Operating Time (min)	181.4	174.4	0.165
EBL* (mL)	34.6	63.1	0.929
Open Conversion	0	1	0.664
LOS* (days)	1.8	2.1	0.710
Maximum SBP (mm Hg)	140.0	143.4	0.291
Minimum SBP (mm Hg)	97.7	102.9	0.197
Preop Hb (g)	12.8	13.7	0.411
Postop Hb (g)	11.7	12.4	0.068
Blood Transfusion	1	1	0.177
Minor Complications	1	6	0.939
Tumor Size (cm)	3.5	3.7	0.453
ASA Class	2.9	2.8	0.570

*EBL=estimated Blood Loss; LOS=length of stay; Pheo=pheochromocytomas; OAD=other adrenal diseases.

The mean follow-up evaluation was 27.4 months (range, 1 to 61). To date, no pheochromocytomas have recurred. Four patients were treated for malignant diseases, 3 adrenocortical carcinomas and one metastatic melanoma. In the follow-up of these patients, no recurrences have been noted. No patients with aldosteronomas had an elevated serum aldosterone level at standard 4-week follow-up.

DISCUSSION

The validity of laparoscopy for the spectrum of adrenal disease has been widely accepted. In this study, we retrospectively compared operative outcomes for patients who underwent LA based on pathological diagnosis groups. In particular, we investigated whether differences existed between pheochromocytomas and other adrenal diseases. Our data analysis demonstrated no statistical differences between patients with pheochromocytomas and those with OAD based on a number of operative parameters. Importantly, laparoscopic dissection did not represent significant cardiovascular problems in our series. Although our data show no difference in intraoperative average maximum and minimum SBP between pheochromocytomas and other diagnoses (P=0.291 and 0.197, respectively), only 6 of 11 pheochromocytomas had significantly elevated preoperative catecholamines and may explain these results. Some investigators have suggested that a laparoscopic approach to pheochromocytoma decreases the intraoperative release of catecholamines compared with open surgery, thus reducing the risk of a hypertensive crisis.[11] A recent study in a large number of patients confirmed that laparoscopic adrenalectomy for pheochromocytoma was superior to the traditional open approach for intraoperative control of blood pressure.[12] This may be directly related to operative time as some groups have reported longer procedure times when performing open versus laparoscopic adrenalectomies for pheochromocytomas.[13,14] If this holds true, an

Table 3.
Complications in 72 Consecutive Laparoscopic Adrenalectomies

Complication	Indication	Clavien Grade[10]	N
Postoperative anemia	Aldosteronoma	II	2
Postoperative anemia	Pheochromocytoma	II	1
Postoperative anemia	Bilateral hyperplasia	II	1
Intraoperative colon perforation	Carcinoma	IIIb	1
Acute renal failure	Other	IVa	1
Respiratory failure	Adrenal pseudocyst	IVa	1

experienced laparoscopic surgeon can significantly reduce the risk of resection for these tumors. In our study, average operative time for pheochromocytomas of 181.4 minutes was not statistically significant from OAD time of 174.8 minutes (P=0.165). Furthermore, we agree with others that central to reducing the risk of excessive catecholamine secretion during surgery is early ligation of the adrenal vein.[15,16] In our experience, this step was performed before dissection of the gland and along with minimizing adrenal manipulation, likely explains the lack of hypertensive crises in this series. We also believe laparoscopy affords improved visualization and faster access to the adrenal vein, further reducing the risk of catecholamine release.

Additionally, our complication rate of 9.1% for pheochromocytomas was not statistically different from that of other adrenal diagnoses (P=0.939). We cannot stress enough that essential factors for successful and safe resection of these lesions are the presence of an experienced anesthesiology team, precise localization of the tumor, and appropriate preoperative medical management and preparation. We caution that in our series the average tumor size of the pheochromocytomas was 3.5 cm. Debate still remains over acceptable pheochromocytoma sizes appropriate for laparoscopic removal. Some believe that tumors larger than 6 cm pose increased risk for malignancy and should be deemed a contraindication to a minimally invasive approach.[17,18] Furthermore, in a 13-year review of 456 laparoscopic adrenalectomy cases, tumor size ≥5 cm, BMI≥24 kg/m^2, and pheochromocytomas were predictors for open conversion.[19] In our series, the 4 malignant adrenal lesions via LA had a mean size of 4.9±2.1 cm. Of note, 2 of these masses were believed to be nonfunctioning adenomas prior to resection and pathologically diagnosed postoperatively. We agree that larger lesions pose a greater operating challenge. Though size is not an absolute contraindication, preoperative imaging plays an even greater role in determining the appropriate surgical approach. Thus, proper localization and careful patient selection can yield acceptable results. In our series, 9 of 11 patients were cured of their hypertension (81.8%) upon an average follow-up of 29.4 months (range, 3 to 58), and no patients displayed radiographic evidence of pheochromocytoma metastases or local recurrence.

A limitation of this study is the inherent selection bias of a retrospective review. Our goal was to compare outcomes of LA for pheochromocytomas with outcomes of other adrenal diseases. We chose to include consecutive patients during a short time period. All procedures were performed later in the surgeon's experience and therefore reflect minimal learning curve effects. Though there were no statistical differences noted in operative parameters, the modest number of total pheochromocytomas resected (n=11) may restrict our interpretation and should be considered a limitation of this study.

CONCLUSIONS

Laparoscopic adrenalectomy is a safe and appropriate surgical technique for most adrenal lesions. In particular, pheochromocytomas should be considered for this approach. Our results with 72 consecutive LAs demonstrate that excellent postoperative outcomes can be expected regardless of pathologic diagnosis. There is no difference between surgical outcomes following laparoscopic adrenalectomy for pheochromocytomas and outcomes following other indications for surgery.

References:

1. Gagner M, Lacroix A, Bolte E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med*. 1992;327:1033.

2. Guazzoni G, Montorsi F, Bocciardi A, et al. Transperitoneal laparoscopic versus open adrenalectomy for benign hyperfunctioning adrenal tumors: a comparative study. *J Urol*. 1995;153: 1597–1600.

3. Jacobsen NE, Campbell JB, Hobart MG. Laparoscopic versus open adrenalectomy for surgical adrenal disease. *Can J Urol*. 2003;10:1995–1999.

4. Linos DA, Stylopoulos N, Boukis M, Souvatzoglou A, Raptis S, Papadimitriou J. Anterior, posterior, or laparoscopic approach for the management of adrenal diseases? *Am J Surg*. 1997;173: 120–125.

5. Thompson GB, Grant CS, van Heerden JA, et al. Laparoscopic versus open posterior adrenalectomy: a case-control study of 100 patients. *Surgery*. 1997;122:1132–1136.

6. Winfield HN, Hamilton BD, Bravo EL, Novick AC. Laparoscopic adrenalectomy: the preferred choice? A comparison to open adrenalectomy. *J Urol*. 1998;160:325–329.

7. Gill IS. The case for laparoscopic adrenalectomy. *J Urol*. 2001;166:429–436.

8. Kim AW, Quiros RM, Maxhimer JB, El-Ganzouri AR, Prinz RA. Outcome of laparoscopic adrenalectomy for pheochromocytomas vs aldosteronomas. *Arch Surg*. 2004;139:526–531.

9. Mobius E, Nies C, Rothmund M. Surgical treatment of pheochromocytomas: laparoscopic or conventional? *Surg Endosc*. 1999;13:35–39.

10. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.

11. Ramacciato G, Paolo M, Pietromaria A, et al. Ten years of laparoscopic adrenalectomy: lesson learned from 104 procedures. *Am Surg*. 2005;71:321–325.

12. Lang B, Fu B, OuYang JZ, et al. Retrospective comparison of retroperitoneoscopic versus open adrenalectomy for pheochromocytoma. *J Urol*. 2008;179:57–60.

13. Kercher KW, Novitsky YW, Park A, Matthews BD, Litwin DE, Heniford BT. Laparoscopic curative resection of pheochromocytomas. *Ann Surg*. 2005;241:919–928.

14. Toniato A, Boschin IM, Opocher G, Guolo A, Pelizzo M, Mantero F. Is the laparoscopic adrenalectomy for pheochromocytoma the best treatment? *Surgery*. 2007;141:723–727.

15. Janetschek G, Neumann HP. Laparoscopic surgery for pheochromocytoma. *Urol Clin North Am*. 2001;28:97–105.

16. Zhang X, Lang B, Ouyang JZ, et al. Retroperitoneoscopic adrenalectomy without previous control of adrenal vein is feasible and safe for pheochromocytoma. *Urology*. 2007;69:849–853.

17. Cobb WS, Kercher KW, Sing RF, Heniford BT. Laparoscopic adrenalectomy for malignancy. *Am J Surg*. 2005;189:405–411.

18. Godellas CV, Prinz RA. Surgical approach to adrenal neoplasms: laparoscopic versus open adrenalectomy. *Surg Oncol Clin N Am*. 1998;7:807–817.

19. Shen ZJ, Chen SW, Wang S, et al. Predictive factors for open conversion of laparoscopic adrenalectomy: a 13-year review of 456 cases. *J Endourol*. 2007;21:1333–1337.